Attention Deficit Hyperactivity Disorder

Concepts, Controversies, New Directions

Medical Psychiatry Series / 37

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Preface

This book bridges the gap between the several existing introductory works on attention deficit hyperactivity disorder and those more advanced texts that focus on a narrow issue or subpopulation. It targets readers in training (medical and nursing students, residents, graduate students, etc.) rather than a lay audience, and thus it is a natural companion to the attention deficit hyperactivity disorder section in the *Diagnostic and Statistical Manual of Mental Disorders* -IV-TR. Although it can be used as an introductory text, it also covers specialized topics that will be of interest to seasoned clinicians and to anyone affected by attention deficit hyperactivity disorder who wishes to broaden their understanding of the disorder.

We asked experts around the world to contribute chapters, with the guideline that they be brief and concise. We granted significant "wiggle room" when contributors needed more length. Some topics received extra emphasis, in order to present readers with more of what they might need to know rather than what they already know about attention deficit hyperactivity disorder. For example, because most of what is known about the disorder comes from research with school-age boys, we thought it essential to include chapters spanning ages and genders. We also overweighted psychosocial approaches to treatment, because the sub-modalities of evidence-based psychosocial treatment are rarely presented. Coverage of medication was limited to the essentials, because pharmacotherapy of attention deficit hyperactivity disorder is already widely disseminated online and in book form and because continuing medical education and pharmaceutical-medical liaisons are sources of continual updates for the prescribing community.

This book also asks readers to challenge their assumptions about attention deficit hyperactivity disorder. The chapter by Pelham is an iconoclastic manifesto on the primary importance of psychosocial treatment. It stems from the fact that the first reported result of the Multimodal Treatment of ADHD Study—that well-managed pharmacotherapy is more effective than psychosocial treatment, and that little is gained from adding psychosocial treatment to pharmacotherapy alone—is often over-interpreted. By considering a broader context, Pelham's chapter stimulates the reader into becoming more sophisticated about medication versus psychosocial issues. Diller's chapter reminds the reader that, even with the amount of research

currently available on the disorder, much work remains to be done before some fundamental questions can be put to rest. Regardless of the reader's viewpoint, the chapters in the "Controversies" section will leave the reader better able to defend their views.

Our choice of emphases should not be misconstrued. Our personal views are that attention deficit hyperactivity disorder is a valid and under-treated disorder, that multimodal treatment (medication *and* psychosocial) is often the best treatment, that federal funding of research on this and related disorders should be quadrupled, and that major revisions are needed to how treatment is provided and reimbursed. Everyone is affected by attention deficit hyperactivity disorder, whether they have it or not. Given the worldwide estimated prevalence of 5.29%, chances are that one out of every 20 people one encounters (including drivers of other cars) has the disorder. Untreated and under-treated, it closes off many paths to better education, better jobs, better health, and better social relationships. It is a costly disorder for everyone. We know a great deal about identifying and helping individuals with attention deficit hyperactivity disorder, but we mustn't allow ourselves to smugly think we know enough. If our book stimulates readers to consider new views on it and to develop their own insights, it will have done its job.

We owe a debt of gratitude for the scholarly efforts of the contributors to this book. Special thanks are due to Russell Schachar, Joel Nigg, and Glen Elliott, who helped in the conceptualization and early planning.

Keith McBurnett
Linda Pfiffner

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Section I: Assessment

1

The Diagnosis and How We Got There

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The standard for diagnosing attention deficit hyperactivity disorder (ADHD) is to apply diagnostic criteria from DSM-IV (1). These criteria were derived using the most empirically sound methods ever used to formulate criteria for a psychiatric disorder. They have been adopted almost universally, and yet somehow they manage to foster both consensus and controversy about what ADHD is and how it should be identified. This chapter outlines the historical and scientific underpinnings of DSM-IV ADHD, and implications for ADHD in DSM-V.

The history of psychiatric diagnosis can be divided into two eras: before DSM-III and after DSM-III. There are several good accounts of the early history of psychiatric diagnosis, so only a brief synopsis need be covered here. One interesting historical fact is that the reason that we have a *Diagnostic and Statistical Manual of Mental Disorders* instead of simply a *Diagnostic Manual of Mental Disorders* is because the DSM was developed from national statistical records. The U.S. Constitution mandates the collection of census data for purposes of representation and taxation. Over time, questions were added to the census to gather additional informational. The first tallies of mental disorders (intended to learn about the institutionalized population) were obtained in the 1840 census, although categories at that time were only idiocy/insanity. In 1918, the Census Bureau published *The Statistical Manual for the Use of Hospitals for Mental Diseases* (2), which was updated in 10 editions through 1942. There were several other important influences leading to the first DSM, but the Census Bureau's *Statistical Manual* can fairly be described as the key precursor (hence the retention of the term *Statistical Manual* despite the smaller role now played by statistics).

Other milestones were the *Standard Nomenclature of Diseases* (3) and the addition of mental disorders to the international classification of diseases, ICD-6 (4). The mental disorders section in ICD-6 was influenced by the attention given to mental disorders by the military, which came to the realization during World War II that recruitment, fitness for duty, and rehabilitation of psychological injury would be enhanced if mental disorders could be better tracked. This was one reason why, when the American Psychiatric Association adopted the first DSM (5), it did not address disorders of children, even though preliminary nomenclature for child disorders had appeared as early as 1886 (6) and was included in the *Standard Nomenclature*.

DSM-II (7) listed a new broad category, "Behavior Disorders of Childhood and Adolescence" and a subordinate subcategory of "Hyper-kinetic Reaction of Childhood." The diagnostic methodology of the era was to obtain insightful descriptions so that a trained clinician could recognize a disorder when presented in the clinic. This is an intuitively appealing process, deeply rooted in Platonic and rational traditions. It is, essentially, a match to prototype method. There is nothing inherently wrong about this method—we use it everyday to identify all manner of things. Problems arise when it is applied to conceptual entities like disease states, especially abnormal behavioral syndromes. Differences in training, experience, cultural background, and theoretical orientation cause clinicians to gather information selectively and to weigh data differently. These difficulties might be surmounted by standardizing diagnostic training, but the more mercurial problem is that nature does not present mental disorders in discrete categories. Individual cases display different patterns of prototypical features, and it is the exceptional case that closely approximates one prototype and has few features of others. We can easily recognize those cases that clearly fit or do not fit a category. Those cases that only moderately fit are the ones that cause disagreement.

How good are we at matching to a prototypical description? Most of us would trust our own skill, but we might be more skeptical of the skills of others. Such skepticism appears warranted for the descriptive approach. When pairs of clinicians were asked to diagnose the same case independently using DSM-II, they often failed to agree on the results. Such unreliability threatens the validity of the diagnosis. After all, if diagnosticians disagree, at least one of them has given the wrong diagnosis and there is not an easy way to know which. An unreliable diagnosis cannot possibly be valid, or to use more precise psychometric terms, reliability places a ceiling on validity.

One cost of diagnostic unreliability is its hindrance of research. Feighner and colleagues at Washington University addressed this problem by developing specific criteria for several mental disorders (8). As these research diagnostic criteria (RDC) were further developed (9), they were shown to increase the reliability of psychiatric diagnosis. This benefit partly derived from the efforts to make the criteria clear and specific, and to

generally focus on behavior rather than inferred states or traits. Improved reliability also derived from the use of multiple criteria. Thus, RDC nudged the diagnostic process from its total reliance on clinical judgment toward incorporating aspects of measurement theory.

The RDC approach was adopted for DSM-III (10), resulting in generally good diagnostic reliability. Hyperkinetic reaction was dropped in favor of attention deficit disorder (ADD), largely in response to reports of inattentive behavior and impaired performance on laboratory measures of attention in children with the disorder (11,12). DSM-III distinguished between ADD with hyperactivity and ADD without hyperactivity. Both types were considered to have significant attention problems and impulsiveness and were distinguished only by the severity of hyperactivity. An important result of this distinction was the emergence of a small research literature on ADD without hyperactivity. However, when the DSM was revised only 7 years later, the DSM-III-R (13) committee was not convinced that the then available research on ADD without hyperactivity was sufficient to validate the subtype. ADD without hyperactivity was not killed off, but it was relegated to a fate close to death: it was stripped of its diagnostic criteria and relegated to a catchall category of undifferentiated attention deficit hyperactivity disorder (UADHD). This had a chilling effect on research into an inattentive type. Not only did UADHD have no DSM-III-like RDC, it had no DSM-II-like clinical description. The real diagnosis (ADHD) could be met by having any 8 from a list of 13 symptoms of hyperactivity, impulsivity, and inattention.

The application of measurement theory to psychiatric diagnosis made a quantum leap in the development of behavior disorder diagnoses in DSM-IV (14). The DSM-IV committee explicitly sought to substitute the reliance on expert clinical opinion wherever possible in favor of generating questions to be addressed with empirical data. Proposals for changes to the DSM were widely solicited. Proposed changes were evaluated with literature reviews, secondary analyses of existing data, and newly designed field trials of proposed diagnostic criteria. For ADHD, three reviews were commissioned (15–17), and a nationwide field trial of all of the symptoms from the attention and disruptive behavior disorders was funded.

The DSM-IV committee gave the job of executing the field trial for attention and disruptive behavior disorders to Ben Lahey. Lahey, working closely with the rest of the committee, was methodical in using psychological measurement to address proposed changes. A large set of proposed symptoms of ADHD and disruptive behaviors was collected from 440 subjects in 11 different sites, including items proposed as sluggish cognitive tempo (SCT) identified from DSM-III era research. Impairment was captured as overall impairment and as domain-specific (e.g., academic, sociobehavioral) impairment. The latent structure (how well symptoms tend to aggregate and appear related to a single dimension) of ADHD symptoms was investigated

using factor analysis. At one level, factor analysis identifies latent (meaning not observable, but detectable with statistics) groups of items. At the level of the item, it measures how closely each item is associated with each of the latent dimensions. The results confirmed prior hypotheses that ADHD symptoms appear grouped into only two dimensions: inattention and hyperactivity-plus-impulsivity. After these two sets of symptoms were demarcated, each item was tested for its symptom utility (18). Symptom utility means how well a symptom predicts the presence of the rest of its symptom group, combined with how well its absence (finding that it is not present) predicts the absence of the rest of its symptom group. The symptom utility analyses found that most symptoms functioned well, with the notable exception of the SCT symptoms. There was no problem with the positive predictive power of SCT symptoms: their presence was strongly associated with the presence of the group of inattentive symptoms. However, when SCT symptoms were not present, other inattentive symptoms were sometimes present and sometimes not. Thus, the SCT symptoms failed to meet the negative predictive power requirement. They were dropped from further investigation.

Lahey now had his final symptom lists. The final task was to use statistical measurement to empirically find the best cutpoints. A cutpoint, or diagnostic threshold, is the number of symptoms from a symptom group that are required to be present in order to determine that an individual has or exhibits that symptom group. (In other words, should we require four inattention symptoms, or five, or six or seven, in order to conclude that an individual case has inattention?) The committee took the innovative approach of selecting cutpoints based on how well different cutpoints predicted impairment, and by looking at how reliable were the categorical decisions made by using different cutpoints in test-retest and cross-diagnostician analyses. The final cutpoints could then be used in a two-by-two contingency table for subtyping ADHD: exceeding the inattention cutpoint but not that for hyperactivity-impulsivity would place a case in the box for predominantly inattentive type; if vice-versa, the box for predominantly hyperactive-impulsive type; if both, the combined type; and if neither, no ADHD diagnosis. (The reader is encouraged to retrieve the original report of these analyses to see the clear relationships between numbers of symptoms and impairment) (19). In toto, the data indicated that the best cutpoints were at six of the nine inattention symptoms, and five of the nine hyperactivity-impulsivity symptoms. However, for the hyperactivity-impulsivity symptoms, a cutpoint of five symptoms was supported by some of the data, but other data showed little difference between five or six symptoms. Given this ambiguity, the committee found favor in the symmetry of requiring six of nine symptoms for both categories. The committee also favored the use of a more stringent cutpoint in order to protect against overdiagnosis. After the criteria were finalized, a cross-validation study applied the new

criteria to existing real-world clinical cases. The study confirmed the association of cutpoints with domain-specific criteria, and concluded that DSM-IV was superior to DSM-III-R in subcategorical homogeneity (the similarity of cases within a type) and in exhaustiveness (ability to classify all apparent cases) (20).

It is often overlooked that DSM-IV ADHD diagnosis is based on the "or rule." This procedure identifies a symptom as present if either the teacher or the parent reports the symptom as being present. So a cutpoint of six symptoms using the or rule is considerably less stringent than using the same cutpoint with a single informant. Using a single informant (generally this would be the primary caretaker), particularly when relying on a symptom checklist, will bias the results toward underdiagnosing ADHD. This bias might be mitigated when using a clinical interview with a parent who is keenly aware of school-based impairment, but this is an inference. Single-informant diagnoses will almost certainly be confirmable cases of DSM-IV ADHD, but they will not represent the population defined by DSM-IV criteria because they will tend to be more severe. There may also be a bias against identifying the inattentive type when relying on parent report only, because teachers appear to be more sensitive to inattention symptoms than are parents. The ice becomes much thinner when we try to apply DSM-IV criteria beyond the age range from which they were derived, due in part to the fact that the classic "or rule" cannot be implemented.

As well-derived as DSM-IV ADHD was, imperfections slowly began to appear. By requiring six symptoms of hyperactivity-impulsivity instead of five, cases that might otherwise be classified as combined type were instead assigned to predominantly inattentive. This meant that the inattentive type was made less homogenous simply by being contaminated with a few extra cases of combined type. One result was that correlates such as anxiety that were previously associated with DSM-III ADD without hyperactivity were not clearly associated with DSM-IV predominantly inattentive type, and the higher prevalence of girls in DSM-III ADD without hyperactivity (vs. with hyperactivity) was lessened in DSM-IV inattentive versus combined type (21). The elimination of SCT symptoms was questioned, and it was found that if SCT items were evaluated only in a subset of cases with predominantly inattentive type (the only type that would be expected to exhibit SCT), their symptom utility was perfectly adequate. Even the grouping of inattentive type in the same general category with other types of ADHD was assailed by airing a laundry list of reasons why the inattentive type might actually be a separate disorder altogether (22).

As we approach DSM-V, we face more questions than before about how to conceptualize and diagnose ADHD. If we continue to apply statistical methods to diagnoses, using methods such as latent class analysis, we

must grapple with a proliferation of empirically derived categories that do not clearly map onto clinical observations and that rely on the severity of symptoms as one boundary between categories. If we appeal to genotypes, or to neuropsychological endophenotypes, we must reconcile that those variables do not fall into well-demarcated categories any better than behavioral symptoms do. The prospects that we might reverse engineer or reverse translate from genotypes or endophenotypes to refined behavioral diagnoses (phenotypes), and then discover a wealth of validity in the new diagnoses, are not likely. This is not to say that the holy grail of a laboratory test for ADHD is entirely futile. It may be possible at some stage to incorporate nonbehavioral laboratory tests into the diagnostic criteria. At this juncture, however, we seem destined to rely on behavior to diagnose ADHD when DSM-V arrives.

Some changes to the diagnostic system can be predicted. The requirement that the disorder must be present by the age of seven will almost surely be modified. Not only does this requirement ignore the normal development of attention problems, it also has been shown to lack validity (23,24). There may be proposals to adjust the content of some items to make them more applicable to older adolescents and adults. Another question is whether to adjust symptom cutpoints. It has been argued that, because the base rate of ADHD symptoms is lower in the population of girls compared to boys, the cutpoints should be lower for girls. This can be readily determined using DSM-IV field trial methods by testing the relationship of symptoms to impairment within gender. It has also been suggested that cutpoints be lowered for older age ranges, particularly for hyperactivity-impulsivity, because of the observed declines in symptoms as age increases. Because so many children with combined type drop a few symptoms of hyperactivity-impulsivity as they mature, the predominantly inattentive type in adulthood consists of both lifelong inattentives and what we might call residual combined type.

It also seems clear that SCT will be reconsidered as symptoms of ADD. Because this would mean that an inattentive category would no longer share the same cognitive symptoms as a hyperactive category, the idea of separating these types into entirely different categories may gain traction. Looking back, perhaps the successive approximations of ADHD across DSM editions might inform DSM-V. DSM-III and IV were correct in separating types. But DSM-III-R might have been right in lumping together cases that exhibit some combination of hyperactivity-impulsivity and attention problems, and it might have erred only in not specifying a separate category of predominantly inattention/SCT. One thing is certain; DSM-V will not be the final resolution of the ADHD nosology. There is far more research that is needed than can be done before its publication.

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2

Differential Diagnosis of Attention and Auditory Processing Disorders

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INTRODUCTION

Children with central auditory processing disorders (CAPD) and those with attention deficit hyperactivity disorders (ADHD) may have difficulty in following directions, behave as though they have a hearing loss, frequently ask for repeated directions, and often display difficulty listening selectively in background noise, despite normal hearing (1,2).

CAPD have been observed in various clinical populations such those where morphological or functional disorders of the CNS are suspected: language disorders, dyslexia, learning disabilities, prematurity, attention deficit disorders (3–13). Does these pathologies are independent developmental disorders or simply comorbid?

DEFINITION OF CENTRAL AUDITORY PROCESSING DISORDERS

Central auditory processing disorders (CAPD) can be defined as syndromes in which hearing impairment is not due to a loss of peripheral auditory function. Since 19th century, only a few classical clinical presentations have been described mostly after large bitemporal lesions. In cortical deafness, the patient does not hear any sound stimulus and behaves like a profoundly deaf person (14,15). Auditory agnosie is defined as an incapacity to recognize any sound or noise although they are detected. In verbal deafness (16), the disability is limited to spoken language. Verbal expression as well as lecture and writing are preserved. Amusia is the incapacity to recognize

or appreciate music (17). Depending on the extent and the importance of the lesion, there is a continuum between these various forms of central deafness which are sometimes associated to others cognitive or sensory disorders.

In addition to these major disorders, many other minor central auditory deficits can be frequently identified. The most common one is probably the impairment of intelligibility with low redundant messages which, of course, can also be associated with a peripheral deficit. In children delayed learning, with normal intelligence and normal peripheral auditory function, can be due to CAPD (18,19). Obscure auditory dysfunction or King-Kopetzky syndrome (20) occurs in patients presenting hearing disabilities despite a normal peripheral auditory function. Hemianacusia (14) is for the auditory modality the equivalent of hemianopsia for the visual modality. It signals a damage of unilateral, temporal, or callosal lesion. Hemianacusia is suggested by a severe or, more often, complete extinction of the contralateral ear, exclusively observed on verbal dichotic tests. In adults over 60 years old, the involution of the central auditory pathways, in particular the demyelinization of the transcallosal connexions, increase the hearing disabilities created by an inner ear lesion (21).

Because these disabilities can be due to other dysfunctions such as language processing disorders or attention deficits, the American Speech-Language-Hearing Association (ASHA) convened a task force in 1996 to develop a consensus statement. The task force defined the Central Auditory Processes (CAP) as the auditory system mechanisms and functions responsible for the following behavioral phenomena: sound localization and lateralization, auditory discrimination, auditory pattern recognition, temporal aspects of audition including temporal resolution (i.e., detection of changes in frequency, amplitude and duration of auditory stimuli, and detection of time intervals between auditory stimuli), temporal masking (i.e., obscuring of probe by pre- or poststimulatory presentation of masker), temporal integration (i.e., summation of power over durations less than 200–400 msec), and temporal ordering (i.e., detection of sequence of sounds over time), auditory performance with competing acoustic signals, and auditory performance with degraded acoustic signals (22).

Beside the above definition which concerns processes specifically dedicated to audition, attention, memory, long-term language representations, and other nondedicated neurocognitive mechanisms are involved in the processing of acoustic signals.

The current model of CAP, whereby a listener actively controls processing, requires reciprocity between bottom-up and top-down processes. This model and the association of both CAPD and metacognitive deficit, necessitate comprehensive intervention programming targeting development of both basic auditory and metalinguistic skills and metacognitive strategies.

CAPD is an observed deficiency in one or more of the above-listed behaviors. For some individuals, CAPD is presumed to result from the dysfunction of processes and mechanisms specifically dedicated to the auditory system. For others, CAPD may originate from a more general dysfunction, such as an attention deficit or neural timing deficit, which affects performance across modalities (i.e., visual, sensitive…). It is also possible for CAPD to reflect coexisting dysfunction of both types (22). Thus, besides pure auditory mechanisms, learning, long-term phonological representation, and other higher level neurocognitive processes, memory and attention are considered in the definition of CAPD. The deployment of these nondedicated global mechanisms and processes in the service of central auditory processing underlies the frequently observed clinical association between CAPD and speech and language disorders, learning disabilities, attention deficit disorders with or without hyperactivity, psychological, emotional, and social problems (21).

Recently, APD has been more widely defined as a deficit in the processing of information that is specific to the auditory modality. The problem may be exacerbated in unfavorable acoustic environments. It may be associated with difficulties in listening, speech understanding, language development, and learning. In its pure form, however, it is conceptualized as a deficit in the processing of auditory input (23). This definition tends toward the view of the potential for interaction between disorders originating at both nondedicated processes and mechanisms in the processing of acoustic information.

Prevalence of CAPD

There is a lack of well-designed epidemiological studies on the prevalence of CAPD. Based on the prevalence of comorbid associations (e.g., serous otitis media, language impairment and learning disabilities, attention deficit disorders), the prevalence of CAPD in children has been estimated to be between 2% and 3% (18). In the aging population, this prevalence ranges from a low of 17% to a high of 90% (18,24) according to the central tests administered and the inclusion or exclusion of subjects with peripheral hearing loss or cognitive deficits (21).

Appeal Signs of CAPD

In children, many appeal signs, although not specific, raise the likelihood of CAPD. Particularly in noisy or low-redundancy listening situations, the child can behave as if he or she has peripheral hearing loss, which is within normal limits. They have difficulty following long or complicated verbal instructions, request they be repeated, or are unable to remember them. They have verbal IQ scores often lower than performance scores or significant scatter across subtests, e.g. math- and language-based subtests, or subtests that tap auditory perceptual skills. Many of these children have significant reading

problems, are poor spellers, and have poor handwriting. To minimize over referrals, CAP questionnaires have been designed to assess the teacher's and parent's perception of a child's auditory processing (25,26).

In adults, by far the most frequent symptom of CAPD is the inability to understand speech in low redundant conditions. The most commonly reported symptoms include: poor utilization of prosodic information, difficulty localizing sound sources or following complex auditory directions, subjective tinnitus, typically localized to the midline of the head, or unusual auditory sensations, e.g. marked decrease in the appreciation of music.

Beside children with learning disabilities and adults with poor in noise intelligibility, a large population can take benefit of central auditory testing. Many reports indicate that patients who have degenerative neurological diseases, multiple sclerosis among others, can have auditory deficits (27). A CAP deficit should be the first sign of senile demence or Alzheimer's disease (28). Occasionally patients with mass lesion of the brain may consult an ENT specialist before a diagnosis is made. Sometimes the auditory complains of patients who have received head trauma can be objectively acknowledged as central processing disorder.

Central Auditory Processing Tests

Tests of central auditory function can be categorized in a variety of ways, e.g., monotic, diotic, dichotic, speech, or nonspeech tests. In the author's commitment, we will follow the lead of Baran and Musiek (29) and categorize central tests in the following manner: low-redundancy speech tests, dichotic speech tests, temporal processing tasks, and binaural interaction tests.

Low-redundancy Speech Tests

Filtered, compressed, expanded, interrupted, and reverberated speech signals have all been used as central low-redundancy tests.

Since from the reports of Bocca et al. (30), low-pass filtering is by far the best known low-redundancy test. In the time compression or expansion technique, the temporal characteristics of the signal are electronically altered without affecting the frequency spectrum (31). Increasing the reverberation time of the speech signal provides an additional method of reducing the extrinsic redundancy (32).

A final method of reducing the redundancy of the speech signal is to imbed the signal in a background of noise (33–36). In spite of specific spectrum noise, cocktail babble has been used as competing signal (37).

Dichotic Speech Tests

Dichotic speech tests involve tests in which a different speech material is presented to both ears in a simultaneous or overlapping manner (38). Based

on her observations, Kimura developed a model to describe dichotic speech perception (39,40). When the central auditory nervous system is stimulated with dichotic speech materials, the weaker ipsilateral ascending pathways tend to be suppressed, and the neural impulses travel up the predominant contralateral pathways to reach the auditory temporal areas. Because the language processing region resides in the left hemisphere for most individuals, stimuli presented to the left ear must ultimately cross over from the right hemisphere to the left-dominant hemisphere, via the corpus callosum. This longer route for left ear presented stimuli induces a Right Ear Advantage (REA) apparent only upon dichotic stimulation. Dichotic speech tests are particularly sensitive to lesions of the auditory cortices and corpus callosum and to a lesser degree to brainstem lesions.

One of the most common dichotic tests in use today in English speaking countries is the Dichotic Digits Test (DDT) (41). For each stimulus presentation four digits are presented to the patient with two digits presented to each ear in a dichotic fashion.

The Competing Sentences Test (CST) developed by Willford (42) is easier and more convenient for child testing and uses a target sentence presented to one ear at 35 db re: spondee threshold and a competing sentence at 50 db re: spondee threshold. Perhaps the most widely used dichotic speech test is the Staggered Spondaic Word (SSW) Test, first described by Katz in 1962 (43). In this procedure, two spondees (compound words with equal stress) are presented in an overlapped fashion so that the second syllable of the first spondee occurs at the same time as the first syllable of the second spondee.

Temporal Processing Tests

Temporal processing is critical to a wide variety of everyday listening tasks, such as environmental signals, melodies, and speech. Many speech sounds are characterized by rapid frequency and intensity transitions that provide information for their identification. The temporal aspects of audition include many processes among which only few are well-codified clinically and widely used.

Temporal resolution refers to the ability of the ear to follow relatively slower transitions (infra 500 Hz) in the amplitude envelope of a stimulus. It has most often been investigated using either the Gap Detection method (44) or the Temporal Modulation Transfer Function (TMTF) method (45).

Temporal masking may be forward or backward type. Forward type refers to masking that occurs when the masking sound comes before the signal, while backward masking means the reverse.

Temporal integrations or summation describe the function relating signal detection threshold to its duration. Stable above 200 msec, the threshold increases as the signal duration decreases (approximately 3 db for every division of duration by two) (46).

Due to equipment sophistication involved in administering these tasks combined with the lack of standardized test protocols, these temporal processing functions are not explored in widespread clinical practice not withstanding their good clinical potential (18,19).

A fourth temporal processing concerns an ordering or sequencing task, i.e., to make discrimination based on the temporal order of auditory stimuli.

Pinheiro and Musiek (47) introduced a test of temporal processing involving triads of tone bursts, the Pitch Pattern Sequence Test (PPST). The subject has to report the pattern perceived from a sequence of three tone bursts: two of one frequency and one of another.

A related test of temporal ordering is the Duration Pattern Test (DPT) described by Pinheiro and Musiek (48). The test is similar to the PPST, but has as its elements 1000 Hz tones which vary only in duration (either 250 or 500 msec with a 300 msec interstimulus interval).

Binaural Interaction Tests

Binaural interaction tests encompass those tests that require the interaction of both ears in order to effect integration of information that is separated by time, intensity, or frequency factors to the two ears. Functions that rely on binaural interaction include binaural fusion, localization (determining direction of the source) and lateralization (place perception in the head) of auditory stimuli, binaural release from masking, and detection of signals in noise.

The task of integrating a portion of one signal presented to one ear and a complementary portion presented to the other ear is referred to as binaural fusion in literature. This task assesses the ability of the CANS to take disparate information presented to the two ears and to unify this information into one perceptual event. The two most used tests in this category of task include the Rapidly Alternating Speech Perception (RASP) and the Band-Pass Binaural Fusion test.

RASP is a procedure in which sentence material is switched rapidly between ears at selected periodic intervals causing unintelligibility when monauraly presented (49). It seems this test should be sensitive only to grossly abnormal brainstem pathology (42).

The test of binaural fusion uses stimuli (mono- or bisyllables) which are band passed so that a low-pass band (500–800 Hz) segment is presented to one ear and a high-pass band (1815–2500 Hz) segment to the other (50). The poor sensibility and acoustic technical problems preclude the wide use of these two last tests.

Interaural difference timer tasks involve the use of pairs of tonal or click stimuli that are presented to both ears simultaneously. Either the onset time or the intensity of the stimulus to one ear is manipulated relative to the other ear. The listener is required to indicate when he or she perceives the signal as lateralizing to one side or the other (27,50,51).

The binaural release from masking refers to the improvement in intelligibility under noise in phase conditions when a speech signal is presented out of phase rather than in phase condition (52,53). Any acoustical stimulus presented in phase to the two ears results in a perception located in the midline of the head, whereas presented 180° out of phase, it will be perceived at the ears. When both speech and noise were in phase (homophasic condition) and perceived both at midline, the speech intelligibility is lower than when the speech is 180° out of phase and noise is in phase (antiphasic) and respectively perceived at the ears and at the midline. The difference in binaural threshold between homophasic and antiphasic condition constitutes the Masking Level Difference (MLD). Variation of the size of the MLD depends on the type of stimuli and masker and of the specific protocol used. It may be as high as 10 to 15 dB when pure tones are used instead of approximately 5 db with speech material (54). Experimental results have shown that the MLD is highly sensitive to brainstem dysfunction while largely unaffected by rostral brainstem and cortical lesions (55,56).

RELATIONS OF APD WITH ADHD

The characteristics of ADHD are defined in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) (57). As said before, comparison of the definition of APD and ADHD reveals much overlap in behavior which could reflect a single developmental disorder (58). It has even been suggested that this difficult differential diagnosis may depend upon whether it is the audiologist or the psychologist who first evaluated the child (1). Nevertheless, some observations illustrating the differences between APD and ADHD support the clinical utility of these diagnosis (18).

The attention deficits of ADHD are typically restricted to sustained attention (59). They are supramodal, i.e., affecting more than one sensory modality (1). In contrast, subjects with APD experience selective and divided attention deficits restricted to the auditory modality. According to a recent study of Seikel et al. (60), inattention and distractibility seem to be the predominant overlapping symptomatology in APD and ADHD. APD should be characterized by a selective attention deficit associated with language processing and academic difficulties. On the other hand, ADHD should be characterized by a behavioral deregulation with inappropriate motor activity, restlessness, and socially inappropriate interaction profiles.

About this relation between APD and ADHD, some authors have suggested that auditory processing assessment could be useful in the evaluation of the methylphenidate (Ritalin®) treatment efficacy in ADHD. Another point is to know if a child with ADHD should be tested with or without treatment since this one could mask a true APD. An elegant way to answer to these questions is to statistically evaluate the effect of Ritalin

upon APD. If APD are improved it can be assumed that there is a common neurodevelopmental disorder with ADHD. On the contrary, no modification of APD would lead to the conclusion of their comorbidity.

To date, only four studies have investigated the effects on Ritalin on auditory process of children with ADHD and/or APD. Three of them have demonstrated a significant improvement of APD in small group of children with ADHD (58,61,62) and in the last one no differences were found in a group of 66 children (63). Methodology, small group, and variation in the inclusion criteria may have influenced the significant medication effect found on the three first studies. Two of them (61,62) evaluated a population of children diagnosed with ADHD for two successive conditions: first without the treatment and then with it, so the improvement observed may be due to a learning effect. In the third one (58), a placebo was used in a double-blind session but the sample population was small ($N = 15$).

The Tillery study was made on a larger sample ($N = 32$). All the children were diagnosed with ADHD and APD. They were submitted to three CAP tests (the SSW, PS, and speech-in-noise tests) and to the Auditory Continuous Performance Test (ACPT), a measure of attention/impulsivity. The study was double-blind and placebo-controlled in a split-unit design. No effect of the Ritalin on the three CAP measures used was observed. However, improvement of ACPT performance was show in the Ritalin group. This underlies the probability that APD and ADHD are independent problems and that, although the treatment improved attention and lessened impulsivity, it was not sufficient to alleviate the auditory dysfunction (63).

CONCLUSIONS

APD refer to an observed deficit in one or more of the central auditory processes responsible for the following behaviors: sound localization and lateralization, auditory discrimination, auditory pattern recognition, temporal aspects of audition including temporal resolution, temporal masking, temporal integration and temporal ordering, auditory performance with competing acoustic signals, and auditory performance with degraded acoustic signals (22).

APD have been frequently observed in association with many other neuromorphological disorders including ADHD, the most common neurobehavioral disorder of childhood affecting 3% to 5% of children aged 2 to 8 years.

Many studies have been made on the co-occurrence of APD and ADHD. A few of them tried to evaluate the efficacy or the effectiveness of the ADHD pharmacological treatment on APD. Some of them seem to show a direct association between ADHD and APD but some methodological mistakes may have been made. On the contrary, a more recent study has demonstrated that these pathologies are two independent problems even if they frequently occurred together.

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Section II: Clinical Conceptualizations

3

Clinical Testing of Intelligence, Achievement, and Neuropsychological Performance in ADHD

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According to the DSM-IV, diagnosis of attention deficit hyperactivity disorder (ADHD) is primarily based on behavioral criteria. If an individual manifests six of nine symptoms of ADHD, inattentive type or ADHD, impulsive hyperactive type in two or more settings with a history of onset before age seven, ADHD may be diagnosed. However, a more complete assessment of an individual who meets behavioral criteria for ADHD is often necessary for several reasons. To firmly establish the diagnosis of ADHD, it is important to rule out other disorders that may have similar behavioral manifestations. After confirmation of the diagnosis of ADHD, the possibility of comorbid disorders must be evaluated since they may effect treatment. Finally, an assessment of an individual's patterns of strengths and weaknesses in various neurocognitive and emotional realms is critical in designing a treatment program in areas such as academic accommodations, career planning, and therapeutic modalities. To that end, a comprehensive neuropsychological evaluation including assessment of intelligence, neuropsychological functioning, academic achievement and psychological functioning is often clinically indicated for individuals with ADHD.

USE OF INTELLIGENCE TESTING IN ADHD

In order to establish a differential diagnosis of ADHD, several conditions that include problems in attention most be ruled out. According to the DSM-IV, individuals with mental retardation and pervasive developmental disorders may meet behavioral criteria for ADHD and need to be differentiated from individuals with true ADHD. In addition, individuals with low average or borderline IQs may be misclassified as having ADHD when they fail to perform adequately in the school setting. Therefore, an accurate assessment of IQ is crucial in evaluating individuals who are underperforming in school and seem to be inattentive or excessively active to see if they are capable of meeting the demands placed upon them. Conversely, an individual who is gifted and placed in an unstimulating or restricted school environment may exhibit symptoms of ADHD due to lack of challenge.

Studies have generally shown that mixed groups of individuals with ADHD have slightly lower IQs than control samples. However, these studies generally do not differentiate between subtypes of ADHD or individuals with ADHD who have a comorbid learning disorder.

By far, the most commonly used IQ measure in assessing individuals with ADHD is the Wechsler Intelligence Scale for Children-IV (WISC-IV). Other tests that have been used are the Kaufman Assessment Battery and the Cognitive Skills Index (CSI).

The WISC-IV has been separated by means of factor analysis into four indexes: verbal comprehension, perceptual organization, working memory, and processing speed. Research has shown that the Working Memory Index score cannot be used to diagnose ADHD as it is not routinely lower in samples of children with the disorder. One of the two subtests that comprise the index, digit span, involves repeating digits forward and backward. However, in the total score there is no differentiation between digits forward, a fairly simple task and digits backwards, which places a larger load on sustained attention and working memory (the ability to hold information in mind to manipulate it). Letter-number sequencing, new on the WISC-IV, is difficult for some younger children to understand. Deficits on these tests may be related to factors other than distractibility, such as slow mental processing, language comprehension difficulties, auditory processing problems, or poor hearing.

Other indicators on the WISC-IV are important in ascertaining the particular neuropsychological profile of the individual being assessed. A discrepancy between the verbal comprehension and perceptual organization composites can delineate strengths and weaknesses important in educational planning. The processing speed index, which assesses the ability to quickly perform straightforward perceptual motor tasks, is an important determinant of functioning in individuals with ADHD. An individual with ADHD, impulsive hyperactive type may show rapid processing but make errors

because of performing impulsively without adequate oversight. Other individuals, particularly those diagnosed with ADHD, inattentive type, may show significantly lowered processing speed. This may result in slow reading and difficulty rapidly performing academic tasks.

ACHIEVEMENT TESTING IN ADHD

Due to the high comorbidity rate between ADHD and learning disabilities, an assessment of an individual's academic strengths and weaknesses is an important part of the evaluation of ADHD. The core symptoms of ADHD often result in problems attending to classroom instructions and directions as well as difficulty carrying out independent assignments and complex or multimodal tasks. In addition, an individual with ADHD may have school problems because of a modality-specific comorbid learning disorder such as dyslexia (a language-based reading disorder), dysgraphia (a writing disorder), or a math learning disability. The most widely used tests in the neuropsychological arena to assess academic achievement are the Woodcock-Johnson Tests of Achievement-III, the Wechsler Individual Achievement Test (WIAT), and the Wide Range Achievement Test-IV (WRAT-IV). The WRAT-IV, which screens word reading, spelling, and math calculation takes the shortest amount of time to administer but has limited subtests. The WIAT includes reading, comprehension, and writing subtests and was standardized with the WISC-IV, providing comparable norms. The Woodcock-Johnson Achievement Test has a large number of subtests and was standardized with the Woodcock-Johnson Test of Cognitive Ability. It has the widest use among educators.

In the past, many achievement tests had a common disadvantage in that they did not have a timed component. For this reason, many individuals showed better performance on the screening measures than was evident by monitoring classroom performance. The Woodcock-Johnson III includes measures of reading, math, and writing fluency that help assess an individual's ability to perform tasks rapidly, often necessary in the classroom. Supplementing these achievement strategies with other times tests such as the Gray Oral Reading Test-4 or the Nelson Denny Reading Test is important to assess an individual with ADD in terms of understanding actual classroom functioning.

Accurate assessment of cognitive and achievement functioning is necessary to assess the desirability of instituting classroom modifications or accommodations for students with ADHD. Individuals with ADHD may qualify for accommodations based on the Individuals with Disabilities Education Act (IDEA) or under a 504 plan. In order to render students eligible, an academic as well as psychoeducational or neuropsychological evaluation is necessary.

NEUROPSYCHOLOGICAL TESTING IN AD/HD

ADHD has been conceptualized as a disorder of executive functioning, including attention difficulties with sustained and behavioral inhibition (1–8).

There is a great deal of evidence suggesting that individuals with ADHD show neuropsychological deficits on tests of executive functioning. However, there are significant differences between tests in terms of the effect size and specificity of an ADHD diagnosis based on test performance. It is apparent that the use of neuropsychological tests alone cannot provide reliable clinical diagnosis of ADHD. However, neuropsychological test performance may be very important in determining the severity and extent of life disturbances in an individual with ADHD, as well as being crucial for educational and treatment planning.

Specific tests of executive functioning that have differentiated groups with and without ADHD are the Stroop Color-Word Interference Test, Trails B, Design Fluency, Wisconsin Card Sort Test, Rey-Osterrieth Complex Figure, Continuous Performance Test, and the Controlled Oral Word Association Test.

In addition to assessment of executive functioning, several other neuropsychological domains are important to evaluate in individuals with ADHD. Short-term memory and working memory are often affected. The degree and nature of an individual's memory impairment may have important implications for treatment strategies. In addition, individuals with a comorbid learning disability are at risk for even greater short-term memory problems (9).

In the school setting, children with dyslexia are sometimes misclassified as having ADHD because of difficulty comprehending written directions as well as inattentiveness and distractibility during reading tasks. There may also be behavior problems related to self-esteem issues around the reading disability. It is important to do a thorough neuropsychological assessment of the underpinnings of reading, particularly phonemic awareness and rapid naming, to differentiate between the two disorders. Individuals with attentional problems sometimes show difficulty with rapid linguistic retrieval and verbal fluency (10). However, most studies indicate that children with reading disability only, without ADHD, show deficits in phonological processing, which are not generally shown in children with ADHD (11).

Clinical evaluation of the speed of mental processing of an individual with ADHD is important for treatment planning. Some individuals with ADHD show very high psychomotor speed, often combined with many attentional errors as material becomes more complex. On the other hand, some individuals with ADHD, primarily ADHD, inattentive type, show very slow mental processing. Individuals with the first pattern may need to be taught strategies for slowing down and checking work.

Individuals with the latter pattern may need extended time for completion of tests and to be taught strategies for organizing their approach to complex or multifaceted tasks.

Assessment of Psychological Functioning in ADHD

Assessment of psychological and emotional functioning is important in ADHD for several reasons. To begin with, there is a high comorbidity with anxiety and mood disorders in ADHD. In addition, an individual's motivation, anxiety level, frustration tolerance, and self-esteem are important in determining prognosis and designing an efficacious treatment plan.

Many symptoms consistent with ADHD, inattentive type are also found in depression and it is important to rule out depression as underlying difficulties in attention, concentration, and executive function. In children, the Childhood Depression Inventory may be useful. For teenagers, the Achenbach Youth Self-Report includes a number of emotional symptoms. For adults, a Minnesota Multiphase of Personality Inventory-2 (MMPI-2) and the Beck Depression Inventory may help to evaluate the presence and degree of depression. The presence of concomitant anxiety or mood disorders may have implications for medication management as well as treatment modalities.

IMPLICATIONS FOR TREATMENT

In addition to self-report forms, it is important to query individuals familiar with the patient as to daily functioning. Parents may be asked to complete such behavior rating scales as the Achenbach Child Behavior Checklist or the Behavior Inventory of Executive Functions (BRIEF). Teachers can complete an Achenbach Teacher Report or school version of the BRIEF.

CONCLUSIONS AND TREATMENT IMPLICATIONS

Complete neuropsychological assessment can aid in diagnosis and treatment planning for ADHD. To begin with, conditions which may meet behavioral criteria for ADHD such as low IQ or depression must be ruled out. When ADHD has been confirmed, evaluation of comorbid learning or emotional disorders is important in designing a comprehensive treatment plan. Academic accommodations will differ if a student has learning problems because of ADHD alone or whether there are concomitant learning disabilities. If ADHD alone is affecting learning, accommodations involving more individual attention and repetition of procedures and instructions may be helpful. In addition, the extent to which executive functioning is disrupted will be important to determine the strategy that will be most effective. Individuals with ADHD often have trouble with multistep or complicated

projects. Writing assignments may be particularly difficult and the nature and extent of these difficulties need to be determined so that remediation can be specific.

Individuals with ADHD and a concomitant learning disability appear to be more impaired than those with ADHD alone on tasks of executive functioning as well as having further specific needs such as work on phonological processing for individuals who are dyslexic (12).

The presence or absence of deficits in processing speed affects academic accommodations. Individuals with ADHD and processing speed deficits require extra time for tests, and this accommodation is increasingly being provided by schools and outside testing agencies. In addition, individuals with ADHD who have working memory deficits may need additional time to reread passages to ensure comprehension and may also require extra time for adequate performance.

Individuals with comorbid emotional or self-esteem issues may benefit from psychotherapy in addition to other treatment modalities. When executive functioning deficits are significant, which may occur even when medication management is effective, resource specialist help or educational therapy in school may be indicated. For adults who continue to have executive function deficits after medication management, the use of educational therapists or "life coaches" may be indicated. Neuropsychological evaluation can provide a detailed neurocognitive, psychological, and behavioral profile that will help guide therapy by delineating the nature and extent of specific problem areas and areas of compensating strengths in an individual with ADHD (13).

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4

Self-Esteem and Self-Perceptions in ADHD

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Attention deficit hyperactivity disorder (ADHD) is characterized by problems with hyperactivity/impulsivity and/or inattention (1). Children with ADHD also often experience severe functional impairments in the form of behavior problems, peer rejection, and/or academic and family-related dysfunction (2–4). In nondisordered populations, incompetencies such as these generally are associated with low self-esteem and/or depression (5–8). Research on the self-esteem and self-perceptions of children with ADHD is much more controversial, however, and at this time, there exist two opposing points of view. Some researchers have discovered children with ADHD to have lowered self-views as compared to controls (9–11). In contrast, there exists an increasingly larger body of research demonstrating overly positive self-views in children with ADHD (12–16). The topic of self-perceptions in children with ADHD thus is a matter of some contention, and the somewhat speculatory nature of this chapter is merely a reflection of the current state of research in this area.

As Hoza and colleagues (13) noted, dividing research on self-concept in children with ADHD into the categories of research on global self-esteem, research on domain-specific self-perceptions, and research on task-specific self-perceptions somewhat clarifies a picture that appears at first glance to be rather hazy. In the current chapter, we therefore consider each of these

constructs in turn, and review both the literature indicative of lowered self-views in children with ADHD as well as that indicating unrealistically positive self-views in these children. As our particular interest lies in overly positive self-perceptions, termed "positive illusions" in our recent research (13), we also will discuss the specificity of self-enhancement findings to ADHD populations, as well as potential mechanisms that may explain this phenomenon. Finally, we will reflect upon the relevance of self-esteem and self-perception research to clinical interventions for children with ADHD.

GLOBAL SELF-ESTEEM

Research focusing on the global self-esteem of children with ADHD as compared to controls has generally shown that the estimates of self-esteem provided by children with ADHD are either lower or approximately equivalent to those provided by comparison children (9,11). For example, Treuting and Hinshaw (11) compared the self-esteem of aggressive boys with ADHD, nonaggressive boys with ADHD, and comparison boys. They discovered that the aggressive subgroup of boys with ADHD reported lower levels of self-esteem than did either nonaggressive boys with ADHD or comparison boys, but failed to discover any significant differences between the nonaggressive ADHD group and the comparison group.

Similarly, Hoza and colleagues (14) compared the estimates of global self-worth provided by children with ADHD to those provided by comparison children. Results indicated that the reports of self-esteem provided by children with ADHD did not differ significantly from the appraisals provided by comparison children, despite the numerous functional impairments typically associated with the diagnosis of ADHD. This finding was replicated by Hoza et al. (13) with a substantially larger sample. The self-esteem of boys with ADHD, therefore, may be unjustifiably positive.

DOMAIN-SPECIFIC SELF-PERCEPTIONS OF COMPETENCE

As with research on self-esteem, a great deal of past research has examined absolute levels of self-perceptions of competence (i.e., examining subjective self-perceptions without comparing them to an external criterion). The results of this research are similar to those reviewed for self-esteem. Again, some research suggests that children with ADHD exhibit lower absolute perceptions of domain-specific competence (10), while other research indicates that children with ADHD provide estimates of their competence that are similar to those provided by comparison children (14). For example, Hoza and colleagues (14) investigated self-perceptions of scholastic competence, social acceptance, athletic competence, physical appearance, and behavioral conduct in boys with ADHD and comparison boys. They

discovered that the self-reports of children with ADHD differed from those of control children only in the domain of behavioral conduct, boys with ADHD reported lower levels of competence (i.e., poorer behavioral conduct) than control boys. Hoza et al. (13) utilized a larger sample in order to perform a between-groups comparison (ADHD vs. control) of absolute levels of self-perceived competence in the above domains, although the researchers chose not to examine the domain of physical appearance. Results indicated that the absolute self-perceptions of boys with ADHD did not differ significantly from those of comparison boys in any of the four domains. These findings indicate that the self-perceptions of children with ADHD may be overly positive.

Several researchers have commented that it is necessary to compare self-views to objective criteria in order to determine their value or accuracy (13,17). Some children's positive self-views may be realistic reflections of actual competence, while other children may be overly positive reporters of their own competencies. As Hoza and colleagues (13) note, it is likely that these two groups of children differ on dimensions that are relevant to adjustment and response to clinical intervention.

Recent research comparing the domain-specific self-perceptions of children with ADHD to control children therefore has compared the perceptions of each child to ratings provided by external raters in order to obtain an index of over- and underestimation (13,18). For example, Hoza and colleagues (13) examined the self-perceptions of children with ADHD and comparison children relative to competence ratings completed by the boys' teachers. These researchers discovered that the reports of children with ADHD regarding their own competence were more inflated relative to teacher reports than the reports provided by comparison children. Further, the researchers found that children with ADHD provided the most positive self-reports in domains in which the teachers had rated them as being most impaired.

Hoza et al. (18) replicated these results with a separate sample of children with ADHD. This study further extended previous work by examining the self-perceptions of children with ADHD and control children in comparison to competence ratings provided by the children's mothers and fathers as well as to ratings supplied by the children's teachers. Regardless of which comparison rater was utilized as the criterion (i.e., mother, father, or teacher), results indicated that children with ADHD overestimated their competence to a greater degree relative to the criterion than the comparison children. These results lend additional support to the hypothesis that children with ADHD provide overly positive reports of their own abilities.

TASK-SPECIFIC SELF-PERCEPTIONS OF COMPETENCE

In addition to examinations of the domain-specific self-perceptions of children with ADHD versus comparison children, both on an absolute level

and in comparison to criteria, children's task-specific evaluations of competence have been examined on laboratory tasks where actual performance on the task is known. For example, Hoza and colleagues (15) administered a find-a-word puzzle task to both boys with ADHD and comparison boys. The researchers found that in comparison to the group of control boys, the group of boys with ADHD solved fewer puzzles, stopped early more frequently, and were able to find fewer words on a subsequent generalization task. Further, research assistants rated the boys with ADHD as trying less hard and less cooperating than control boys. Despite the poorer performance of the ADHD group on the behavioral measures and the lower ratings of effort and cooperation that this group of boys received, the pretask performance expectations and posttask evaluations of performance provided by boys with ADHD were not significantly different from those of control boys. These findings further support the idea that children with ADHD provide evaluations of their own competence that are positively biased.

Hoza et al. (16) further investigated the construct of positive illusions through an examination of the self-ratings of boys with ADHD on a social laboratory task. Specifically, both boys with ADHD and control boys were asked to convince a child confederate to attend a camp under either a success or a failure manipulation. In addition, following the manipulation, an adult research assistant also provided each boy with either positive or negative feedback regarding his performance on the task. Consistent with similar research in the academic domain, the boys with ADHD provided more positive ratings of the child confederate and of their own performance on the task than did the comparison boys. For a subset of the dependent variables, these differences between boys with ADHD and comparison boys were even more marked after the boys had experienced the failure manipulation. Evidence that self-reports of the boys with ADHD were overly positive, came from objective raters, who evaluated the boys with ADHD as being less socially effective than the control boys. These findings are further evidence toward the conclusion that children with ADHD are overly positive reporters of their own performance. In addition, they indicate that these children may be most unrealistic about their performance when they have failed at a task.

This finding is consistent with research demonstrating that children with ADHD manifest positive illusions to the greatest degree in their domains of greatest deficit (13,18). In other words, the discrepancies between positive illusory estimates of their own competence provided by children with ADHD and the competence ratings provided by adults familiar with the children are greatest in the domains where children are evaluated as being least competent by the adult raters. Thus, aggressive children with ADHD provide the most inflated evaluations of their own competence in the behavioral domain, while low-achieving children with

ADHD provide the most inflated estimates of competence in the academic domain (13).

Comorbid depressive symptoms, on the other hand, appear to exert a different effect upon the self-views of children with ADHD than do the comorbidities described above. In fact, comorbid depression appears to alleviate the positive bias to a certain extent (13,14,18). For example, although Hoza and colleagues (13) discovered that the absolute self-perceptions of children with ADHD and control children did not differ significantly, subgrouping the children with ADHD into those with and without comorbid depressive symptoms produced an interesting pattern of results. The self-perceptions of boys with ADHD and comorbid depressive symptoms were significantly lower than the self-perceptions of both, the boys with ADHD but without comorbid depression and the comparison boys. These two latter groups did not differ significantly from one another. Further, when the researchers examined the boys' self-perceptions relative to ratings provided by the boys' teachers, they discovered that the boys with ADHD and comorbid depressive symptoms provided estimations in key domains (e.g., social) that were similarly realistic to those provided by comparison boys. Boys with ADHD but without depressive symptoms, on the other hand, overestimated their competence in multiple domains as compared to both of the other groups. In the behavioral conduct domain, however, both groups of boys with ADHD overestimated their competence relative to control boys, although the effect size was smaller for boys with ADHD and co-occurring depression than for nondepressed boys with ADHD. Consistent with research demonstrating a link between depression and diminished self-esteem in nondisordered populations (19), therefore, it appears as if comorbid depressive symptoms may lessen positive illusory tendencies in children with ADHD.

ARE POSITIVE ILLUSIONS SPECIFIC TO ADHD?

Specific ADHD-related behaviors appear to be associated with positive illusory beliefs of self-competence, although there is currently a paucity of research addressing this issue. However, Owens and Hoza (20) studied the presence and extent of overly positive views of academic self-competence in children with symptoms characteristic of ADHD, and discovered that hyperactive/impulsive symptoms were more closely related to positive illusions of academic competence than were inattentive symptoms. In other words, the self-reports of children exhibiting hyperactive/impulsive symptoms were found to be overly positive when compared both to the children's own achievement test scores and to their teachers' reports. Both control children and children with primarily inattentive symptoms provided more accurate self-reports of their academic competence.

Despite this tie to hyperactive/impulsive symptoms, a core component of ADHD, it seems likely that positive illusions also are associated with other disruptive behavior disorders. In the past, overly positive self-esteem and self-perceptions have been linked to problems such as peer rejection (21–23) and aggression (17,24–29). Further, comparisons performed between children diagnosed with conduct problems or oppositional-defiant disorder (ODD) and comparison children indicate that children with these externalizing disorders provide estimates of their own social competence that do not differ significantly from those provided by control children, despite parents' and teachers' reports to the contrary (30). It therefore appears at this time that the positive illusory bias is a construct that is indeed correlated with specific dimensions of psychopathology, namely those associated with the disruptive behavior disorders and specifically with ADHD. The common comorbidity among ADHD and other disruptive behavior disorders (31) may at least partially account for the presence of positive illusions in both ADHD and other behavior-disordered populations.

POTENTIAL MECHANISMS

There are several potential explanations for the existence of positive illusory self-perceptions. First, it seems possible that these inflated self-perceptions reflect other impairments associated with ADHD. For example, Barkley (32) has proposed that the primary dysfunction in ADHD is a deficit in executive functioning, specifically a lack of behavioral inhibition that can account for all of the impairments that are commonly associated with ADHD. Barkley hypothesized that tasks such as the inhibition of task-irrelevant responses, execution of goal-directed responses, sensitivity to response feedback, and persistence toward a specific goal all can be subsumed under the general category of behavioral inhibition. A deficit in behavioral inhibition therefore would cause impairments in self-control and self-regulation much like those demonstrated in ADHD. It seems likely that accurate self-perception requires the ability to self-regulate in response to external feedback, and an impairment in executive functioning thus may prevent children with ADHD from being aware of their deficits. Indeed, past research has demonstrated a connection between impaired executive functioning and diminished self-awareness (33).

Research on clinical assessment (3) and cognitive interventions (34) also emphasizes the idea that children with ADHD may lack certain cognitive skills relevant to self-perception. For instance, clinicians are encouraged to discount the self-reports of externalizing children in the assessment and diagnostic process (3). In addition, cognitive treatment strategies such as self-instructing, problem solving, self-reinforcement, and self-redirection appear ineffective when used as primary interventions to ameliorate

the problems of children with ADHD (3,34). In fact, current empirically supported treatments for ADHD are all treatments that emphasize altering the environment of the child rather than fostering changes within the child (35). Current clinical wisdom therefore accentuates the possibility that these children lack the self-regulatory abilities necessary to effectively process and apply external criticism in order to regulate their own behavior.

Alternatively, another group of researchers has proposed a self-protective interpretation of the positive illusory bias (12,36). This explanation posits that overly positive views of self-competence are a façade for actual insecurities on the part of children with ADHD, serving the function of preventing these children from feeling inadequate as a result of their deficits. There is some evidence to support this hypothesis, most notably in the social domain. For example, Ohan and Johnston (36) presented children with ADHD with a social task, and then asked the children to evaluate their own performance. The researchers found that children with ADHD who initially provided overly positive estimates of their performance on the task were able to provide more realistic evaluations of their performance after an adult research assistant gave them positive, task-specific feedback. Similarly, Diener and Milich (12) discovered that providing boys with ADHD with positive feedback that was supposedly from a peer partner in a laboratory interaction task served the function of reducing overly positive performance evaluations on the part of the boys with ADHD to a more realistic level.

However, evidence regarding the validity of the self-protective hypothesis has been inconsistent across domains. Ohan and Johnston (36) also presented their ADHD and control sample with an academic task. As expected, the boys with ADHD provided pretask estimates of their performance that were similarly high to those of comparison boys, even though the boys with ADHD subsequently performed at a significantly lower level than the comparison boys. Contrary to findings in the social domain, however, providing the boys with positive feedback resulted in increased performance evaluations from both boys with ADHD and control boys in this condition, as compared to boys who received either average or no feedback regarding their performance. These results are inconsistent with the self-protective hypothesis. Ohan and Johnston posited that academic tasks may be less salient than social tasks for children with ADHD. If children with ADHD view academic competence as being less important, they may be able to discount their failure in the academic domain. If this is the case, then these children would have no reason to self-protect. Alternatively, Ohan and Johnston suggested that the explanation for positive illusory estimates of competence may vary from domain to domain. They proposed the possibility that although positive biases in the social domain may be best explained by the self-protective hypothesis, overly positive estimates of academic competence may reflect children's actual judgments of their academic performance.

This suggestion is consistent with research from the adult social psychology literature that points toward another potential explanation for inability to acknowledge incompetence. Kruger and Dunning (37) claim that individuals who are incompetent are, by definition, less able to recognize competence (and thus incompetence) in themselves or in others. If this is the case, the skills deficits demonstrated by children with ADHD ironically may prevent them from realizing their own incompetence. If these children do not understand what it means to be competent, they are free to consider themselves as being competent. This explanation should be considered in future research.

CLINICAL RELEVANCE

Research on the self-perceptions of children with ADHD is relevant in shaping clinical interventions. Although many clinicians, parents, and researchers cite increased levels of self-esteem as a key treatment goal (38), there exist several studies demonstrating poorer treatment response in subsets of externalizing children with either elevated self-esteem (39) or self-confidence (40). This research highlights the possibility that current clinical practice may promote inaccurate and overly positive self-perceptions in these children, therefore making them more resistant to therapeutic change. It seems likely that the failure of these children to recognize their own incompetence in essential domains of functioning means that they see no need for improvement and thus have no motivation for treatment. In fact, Gresham et al. (21) suggest that this population of children may best be served by interventions targeting self-control and "humility training" (p. 405), the goal of which would be to decrease these children's self-views to a more realistic level. However, this is a radical departure from common clinical intuition, and we feel that outcomes associated with a positive illusory style of self-perception over time should be examined before definite recommendations are made.

The competing explanations for the existence of positive illusions imply different effective treatments for children with positive illusory biases, and it consequently is impossible for us to make specific recommendations at this time. If the positive illusions of children with ADHD stem from cognitive skill deficits, then this bias may not be easily altered by feedback of any kind. Current behavioral treatments that operate by modifying the child's environment through the use of incentives may therefore remain the best strategy. The self-protective hypothesis, however, implies that clinicians and parents may need to praise the successes of children with ADHD and downplay their failures. Taking this tactic may permit positive illusory children with ADHD to relax their defenses, evaluate their competence more realistically, and therefore perhaps understand the necessity of change. Finally, accepting Kruger and Dunning's (37) explanation of positive

illusions as the inevitable consequence of incompetence implies that teaching positive illusory children to become competent in their domains of greatest deficit may ameliorate positive illusory self-perceptions. All of these recommendations, however, are purely speculatory at this time; at present, it seems most prudent to recommend that clinicians continue to employ existing interventions in order to increase the competence of children with ADHD (consequently making these children's competence more congruent with their self-views). Future researchers must determine the true cause of positive illusions and the function that these illusions serve prior to amending existing interventions.

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5

The Family Context of ADHD

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The families of children with attention deficit hyperactivity disorder (ADHD) have been the focus of investigations for more than a quarter of a century (1,2), with interest in areas such as parent–child interactions, parental characteristics, as well as marital relations and family involvement in the treatment process. This research, although largely descriptive in nature, has provided ample documentation of the areas in which these families are likely to face challenges, as well as areas of strength. Recently, research concerning families of children with ADHD has been characterized by a progressive understanding of the relation between family or parental characteristics and the conduct problems that commonly co-occur in children with ADHD. Given necessary space limitations, in this chapter we have chosen to highlight research in five domains of functioning within families of children with ADHD including parent–child interactions, parental psychopathology, parental cognitions, marital relationships, and the role of families in treatment.

As a background to this review, we note the need for a developmentally informed and interactive model for understanding how childhood ADHD interacts over time with the family context in which the child resides (3). Such a developmental psychopathology conceptualization is necessary to allow integration of what is known about the families of children with ADHD with new and increasing information concerning the characteristics of children with the disorder, including their biological or genetic make-up. Despite strong evidence for an underlying biological origin in ADHD (4), the heterogeneity of clinical presentations of ADHD suggests diverse pathways in the development of the disorder, and it is likely that this

diversity reflects the interaction of cultural, social, and biological factors over time (5,6). Within such a framework, the child's behavior is understood to influence the functioning of the family, and at the same time, the behaviors of other family members exert an impact on the child. This approach encourages identification of risk and protective factors within the child and family context that, acting at different points in time across the child's development, might serve to accelerate or buffer the development of ADHD symptomatology or accompanying conduct problems. For example, a child's early difficult temperament may serve as a risk factor for emerging problems in parenting responsiveness and together these child and parent difficulties may exacerbate the child's inattentive or impulsive behavior. Alternately, a family's ability to respond to challenging child behaviors with sensitive modeling or teaching of effective self-regulation strategies may serve to protect the child from escalating difficulties with inattention/impulsivity, or alternately, to prevent the development of an oppositional pattern of behavior. Thus, we argue that conceptualizing the relations between family characteristics and child ADHD as interactive and constantly evolving is important in understanding, not only the development of ADHD, but also the co-occurrence of ADHD and oppositional or conduct problems (7,8).

PARENT–CHILD INTERACTIONS AND PARENTING BEHAVIORS

Numerous studies have identified high levels of both parent and child aversive behaviors in interactions in families of children with ADHD. Compared to families of nonproblem children, children with ADHD are more aversive and less compliant, and their parents are more negative, directive, and less socially engaging (9,10). Similar difficulties in parent-child interactions have been reported for both boys and girls with ADHD (11), from preschool through adolescent ages (12,13), and in father–child as well as mother–child interactions (14). Thus, parent–child interaction difficulties are a well-established characteristic of families of children with ADHD.

However, questions remain regarding the extent to which these difficulties are associated with ADHD versus with comorbid child conduct problems. Johnston (15) and Gomez and Sanson (16) both found higher levels of negative and noncompliant child behavior in children with comorbid ADHD and conduct problems compared to children with only ADHD or to nonproblem children. However, Gomez and Sanson observed more directive, negative, and less rewarding behaviors by mothers in a comorbid group as compared to the other two groups, whereas Johnston reported no differences in observed mother or father behavior among the three groups. Johnston did find, however, that parents in both the ADHD only and ADHD/conduct problems groups reported less optimal parenting strategies compared to the nonproblem group. Supporting the need to focus on positive as well as problematic aspects of parent–child interactions,

Lindahl (17) found that, although parent–child conflict distinguished both ADHD and comorbid children from nonproblem families, it was positive family interactions that best discriminated between families of children with only ADHD and families of children with conduct problems. Similarly, Johnston et al. (18) found that, among families of children with ADHD, maternal responsiveness in parent–child interactions was related to the child's level of conduct problems, but was not related to the child's level of ADHD symptomatology.

In general, across the range of child ages and a variety of dimensions of parenting or parent–child interactions, results from cross-sectional studies clearly suggest more difficulties in families of children with ADHD and co-occurring conduct problems in contrast to families of nonproblem children. However, whether parent–child interactions in families of children with only ADHD are most similar to nonproblem families or to the comorbid group, or fall between these groups varies across studies. Unfortunately, cross-sectional studies are unable to address issues related to how parenting and child characteristics may interact in the development of child problems or parent–child interaction difficulties over time. Longitudinal studies conducted in community samples have suggested that difficulties in parenting behavior are more strongly predictive of continuation of child conduct problems than of the continuation of ADHD symptoms (19) and that parenting problems may combine with child ADHD behaviors to predict the highest risk of child aggression (20). More such longitudinal, prospective studies measuring a range of parenting behaviors and styles and a range of child behavioral tendencies are needed to elucidate the development and course of these family problems and child outcomes.

PARENTAL PSYCHOPATHOLOGY

Elevations in a variety of forms of parental psychopathology have been found in families of both male and female children with ADHD, in both mothers and fathers, and across a range of child ages (11,21,22). However, as with the research into parent–child interactions, in many instances it appears that difficulties in parental psychological functioning may be linked more closely to conduct problems than to ADHD (13,23), although such findings are not entirely consistent (15,24).

One aspect of parental psychopathology that has received considerable attention, particularly among mothers of children with ADHD, is depression. Several studies have identified higher rates of depression in mothers of children with ADHD as compared to mothers of nonproblem children (11,22). Many, although not all, of these studies suggest that problems with depression are particularly likely among mothers of children with both ADHD and conduct problems, or in families with more than one child with

ADHD (25). Other studies have focused on parental antisocial behavior, particularly among fathers of children with ADHD. These studies quite clearly indicate that parental antisocial behavior is most closely related to the presence of comorbid child conduct problems rather than to ADHD per se (23,26). Still other studies have focused on parental alcohol problems and found higher rates of alcohol use in parents of children with ADHD as compared to parents of nonproblem children (22,27). Again, it seems clear that this elevation in parental alcohol abuse is more strongly associated with child conduct problems, including physical aggression, than with ADHD symptomatology (28). High rates of ADHD also have been reported among parents of children with ADHD (29). Here, in contrast to the findings for depression, antisocial behavior, and alcohol abuse, where the relation seems to be stronger with child conduct problems, ADHD among parents appears most closely related to the child's problems with ADHD (25,30).

As with the study of parent–child interactions, much more work is needed to understand how various aspects of parental psychological functioning interact with child characteristics in the development and maintenance of child ADHD and conduct problems. A few glimpses of the types of research that will inform this area can be found. For example, one can easily imagine how a parent's own difficulties with ADHD would interfere with his/her ability to monitor and manage challenging child behavior. So far, both case studies and more controlled studies have supported this speculation that impairment of parenting skills may play a role in mediating the association between parent and child ADHD symptoms (31,32,33). Another example of the type of work that is needed in this area comes from an interesting series of studies by Lang and colleagues (34,35). These studies demonstrated both that difficult child behavior can elicit increased alcohol consumption among parents, and that consumption of alcohol increases inappropriate parenting behaviors such as demandingness, indulgence, failure to attend to the child, and off-task comments.

PARENTAL COGNITIONS

The study of social cognitions among parents of children with ADHD is an emerging area of research. To date, focus has been on two primary types of cognitions: parenting efficacy and attributions for child behavior. Given the parent–child difficulties in families of children with ADHD, it is not surprising that several studies have reported diminished parenting satisfaction and efficacy among parents of children with ADHD, with children ranging from preschool to school age (36,37). Considering how parenting sense of efficacy relates to child conduct problems, Johnston (15) found that both mothers and fathers of ADHD children with comorbid conduct problems reported lower levels of parenting competence than parents of children with

ADHD alone, and both of these groups were lower than parents of nonproblem children. Thus, as with parent–child interactions, parents' thoughts about their parenting competence appear most at risk in those parents who must face the challenges of a child with both ADHD and conduct problems.

Other research has focused on the causal attributions that parents offer for the behavior of children with ADHD. Across a variety of assessment methods, compared to parents of nonproblem children, parents of children with ADHD see both the symptoms of ADHD and child conduct problems as caused by uncontrollable, stable factors within the child, but see children's positive behavior as less dispositional and see themselves as less responsible for child behaviors (38,39). A necessary next step in this research is to determine whether the differences found in attributions across parents of nonproblem children and children with ADHD are related to differences in parenting reactions to the children, and to subsequent differences in child behavior, and to map the mutual influences among child and parent behavior and parental cognitions in families of children with ADHD.

MARITAL RELATIONSHIPS

Studies examining marital relationships in families of children with ADHD have generated inconsistent findings. Some have reported more marital conflict and less satisfaction in couples with children with ADHD as compared to couples with nonproblem children (11,36); however, these results have not always been replicated (40). Although researchers have looked to comorbid conduct problems as an explanation for these mixed findings, here again the results are not entirely consistent. Reports of greater marital difficulties in parents of children with ADHD and comorbid conduct problems as compared to parents of children with only ADHD have been reported (17), but so have reports of no differences in martial functioning among the two groups of ADHD children (15,41). In sum, although disrupted martial relationships may characterize some families of children with ADHD, this is far from universal and much remains to be discovered about which child or parental characteristics are most closely linked to functioning within the marital system.

FAMILY INVOLVEMENT IN TREATMENT

Parents play essential roles in both the pharmacological and psychosocial treatments that have been shown to be efficacious for treating children with ADHD. Parents are central, not only in decisions regarding choice of treatment, but also in the implementation and maintenance of these treatments. For example, the efficacy of stimulant medication in reducing a

child's ADHD symptoms has been suggested to vary depending upon the type of medication management support and advice received by the parents (42). Child attitudes and beliefs (43), as well as parental knowledge of ADHD (44) appear predictive of medication adherence. Greater research of the interplay of these factors as predictors of initial and ongoing treatment utilization will be important in advancing our knowledge of the role that families play in pharmacological treatments. Parents also play a crucial role in implementation of effective psychosocial treatments for children with ADHD (45), particularly behavioral parent training. Such programs are designed to alter parenting strategies so as to reduce disruptive child behaviors. The parents' willingness and ability to engage in psychosocial treatments, as well as their success in implementing the recommended strategies is a crucial determinant of the success of these treatments in improving child outcomes.

Not surprisingly, the elevated levels of intrapersonal or marital difficulties that often occur in parents of children with ADHD or ADHD and conduct problems can stand as significant obstacles to parents' effective involvement in the treatment of the child's ADHD. However, on a more optimistic note, and consistent with the interactional view of child ADHD and family functioning that we presented earlier, both pharmacological and behavioral treatments for ADHD have been demonstrated to hold promise in reducing parental distress, improving marital distress, and improving feelings of parenting competence (46,47).

CONCLUSION

We have presented a brief review of aspects of family functioning that are related to ADHD in children, and tried to elucidate the extent to which these associations between family and child characteristics are specific to the child's ADHD symptoms or to co-occurring conduct problems. We also have argued for a transactional approach as a method to conceptualize how dimensions of family functioning interact with child characteristics over time, and may function to influence, not only the severity but also the type of child problem. This approach recognizes that the vast majority of research is clear in ruling out the possibility that aspects of family functioning, such as parenting, are the primary cause of childhood ADHD. Instead, an interactive model argues that the characteristics of children (including biological predispositions to ADHD) are involved in a mutually influential dance through time with the environment of the family. Difficulties inherent in children are likely to serve as risk factors for a family's functioning, while at the same time aspects of the family context, such as less than optimal parenting, may exacerbate the nature and extent of the child's difficulties.

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6

Comorbidity as an Organizing Principle

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Most children presenting to clinics and meeting the diagnosis of ADHD also have one or more comorbid disruptive behavior or emotional disorders (1). It is increasingly clear that consideration of these disorders is critical to sharpen our conceptualization of ADHD and its etiologies, to the diagnostic process, and to treatment choice and outcome. This chapter discusses the impact and implications of comorbid disruptive behavior, anxiety, and depressive disorders.

OPPOSITIONAL DEFIANT DISORDER AND CONDUCT DISORDER

The two other disruptive behavior disorders, oppositional defiant disorder (ODD) and conduct disorder (CD), are commonly comorbid with ADHD. ODD, present in up to two-thirds or more of cases, is characterized by chronic argumentativeness, defiance, and anger (2). The more pernicious CD, involving serious violations of societal norms, is present in a quarter to half of all cases (2–4). ODD is generally considered a milder disorder than CD, but it is far from benign: it is associated with functional impairment and disturbed interpersonal relations, and in some cases it progresses to CD. Children having both ADHD and CD have more learning problems, neuropsychological deficits, and poorer prognosis with high rates of antisocial outcomes (1). The combination of ADHD and CD is associated with an earlier age of onset for CD and more persistent and serious conduct problems (5).

Multiple risk factors related to heredity and family environment have been linked to each of the disruptive behavior disorders (6). The association

between paternal antisocial personality disorder (APD) and child CD in boys with ADHD has been replicated in several studies (7–9). Weaker associations have been reported for paternal APD and comorbid ODD in children with ADHD (8,10) with some studies showing no association (11). Parental depression also has been linked to disruptive behavior in children, perhaps via common familial vulnerabilities (2), via an association with parental antisocial behaviors (11), or due to the difficulty of raising children with a disruptive behavior disorder. There is less evidence for a specific association between parental anxiety and disruptive behavior disorders, particularly when comorbid anxiety in the child is controlled (2,10).

Parenting practices form a second set of family risk factors for comorbid externalizing disorders. Dysfunctional parenting is common in families with children having ADHD and may partly be a reaction to the difficulties of raising a child with ADHD; it may also serve an etiological role in the emergence of comorbid disruptive behavior disorders (6). Consistent with social learning theory, children with oppositional and conduct problems often have families characterized by coercive interaction styles, inconsistent discipline, lack of parental involvement, and lack of positive and warm interactions between parent and child (12–14). Recent studies with ADHD children suggest that certain kinds of dysfunctional parenting, including maternal lack of responsiveness (6,15), lack of warmth and positive involvement, overly negative discipline (16), lax and inconsistent parenting, and a lack of cohesion among family members (17), are related to comorbid oppositional or conduct problems rather than ADHD per se. Comorbid externalizing problems are also predictive of dysfunction in the sibling relationship with greater conflict and less warmth/closeness among siblings of children with these problems than those without (18).

Pfiffner et al. (11) compared parenting practices of parents of children with ADHD only versus ADHD+ODD versus ADHD+CD. Similarly negative and ineffective disciplinary styles were found among parents of children with either of these disruptive behaviour disorders (DBDs) relative to those of children without a comorbid DBD. In family process theories (14), negative/ineffective discipline is related to compliance problems and to negative, coercive interchanges. The results are consistent with a bidirectional model (6): the behavioral challenges exhibited by difficult children tax and degrade primary caregivers' limit-setting capabilities and in turn, caregivers' ineffective discipline reinforces children's oppositional and conduct problems.

On the other hand, Pfiffner et al. (11) found that mothers' lack of positive involvement (including warmth and interpersonal involvement) was associated with an increased risk that a child with ADHD would develop comorbid CD, but not comorbid ODD. The apparent risk posed by this factor is consistent with long-standing notions that antisocial personality development is often accompanied by impoverished attachment and

affective development (19–21). Interestingly, dysfunctional parenting was related to CD primarily in families without paternal APD. If the odds of developing CD were already increased due to the presence of a father with APD symptoms, dysfunctional parenting was not strongly associated with further increase. A possible interpretation is that dysfunctional parenting can lead to failures of socialization and affective development, but that a similar outcome might occur if children inherit temperamental risks from APD fathers. In other words, this finding of moderator effects is consistent with the idea that CD can result from multiple causal pathways (22).

Treatments effective for ADHD are also useful for comorbid ODD and CD. Stimulant medication shows benefit for ODD and CD symptoms, decreasing ODD and overt and covert conduct disorder symptoms at dosages similar to those used to treat ADHD symptoms (23). Likewise, children with ADHD and comorbid ODD or CD show a similarly positive response to stimulant medication as those with only ADHD (24,25) and antisocial behaviors such as stealing and fighting can be reduced with stimulant medication (26). Behavioral interventions are also beneficial for addressing many of the associated impairments with ODD or CD including parent–child dysfunction (27) and social skills problems (28,29). Treatment implications of the parenting findings reviewed above include the need to target parenting skills on the part of mothers and fathers related to effective limit-setting and discipline as covered in parent training programs (30–32). Deficiencies in bonding, positive involvement, and attachment may be addressed by parent training components such as strategic activities to increase positive, nonjudgmental parent–child involvement (e.g., "Child's Game"), specific praise and positive reinforcement programs as well as effective communication strategies to enhance the quality of the positive relationship between parent and child. The child's sibling relationships should also be strengthened given the likelihood for conflict and lack of closeness. In more serious cases of comorbid CD and delinquency, multisystemic therapy (MST) may be indicated (33).

ANXIETY DISORDERS

As many as one-quarter to one-half of ADHD cases meet criteria for one or more anxiety disorders (1). Although, far less studied than comorbid disruptive behavior disorders, ADHD with comorbid anxiety appears to be associated with distinct correlates, outcomes, and response to treatment that have lead to consideration of ADHD plus anxiety as a distinct subgroup of ADHD (1). Children with ADHD and anxiety are less impulsive (34,35) but have impaired working memory (36), report more school and social difficulties (2) and experience more stressful life events and parental separations and divorce (2,37) relative to those with ADHD only.

Little is known about the origin of anxiety disorders in children with ADHD or about the underlying mechanisms for their differential response to treatment. However, genetic vulnerability is one possible etiological pathway given that genetic heritability of anxiety is estimated to be moderate (38). Several studies with ADHD children support family transmission. Biederman et al. (39) found through a familial risk analysis that relatives of children with ADHD plus an anxiety disorder had a greater risk for anxiety than relatives of children with ADHD but without an anxiety disorder, with risk for anxiety disorders being higher for mothers than for fathers. Pfiffner et al. (10) found a strong association between parental anxiety disorders and child comorbid (with ADHD) anxiety disorders, even while controlling for the significant association of parental depressive disorders and child comorbid anxiety disorders. This finding was replicated in a recent study by Pfiffner and McBurnett (40).

Parenting may also play a role in the development of anxiety. Pfiffner and McBurnett (40) report that positive contingent responsiveness and overprotectiveness/possessiveness are key parenting practices specifically associated with anxiety, rather than with disruptive behavior disorders or general psychopathology. These results are most consistent with a model specifying three family factors (maternal anxiety, overprotectiveness, and lack of positive parenting) as distinct correlates of child comorbid anxiety. The greatest risk for child anxiety occurs when all three of these factors are present. This outcome would be predicted by combining the ideas of Parker (41)—that it is the combination of inadequate care and excessive protectiveness (rather than either in isolation) that is particularly anxiogenic—with the findings of Moore et al. (42)—that child anxiety is related to parenting practices independent of any relationship to maternal anxiety. Using a community sample, Kepley and Ostrander (43) also reported that the family environment of children with ADHD and comorbid anxiety was more insular and discouraging of autonomy than that of children without anxiety. Based on patterns with anxious, non-ADHD youth, additional parenting factors to consider in the development of anxiety among ADHD youth include excessively high parental expectations, modeling of anxious behaviors, and parental support for avoidant solutions to problems.

It is noteworthy that comorbid anxiety in ADHD frequently co-occurs with CD (44) and there is evidence that doubly comorbid children are especially impaired (45). The association between anxiety and CD may have significance for understanding family factors associated with comorbid anxiety based on recent theorizing that anxiety in the presence of CD is quite different than in its absence. The former is reported to reflect negative affectivity resulting from perceptions that negative consequences are inevitable, perhaps due to repeated frustrations and failures. The latter is reported to be "classic" anxiety or fearfulness, resulting from sensitivity to

cues of impending danger, and is the more traditional form of anxiety (46). In children with ADHD, anxiety has been described as being more like negative affectivity than fearfulness, perhaps due to the frequent co-occurrence of anxiety and CD in this group of children (44). It is possible that anxiety accompanied by CD may have family correlates that are more similar to those of CD (e.g., discipline problems) than those of fearfulness (e.g., overprotectiveness). However, the moderating role of CD in the associations between family factors and anxiety has been unexplored.

Based on the findings reported above, children with ADHD and an anxiety disorder will likely benefit from parenting programs that promote frequent, contingent, and specific positive feedback, but they could also benefit from specific strategies to encourage steps toward independence and developmentally appropriate risk-taking. The commonly found presence of anxiety in mothers of children with ADHD and comorbid anxiety is an important consideration, because unrecognized parental anxiety can be an impediment to full participation in the therapeutic process. Also, clinicians should be prepared to assess other likely targets for intervention (e.g., child cognitions, parent anxiety, family support of avoidance behaviors, etc.) based on the presence of comorbid anxiety. The additive benefit of including, for example, a cognitive behavior therapy component for children to the parenting component for parents seems to make clinical sense but has not been evaluated.

Several studies report that comorbid anxiety decreases response of children with ADHD to methylphenidate (47,48). However, more recent studies show similar response to stimulant medication in ADHD children with and without comorbid anxiety (24,49). In the NIMH collaborative MTA study, comorbid anxiety-moderated response to treatment such that those with anxiety responded equally well to medication and/or behavioral interventions while those without anxiety tended to benefit relatively more from medication. Those with comorbid anxiety and ODD or CD responded best to a combination of medication and behavioral interventions (24). While further study is needed, the preponderance of evidence suggests that comorbid anxiety is not a contraindication for stimulant treatment, although monitoring of possible side effects of increased anxiety and over-focusing has been recommended (50). Furthermore, evidence exists that among children with ADHD and anxiety who are being treated with a stimulant, the addition of an selective serotonin reuptake inhibitor (SSRI) does not provide added benefit (51).

DEPRESSIVE DISORDERS

Comorbid depressive disorders appear to be somewhat less common among youth with ADHD than either comorbid anxiety or disruptive behavior disorders during the early school years (24). However, rates of mood

disorders are still estimated in the 10% to 30% range and are higher among those with ADHD than comparison children (2,50,52). Even in the absence of a clinical depressive disorder, demoralization and low self-esteem are very common among youth with ADHD, particularly among those who are also aggressive (53). The repeated social and academic failures experienced by those ADHD may indeed lead to depressive symptoms which usually follow onset of ADHD. Although there is likely an interrelationship between the two, evidence supports the notion that ADHD and major depression (MD) are independent and distinct disorders with their combination, particularly when also accompanied by CD (50), associated with significant long-term difficulties (54) including suicidality (55) and exacerbated and prolonged symptoms (56). The few studies conducted on psychosocial risk factors or correlates of comorbid MD have combined internalizing spectrum disorders and show higher levels of stress and depressive symptoms among parents and generally greater levels of family and psychosocial adversity (1). A later age of onset for ADHD has been reported to be correlated with a greater rate of parent-reported child anxious/depressive symptoms (57).

Ample evidence supports a linkage between parental and child depression (58). However, specificity of this relationship in an ADHD sample is not as clear. To investigate familial relationships between ADHD and affective disorders, Biederman et al. (59) compared rates of attention deficit disorder (ADD) and affective disorders among family members of youth with either ADHD only, ADHD plus an affective disorders or neither. They found higher rates of ADHD diagnoses among family members of those with ADHD relative to normal control children, however, rates of affective disorders were similar among the relatives of those with either ADHD or ADHD+ an affective disorder. These results lead the authors to conclude that ADD children with and without an affective disorder share familial etiological factors. However, other studies have failed to show such a strong relationship between ADHD and parental affective disorder (50). The role of comorbid conduct disorder in this relationship is also not clear, although it is possible that CD could account for at least part of the association between ADHD and parental depression given the strong association between ADHD and CD on the one hand and between CD and parental depression on the other.

Few studies exist to guide the medication decisions for youth with ADHD and comorbid MD. Beiderman et al. (60) reports that a tricyclic antidepressant may be particularly effective in addressing depressive symptoms among ADHD youth who also have ADHD, although direct comparison with stimulants was not made. Garfinkel et al. (61) found that tricyclic antidepressants (clomipramine, desipramine) were more effective in reducing affective symptoms among children with ADD than methylphenidate, but were less effective than methylphenidate in reducing ADHD symptoms. In a small sample of children with ADHD and comorbid

depression, Emslie et al. (62) reported that most ($N = 9/15$) responded to stimulant treatment without need for subsequent medication for depression, but others who had more severe depressive symptoms were treated with either a combination of ADHD and a SSRI or an SSRI alone. In reviewing these and other studies, Pliszka et al. (63) favorably weighed stimulant treatment to antidepressant treatment when ADHD symptoms predominate and suicidal behavior and vegetative signs are minimal. However, for cases in which depressive symptoms are serious and predominate, antidepressants (SSRIs) were recommended as the initial medication choice.

Use of evidence-based behavioral treatments for ADHD may well improve self-esteem and other depressive symptoms due to improvements in school and social impairments. For example, the MTA study reports benefit for depressive symptoms from combined stimulant treatment and behavioral interventions relative to stimulant treatment alone (64). It is also possible that cognitive behavior therapy directed to the comorbid depression would be helpful, but this has yet to be evaluated empirically.

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7

Dysfunctions of Attention, Learning, and Central Auditory Processing: What's the Difference?

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INTRODUCTION

Central auditory processing disorder (CAPD) is a developmental disorder involving dysfunction of the auditory perceptual system that is not due to a peripheral hearing loss (1). Children diagnosed with CAPD typically have poor listening skills, difficulty hearing in background noise, difficulty following oral instructions, academic difficulties, poor auditory association skills, distractibility/inattentiveness, and require increased time to complete tasks (6). This disorder, which is typically diagnosed by an audiologist, was conceptualized in the last 40 years (2). Conceptual and diagnostic concepts surrounding the disorder are typically taught in speech-language pathology and audiology training programs, leaving physicians and psychologists with a paucity of knowledge on the subject (2). Furthermore, CAPD is not a disorder listed in the DSM-IV (8), which provides a framework for diagnosis for many professionals. However, CAPD is an important disorder to understand due to the fact that it shares symptomatology with attention deficit hyperactivity disorder (ADHD) and language-based learning disabilities (language-based LD), which can make accurate differential diagnosis difficult.

The overlapping symptomatology between CAPD, ADHD, and LD has led many researchers to question if CAPD is in fact a separate and distinct disorder from ADHD, and to a lesser degree, language-based LD such as developmental dyslexia (2). Diagnostic criteria for these disorders

overlap significantly (1,2,5), as does behavioral presentation (6). This overlapping symptomatology has led to the assertion that differential diagnosis is extremely difficult, and may depend on whether the child is evaluated by a psychologist, physician, or an audiologist (2,7).

DEFINITION

In 1993, The American Speech-Language-Hearing Association (ASHA) formed a task force on central auditory processing consensus development to provide a definition, assessment strategies, and treatment parameters for CAPD (3). This task force, whose consensus was published in 1995, defined CAPD as an observed deficiency in one or more of the central auditory processes, which include sound localization and lateralization, auditory discrimination and pattern recognition, temporal resolution, masking, integration, and ordering, auditory performance decrements with competing acoustic signals, and auditory performance decrements with degrading acoustic signals (3). These central auditory processes occur after hearing processes but before conscious awareness, and the deficits in CAPD are presumed to apply to both verbal and nonverbal acoustic information (3). Furthermore, the ASHA task force stated that while CAPD is presumed to result from deficits in audition, but it may also result from a more widespread dysfunction, such as difficulties with attention. Despite the efforts of the ASHA task force, there remains little consensus as to the definition, appropriate assessment and treatment of CAPD, and some suggest that research has not supported the idea that there is a specific auditory deficit in CAPD (4). Reflective of this perspective, Cacace and McFarland (1) assert that CAPD, in definition, assessment, and intervention, is "vague and loosely defined."

CAPD AND ADHD

Overlapping Symptomatology

Many symptoms of CAPD overlap with those associated with ADHD, including auditory attention problems, distractibility, and inattentiveness. Children with ADHD demonstrate significant difficulty on tasks used to assess central auditory processing skills (2), and children with CAPD demonstrate difficulties with attention, particularly auditory attention (6). Thus, differential diagnosis between the two disorders can be challenging. Furthermore, there has been a debate in the literature as to whether CAPD and ADHD reflect a single developmental disorder (7) or comorbid disorders (6).

CAPD/ADHD: Evidence for Discrete Disorders

In order to explore the question of whether or not ADHD and CAPD represent independent disorders, Riccio and colleagues (2) explored the incidence of ADHD in children who met criteria for CAPD. Half of the CAPD

sample also met criteria for ADHD, which is higher than expected based on the population base rates. Within the comorbid ADHD/CAPD group, some children were experiencing difficulties with attention alone, while others were experiencing difficulty with attention, hyperactivity, and impulsivity. Impaired language abilities were found in the entire sample, but no significant between-group differences were found in the cognitive, auditory, or language measures. The authors concluded that, for children who were experiencing comorbid ADHD/CAPD, the "inattention, hyperactivity, and impulsivity may be resulting from auditory-linguistic problems rather than the ADHD syndrome per se." Strengthening this argument was the fact that no behavioral disorders associated with ADHD [such as oppositional-defiant disorder (ODD)] were found in this sample.

Chermak and colleagues (6) compared ranking by psychiatrists, audiologists, teachers, and pediatricians of the behaviors related to ADHD and CAPD. Overall, professionals described exclusive sets of behaviors that characterize each disorder. They tended to characterize children with ADHD as inattentive, distractible, impulsive, and as having a heightened activity level. Children with CAPD were described as having difficulty hearing background noise, difficulty following directions, poor listening skills, and academic problems. Only two symptoms were endorsed as falling into both categories: inattention and distractibility. However, these symptoms were ranked ordered first and second for ADHD and ranked seventh and sixth for children with CAPD, showing that the majority of behaviors were seen as unique to one disorder or the other. Thus, it appears that children with ADHD, particularly those children that present with hyperactivity and impulsivity, and children with CAPD have distinguishable clinical presentations (6). While children with CAPD demonstrate inattention and distractibility, these symptoms do not define the disorder as in ADHD; rather, difficulties in listening, hearing, following oral directions, and experiencing difficulty in academic settings are defining characteristics of CAPD (Table 1).

Table 1 Rank Order of Behavioral Means Greater than One Standard Deviation Above the Respective Grand Mean

ADHD	CAPD
Inattentive	Difficulty hearing in background noise
Distracted	Difficulty following oral instructions
Hyperactive	Poor listening skills
Fidgety/restless	Academic difficulties
Impulsive	Poor auditory association skills
Interrupts or intrudes	Distracted
	Inattentive

Source: Adapted from Ref. 6.

Strengthening the argument that ADHD and CAPD represent discrete disorders is a recent shift in the conceptualization of ADHD, led by Barkley and colleagues (9,15). While ADHD has traditionally been viewed as solely a dysfunction of attention, the last decade has seen the disorder characterized primarily as a deficit in impulse control and behavioral regulation (9). Some researchers suggest that hyperactivity is the hallmark of ADHD as opposed to dysfunction of attention, and the use of hyperactivity alone for diagnostic criteria has been proposed (15). CAPD, by contrast, is not characterized by hyperactivity and deficits in impulse control. This suggests that CAPD and ADHD are discrete disorders when criteria beyond auditory inattentiveness are used (15).

CAPD AND LANGUAGE-BASED LEARNING DISABILITIES

As ADHD and CAPD are highly comorbid disorders (2), ADHD and language-based LD are highly comorbid disorders (10), so, not surprisingly, CAPD and language-based LD share significant symptomatology. Disorders of auditory perception have been suggested as the underlying cause of language-based LD such as developmental dyslexia (11). Phonological processing in particular has been well documented as the core deficit in dyslexia (12). The disorders of auditory perception found in language-based LD, such as phonological processing, are very similar to the central auditory processing dysfunctions in CAPD (4) as they involve difficulty in the discrimination and manipulation of auditory stimuli (3). In addition, many children with CAPD have learning problems (4). This overlap has led to difficulty distinguishing between the two disorders and questions as to whether the disorders are distinct (1). However, some have suggested that the auditory processing problems associated with developmental dyslexia are specific to the encoding of speech and are not a more general dysfunction of the encoding of all auditory stimuli (1), which would suggest distinct etiologies of CAPD and dyslexia.

CONCEPTUAL DIFFERENCES BETWEEN CAPD, ADHD, AND LANGUAGE-BASED LD

Cacace and McFarland (1) introduced the idea that modality specificity is the primary way to differentiate CAPD from LD and ADHD. The authors posit that the primary deficit of CAPD is the processing of acoustic information, and that people with CAPD should display impairments during the processing of information in other sensory modalities. This definition of CAPD as a unimodal dysfunction contrasts with the current state of knowledge surrounding ADHD and LD, which are multimodal in nature (1).

There is considerable evidence that supports the idea that developmental dyslexia is associated with a sensory processing deficit that is not restricted to a single sensory modality (1). Although there is a great deal of evidence that anomalies in the auditory cortex of the left temporal lobe may result in dyslexia, there is also evidence that correlates the cognitive and behavioral symptoms of dyslexia with executive symptoms in the frontal lobes (13) and the thalamic nuclei of the visual system (14). Furthermore, neurobiological evidence suggests that variations within brain regions associated with auditory processing, visual processing, and interhemispheric processing exist in developmental dyslexia (15), suggesting multimodal deficits of language-based LD. Thus, dyslexia can have a complex neurological basis involving multiple sensory areas and behavioral deficits are observed across modalities. The multimodal nature of dyslexia differentiates it from CAPD, which is conceptualized as a disorder of only one modality (1).

Both functional and structural imaging studies support neurobiological anomalies in a biological basis of ADHD in the frontal lobe and basal ganglia, areas not related to auditory processing (16). Furthermore, children with ADHD show impaired performance on neuropsychological tasks across modalities, whereas children with CAPD show inattentiveness solely in response to auditory stimuli (1). Cacace and McFarland (1) conclude that children with ADHD have multimodal attentional problems. Again, the multimodal nature of the deficits in ADHD separate ADHD from the unimodal conceptualization of CAPD.

While the Cacace and McFarland model of conceptualizing CAPD and how it differs from other disorders is compelling, the fact remains that research has not shown clearly that a specific auditory deficit exists in CAPD (1,4). The modality-specific model of differentiating CAPD from disorders with overlapping symptomatology is a useful tool provided that research has documented clearly the existence of children who have this specific deficit. A child with ADHD or language-based LD would be likely to present as having a deficit in one or more of the central auditory processes if evaluated by an audiologist, and would likely been diagnosed with CAPD despite the multimodal nature of the child's deficits. Thus, a multimodal assessment is necessary in both clinical practice and research on CAPD.

CLINICAL IMPLICATIONS

Implications for Differential Diagnosis

Although a significant amount of overlapping symptomatology exists between CAPD, ADHD, and language-based LD, evidence suggests that the three disorders are conceptually distinct. When overlapping symptoms exist,

the modality/ies of the deficits must be thoroughly assessed for accurate differential diagnosis (1,7). Collaboration among speech-language pathologists, audiologists, neuropsychologists, physicians, and school psychologists may be necessary to ensure accurate differential diagnosis because these professionals may need to collaborate assess thoroughly across modalities (4,7). If auditory attention problems exist but visual attention is not impaired, there is a family history of hearing problems, and there is evidence of five or more ear infections in the first 2 years of life, a referral to an audiologist for a CAPD evaluation is certainly warranted.

Implications for Pharmacological Intervention

While there is substantial evidence that methylphenidate enhances attention in children with ADHD, the effect of stimulant medication on auditory processing is not fully understood. Some research has found stimulant medication to be effective in both CAPD and ADHD (7,14), while some research has found mixed effectiveness depending on symptomatology. Research has shown that, in a comorbid group, auditory processing improved with the use of stimulant medication (15). In a recent study of a comorbid population, however, Ritalin reduced impulsivity and inattention but did not result in improved auditory functioning (5). Further research is necessary to determine the effects of stimulant medication on the auditory processing and attention of children with CAPD and the comorbid condition. This will allow for appropriate interventions to be designed.

INCONSISTENT FINDINGS AND UNDERSTUDIED AREAS

Future research on CAPD should also focus on the developmental trajectory of children with CAPD into adulthood. It is not clear at this time if the problems remediate as one gets older, if children with CAPD are able to compensate for their dysfunctions in central auditory processing, and what factors may affect remediation and compensation. Furthermore, does the developmental trajectory change if the children with CAPD also have comorbid ADHD or language-based LD? Understanding the developmental trajectory of children with CAPD would pinpoint important areas for intervention.

Finally, there is a dearth of research on the possible biological basis of CAPD. The question remains as to whether or not there are genes that may predispose or cause an individual to develop CAPD. Family and genetic studies are necessary to answer this question. In addition, structural and functional neuroimaging studies would provide valuable information as to what neuroanatomical areas are affected, if any, in children with CAPD. This information would aid researchers in understanding the neurobiological basis

of the central auditory processes and how the biological substrate underlying these processes may be altered in children with CAPD.

Although Cacace and McFarland's definition of CAPD as unimodal disorder is extremely useful in the conceptualization of this disorder, the existence of CAPD as a disorder that is separate and distinct from language-based LD and ADHD has not been well-documented in the literature (1). CAPD may be a solitary disorder with a high comorbidity with ADHD and language-based LD, or it may be an associated feature of those well-defined disorders. Furthermore, the fact that CAPD does not appear in the DSM-IV (8) as a distinct diagnosis makes any such diagnosis questionable in terms of qualifying a child for clinical- or school-related services. Thus, research should attempt to elucidate if in fact CAPD exists as a unitary and distinct disorder as an understanding of the nature of CAPD is essential for communication among professionals, the development or appropriate intervention, and the delivery of services to children.

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Section III: Clinical Neuroscience

8

Neuroanatomy of ADHD

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The third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) marked a paradigm shift from psychoanalysis toward an empirically based classification of disorders, with the implicit goal that psychiatric disorders would eventually be referenced to specific enumerable brain dysfunctions. Although this goal has not yet been achieved for any psychiatric disorder, recent advances in brain imaging could assist in this process. Anatomic magnetic resonance imaging (MRI) is the principal technology used to examine the pediatric brain, mainly because it does not use ionizing radiation, in contrast to methods like computed axial tomography, positron emission tomography, and single-photon emission computed tomography. Therefore, although those approaches will also inevitably contribute to our understanding of the pathophysiology of attention deficit hyperactivity disorder (ADHD), we will limit ourselves to recent MRI studies of children and adolescents (roughly ages 5–18) diagnosed with this common psychiatric condition.

As valuable as MRI can be, we must precede our review with a word about the technique's limitations. Depending on the viewpoint, the neuroanatomical literature on ADHD presents either a reasonable degree of concordance (1), or a distressing absence of truly confirmed findings (2). Early studies, which have been reviewed in detail elsewhere (3–5), had several limitations, some of which continue to represent obstacles in current work. The high cost of obtaining MRI scans results in small sample sizes, which tend to yield insufficient statistical power. As Rossi and coworkers have pointed out, when most studies in a field only have statistical power in the range of 50%, then inconsistent results are to be expected (6).

Comparison of results across studies is also hampered by variability in subject selection, which is driven by factors that are idiosyncratic to each setting and study. Another source of inconsistencies in the anatomical literature has been derived from a focus on lateralization and indices of asymmetry (7), which, perhaps are biologically interesting, but intrinsically much less reliable than the volumetric measures from which they are constructed (8,9). Lastly, the field has not yet adopted standard quantitative analytical methods which would improve comparisons across studies. Current methods include hand-tracing of individual regions of interest, which tends to optimize validity at the expense of reliability; fully automated methods, which maximize test–retest reliability but can still only be applied to a few large regions; and semiautomated methods, which combine the strengths and weaknesses of the other two alternatives. Despite these concerns, progress continues in delineating the brain anatomy of ADHD.

NORMAL BRAIN DEVELOPMENT

ADHD cannot be considered without taking into account developmental factors; likewise, an examination of the brain anatomy of ADHD must be referenced to healthy brain development. Since the late 1980s, converging studies have shown that over 90% of total brain volume of a young adult is attained by age 5 (10,11), though the apparent stability of total brain volume during childhood and adolescence masks complex changes in gray and white matter and subcortical compartments (12). Increasing myelination is reflected in linear increases of white matter volumes during the pediatric age range, which are statistically greater in males (13). Heterogeneity of white matter development has been noted in the corpus callosum, the anterior cross-sectional area of which increases first, followed by posterior growth through late adolescence (14). Gray matter also shows a heterogeneous overall growth pattern: volumes peak at about age 12 in frontal and parietal lobes and at about age 16 for the temporal lobe (12). (In the cerebellum, considered as the sum of both white and gray matter, volumes peak at around age 18.) Total gray matter volume increases until early-to-mid adolescence before decreasing during late adolescence (12), probably reflecting selective pruning of neuronal connections (15). Similarly, the caudate reaches its maximum volume before 10 years of age.

One of the pivotal achievements of pediatric medicine was the derivation of norms for the expected developmental trajectories of weight, height, and head circumference from birth to adulthood. Such growth charts, which have long been commonplace in every pediatrician's office, facilitate the early detection of growth deficits and make possible timely interventions. The availability of noninvasive high-resolution MRI scans now makes it feasible to begin to develop growth charts for the human brain. While such potentially clinically useful tools are not yet at hand, a

multisite project, contracted by three of the U.S. National Institutes of Health with seven sites in the United States and Canada continues to advance toward this goal.

NEUROANATOMICAL ABNORMALITIES IN ADHD

The brains of children with ADHD are significantly smaller, on average, than the brains of healthy comparison children throughout childhood and adolescence (16). Beyond this globally decreased volume, there is more conflicting evidence in support of a distributed circuit, the disruption of which likely underlies ADHD symptoms. At least in boys, this circuit appears to include right prefrontal brain regions, the basal ganglia, the cerebellar hemispheres, and a subregion of the cerebellar vermis. Lastly, the distribution of gray and white matter may be altered in ADHD. We will discuss these abnormalities in turn.

Decreased Global Brain Volume

As Table 1 shows, most studies have found overall reductions in total brain volume in children with ADHD compared to age- and sex-matched controls. In a meta-analysis of published volumetric studies in ADHD, we found a highly significant overall effect ($Z = 19.84$; $P < .0001$; 95% CI: 8.79 to 30.90), which remained significant even when the largest study (16) or the study with the largest effect size (17) were excluded. In the largest study, Castellanos et al. examined 152 children and adolescents with ADHD and 139 controls, and analyzed the results using fully automated methods. Children with ADHD showed overall cerebral volumes that were 3.2% smaller than controls, adjusted for significant covariates ($P = .004$; Fig. 1). All four major lobes were comparably affected, but after adjustment for total brain volume, these differences were statistically subsumed; however, the decreased volume of the cerebellum (−3.5%) remained statistically significant (16). The volumetric abnormalities were at least as pronounced in the 49 medication-naïve children with ADHD as in the 103 children with ADHD who were being treated with stimulants. This finding supports the conclusion that volume reductions in ADHD do not arise from stimulant treatment.

Prefrontal Brain

Anatomic hypotheses of the substrates of ADHD have generally focused on the role of the prefrontal cortex (PFC) in the disorder, which is known to be involved in executive functioning, a group of high-order mental abilities including behavioral planning and response inhibition, selective attention, and the organization of information in problem-solving tasks. Normally, the right PFC is slightly larger than the left (18), but the region is more

Table 1 Meta-Analysis of Total Brain Volume in ADHD

Study	Measure	Mean NC	SD NC	*N* NC	Mean ADHD	SD ADHD	*N* ADHD	Total *N*	% change	Effect size	Estimated difference[b]	95% CI
Aylward et al. (1996)	Representative brain volume	305.6	14.5	11	295.9	17.9	10	21	3.2%	0.60		
Filipek et al. (1997)	Right hemisphere volume	659.4	47.1	15	627.9	47.4	15	30	4.8%	0.67		
Bullmore (1999)[a]	Gray and white matter voxels	1342.1	129.11	16	1302.3	142.5	18	34	3.0%	0.29		
Bussing (2002)	Cerebral hemispheres	1172	89	19	1182.5	93.1	12	31	−0.9%	−0.12		
Hesslinger et al. (2002)	Total brain volume	1075	118.5	17	1174.3	187.8	8	25	−9.2%	−0.69		
Mostofsky et al. (2002)	Gray and white matter voxels	1241.4	54.7	12	1138.0	101.7	12	24	8.3%	1.27		
Castellanos et al. (2002)	Gray and white matter voxels	1104.5	111.3	139	1059.4	117.5	152	291	4.1%	0.39		
	Totals/average			229			227	456	1.9%	0.34	19.84	(8.79–30.90)

[a] Variance estimated.
[b] Estimated true difference in SD units.
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; NC, normal control; SD, standard deviation.

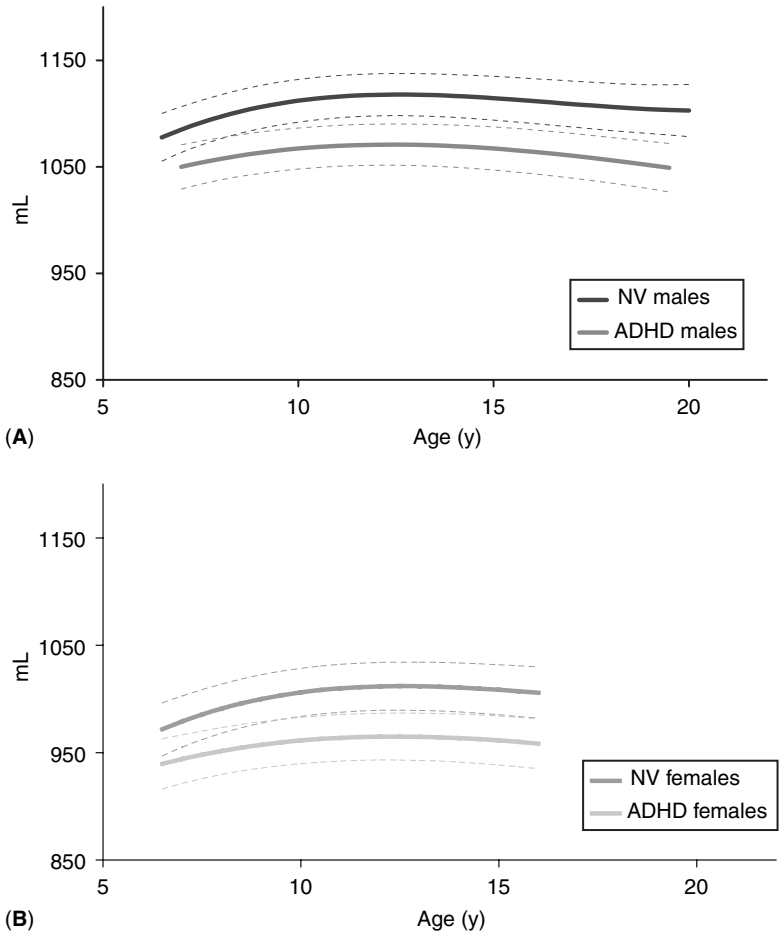

Figure 1 Predicted unadjusted longitudinal growth curves for total cerebral volumes for male (**A**) and female (**B**) patients with ADHD and controls. *Abbreviation*: ADHD, attention deficit hyperactivity disorder. *Source*: From Ref. 16.

symmetrical in ADHD (13,19–21). Also, reduced size of the right PFC was correlated with response inhibition problems in boys with ADHD (22).

While these studies have examined overall volumetric differences in the PFC, other recent studies have differentiated frontal gray and white matter volumes. Reductions in both gray and white matter were reported for the right PFC (23,24), but Kates et al. (25) reported similar reductions in the left PFC. These latter findings were confirmed recently by Mostofsky et al. (17) who reported significant white matter reduction confined to the left PFC, with gray matter reduced in both hemispheres but more so in the right.

Another recent development has been the quantification of PFC subregions. Hesslinger and colleagues (26) found that eight adult patients with ADHD who had never been medicated had significantly smaller left orbital-frontal cortical gray and white matter volumes than did 17 comparison subjects (-12%, $P = .04$). Investigators are also studying the dorsolateral PFC; Yeo et al. reported that right dorsolateral prefrontal volume, measured as a block, was significantly smaller in 23 children with noncomorbid ADHD as compared to 24 controls (27). While these reports are currently difficult to integrate because of many differences in methods and subjects, automated image analysis techniques should alleviate this problem in future studies.

Basal Ganglia

Along with the PFC, the caudate nucleus and its associated circuits have long been implicated in ADHD (28). The caudate nucleus and the putamen serve as the entry point to the basal ganglia, and abnormalities of both structures have been reported in this disorder. Researchers have noted both volumetric differences (most studies have reported a decrease, with one exception) (21,23) and loss of asymmetry (21,29,30) in ADHD—although it is still unclear whether the normal caudate is asymmetric, and if so, whether this asymmetry normally favors the right (21) or the left side (12,23,29–31). When total caudate volume was analyzed in a mixed cross-sectional/longitudinal design, decreased volumes were detected in the group with ADHD for ages below 16 (Fig. 2), but not beyond that age (16). Such transient

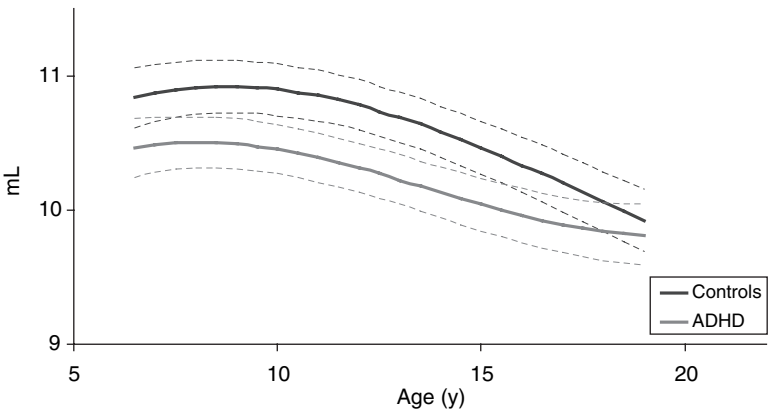

Figure 2 Predicted unadjusted longitudinal growth curves for total caudate volume for patients with ADHD and controls. *Abbreviation*: ADHD, attention deficit hyperactivity disorder. *Source*: From Ref. 16.

abnormalities may relate to the diminishment of motoric symptoms in ADHD with increasing age, but this speculation should be tested directly.

Studies of the putamen, a region associated with primary and supplementary motor areas that may contribute to the motoric symptoms of ADHD, have yielded equally ambiguous results. Investigators who examined putamen volumes as regions of interest did not detect significant differences (21,32). On the other hand, a recent preliminary functional imaging study detected decreased blood flow in the putamen of objectively hyperactive boys with ADHD compared to those boys whose activity level resembled that of controls (33). Putamen lesions are also associated with greater likelihood of ADHD. Two instructive cases of severe ADHD associated with a traumatic amniocentesis at 17 weeks gestation revealed complete elimination of the right basal ganglia (34). In addition, lesions of the right putamen and posterior ventral putamen have been associated with higher incidence of secondary ADHD (S-ADHD) and ADHD, respectively (35,36). The relationship between injury and the disorder's symptoms will be further explored below. Lastly, the globus pallidus, which receives input from caudate and putamen, has been examined; although it is difficult to measure reliably, it was found to be significantly smaller in boys with ADHD (21,32). However, the two studies differed as to whether the size reduction was greater in the left or right side.

Cerebellum

The cerebellum is associated with coordination of motor movements, but functional neuroimaging studies have clearly demonstrated cerebellar involvement in nonmotor functions (37–43). MRI studies of the cerebellum in ADHD have detected smaller cerebellar hemispheric volumes (21) which are sustained throughout adolescence (Fig. 3) (16). Within the cerebellum, the posterior-inferior vermal lobules (VIII-X) were particularly smaller compared to the contrast group of right-handed boys (44). This finding has been independently replicated in both boys (45) and girls with ADHD (31). Consequently, the cerebellar hemispheres and the posterior-inferior cerebellar vermis are becoming increasingly incorporated into hypotheses of ADHD (46).

ASSOCIATION OF HEAD TRAUMA AND ADHD

In addition to comparisons between children with ADHD and controls, several investigators have begun focusing on the effects of early brain lesions or head trauma on the secondary development of ADHD. The disorder is associated with increased pre- or perinatal adverse events (47) and with closed head injury (48). ADHD is the most common psychiatric disorder to develop after brain injury (49) or stroke (50) in childhood, and its

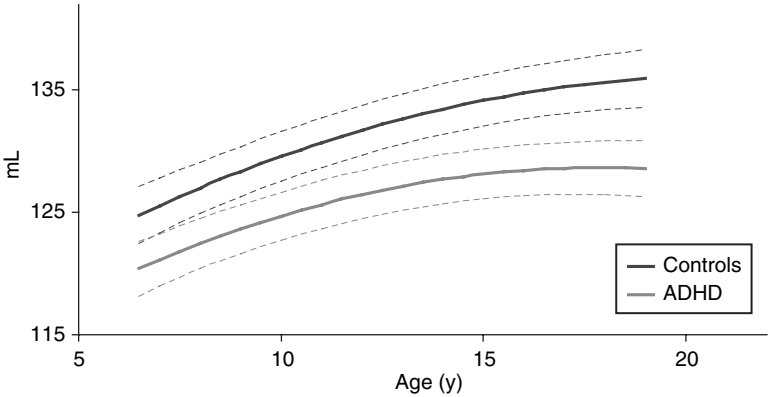

Figure 3 Predicted unadjusted longitudinal growth curves for cerebellar volumes for patients with ADHD and controls. *Abbreviation*: ADHD, attention deficit hyperactivity disorder. *Source*: From Ref. 16.

occurrence is correlated with severity of injury (51). The most common form of head trauma in childhood and adolescence is closed head injury, which can particularly affect inhibitory capacity (52) and executive function, deficits of which are symptomatic of ADHD, and can result in personality changes (e.g., increased aggression). In the interest of delineating a potential circuit underlying ADHD, MRI has been used to identify the specific sites of injury, which have then been correlated with the emergence of S-ADHD, in which symptoms can appear after age 7 (48). When 99 children who suffered closed head injury, ranging in age from 4 to19 years, were followed for a year, the odds of developing S-ADHD were 3.6 times higher among children with thalamus injury and 3.2 times higher in children with basal ganglia injury (53). Further brain injury studies, especially those using imaging techniques, should shed further light on neurodevelopmental susceptibilities.

CONCLUSIONS

Although methodological inconsistencies and low statistical power are still important limiting factors, there is increasing evidence that ADHD is associated with globally decreased brain volumes which appear to represent a nonprogressive deficit presumably resulting from early genetic and/or environmental factors. Putative sex differences are probably best understood as the result of sampling variations; referred samples of boys and girls with ADHD differ from community-based samples (54), but when patient samples have been recruited to meet equivalent severity criteria (55), results have been comparable, though slightly less prominent, for girls (16).

Beyond global volumetric differences in the brain, there is more evidence for right prefrontal deficits, although there are also several findings of decreases on the left. The same sort of inconsistency is reported for findings in basal ganglia structures. The safest conclusion, supported by cases of head trauma, is that basal ganglia are an important link in the circuits implicated in ADHD, but that we cannot specify whether such deficits are truly lateralized. At least for the caudate nucleus, the volumetric abnormalities seem to be age-dependent, as they are no longer detected after mid-adolescence (7,16).

The most robustly deviant region in brain associated with ADHD is the cerebellum, both when measured algorithmically as a single unit, which is mostly composed of the hemispheres (16), and even more so in hand-traced measurements of the posterior-inferior cerebellar vermis (31,44,45). Thus, one of the most promising and unexpected frontiers of ADHD research is the exploration of the cerebellum's influence on cortico-striatal-thalamo-cortical (CSTC) circuits (56), which choose, initiate, and carry out complex motor and cognitive responses (57). The posterior-inferior lobules of the cerebellar vermis appear to differ from the remaining cerebellar hemispheres and vermis in selectively containing dopamine-transporter-like immunoreactive axons (58).

Despite the suboptimal variability of recent results, the current literature has begun to reveal several key brain structures involved in ADHD. The increasing availability of neuroimaging, along with growing interest in developing convergent methods and standards, will facilitate the elaboration of testable models of the disorder's pathophysiology.

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9

Interactions Among Motivation and Attention Systems: Implications for Theories of ADHD

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Temperament models approach attention deficit hyperactivity disorder (ADHD) in terms of neural systems involved in motivation, emotion, arousal, and attention. This chapter emphasizes individual differences in two motivational systems that are activated in appetitive and defensive situations, along with an attentional system related to voluntary or effortful control. The basic framework suggests that the two motivational systems exert relatively reactive or involuntary effects on behavior and attention. With the development of frontal circuits, however, the motivational systems become capable of recruiting executive attentional systems that allow for more refined and voluntary motivational functions. Individual differences across these systems leave some children vulnerable to impulsive disorders such as ADHD, as characterized by hyperactivity, attentional deficits, and impulsive behavior.

In the following sections we briefly discuss the various systems, emphasizing their effects on both behavior and attention. We then discuss interactions between the systems, illustrating how some profiles might increase vulnerability whereas others serve a more protective function. Our approach suggests that symptoms of ADHD can arise from several different developmental pathways. For some children, the problem may involve only a single system, such as an overly strong approach system or a weak frontal attentional capacity. In others, two or more systems might be involved,

such as strong approach accompanied by weak inhibitory capacities. An important theme is that the three systems are highly interactive, with reciprocal influences upon one another. In some cases interactive influences may prove beneficial for voluntary control, but in others, the interactive effects may constrain the child's ability for self-control. Thus, it is essential to consider the various ways in which these systems influence one another.

REWARD-RELATED APPETITIVE MOTIVATION

An initial neural system relevant to ADHD is responsible for producing approach behavior in response to expected rewards (1–3). Although the precise formulations vary, this appetitive system is thought to be focused within subcortical limbic regions and to receive reward-related inputs from the cortex. Upon detecting a potential reward, the system recruits dopaminergic projections to facilitate approach behavior and emotional states such as "hope" and "anticipatory eagerness". In addition, some have suggested that strong appetitive systems may produce frustrative reactions when a reward is blocked (3–5). Individual differences in this system are thought to underlie personality dimensions related to extraversion (or neurotic extraversion). For example, as one moves from the "introverted" to the "extraverted" pole of this dimension, the person becomes more sensitive to potential rewards, shows faster and more vigorous approach behavior, and greater hope and eagerness. In terms of psychopathology, this system may contribute to the hyperkinetic and impulsive behaviors evident in ADHD, as well as the proneness to emotions such as hope and frustration.

In addition to these behavioral and emotional effects, the appetitive system also exerts effects on attention. In many cases these are reflexive or involuntary effects, mediated by projections from the motivational system to the "posterior attentional system" described by Posner (6). The posterior system is a distributed system that produces reactive orienting through operations of "disengaging," "moving," and "engaging" attention. Our research with college students suggests that appetitive motivation makes it more difficult for individuals to disengage attention from a reward-related spatial location, with the effect strongest in neurotic extraverts (7). Such a bias may also occur in ADHD, causing such children to have difficulty shifting from a salient rewarding activity in favor of less-rewarding tasks.

Another attentional process influenced by motivational and emotional states involves adjustments in the breadth of attention. Relevant neural mechanisms appear lateralized, with posterior left hemisphere circuits supporting a "focusing" or "narrowing" of attention, and posterior right hemisphere circuits promoting a "broadening" or more global attentional scope. In emotional terms, evidence suggest that negative states such as anxiety promote a narrowing of attention while positive or appetitive states promote a broadening of attention (8). If an ADHD child is subject to

strong appetitive motivation, they may often show a relatively broad attentional focus. As a result, they may have more difficulty focusing on the details of the situation, and may be more responsive to task-irrelevant information sources.

In addition to these reactive influences, the approach system can also access frontal attentional mechanisms that allow for voluntary control. As discussed in more detail below, voluntary attentional mechanisms allow the individual to access additional information (rules, beliefs, feelings) that helps in selecting, planning, and controlling approach responses. In delaying gratification, for example, the child may be able to access knowledge that a delayed reward will be greater than an immediate reward, and voluntarily shift attention away from cues that intensify the immediately rewarding aspects of the situation (9).

Unfortunately, evidence relating individual differences in approach motivation to ADHD remains inconsistent. Early concept identification studies suggested that children with ADHD may be overly sensitive to rewards, to the loss of reward, and to the failure of expected rewards to appear (10). More recent studies suggest that ADHD children are especially sensitive to individual instances of reward, which bias their responses in relation to more frequently rewarded stimuli (11). In addition, ADHD children may have particular difficulty in delaying reward, with a strong preference for immediate over delayed rewards (12,13). While these studies suggest an oversensitivity to salient rewards in ADHD children, other findings are more difficult to interpret. For example, children with ADHD slowed down more dramatically in the reward condition on a stop task than normal controls, and this slowing was interpreted as a strategy to increase the chance of being rewarded (14). Also problematic are findings that ADHD children make more errors of commission in a go/no-go task, regardless of whether the conditions involved reward or response costs (15).

Also supportive of strong appetitive motivation are findings suggesting that ADHD children are prone to frustration. It is worth noting that our view linking frustration to reward and appetitive motivation differs from models such as Gray's, which view frustration as an output of the anxiety-related behavioral inhibition system. Along with others (3,4), we suggest that it makes more functional sense to link frustration to a general appetitive motivational system that responds to nonreward as well as reward. In any event, Douglas and Parry (16) found ADHD children to show more frustrative behavior (i.e., more vigorous lever pulling) under conditions of low reward probability and reward extinction. ADHD children have been found to show greater frustration than controls in a nonsense word spelling task under partial reinforcement (17). In a more general model of impulsive problems, Newman and his colleagues have suggested that disorders such as ADHD may involve a facilitation of a dominant

response set (e.g., approach) by the nonspecific arousal resulting from a negative outcome (e.g., frustration) (18,19).

PUNISHMENT-RELATED INHIBITORY MOTIVATION

A second motivational system often related to ADHD is Gray's "behavioral inhibition system." Relevant circuitry is distributed across the orbital cortex, hippocampus, amygdala, hypothalamus, and periqueductal gray, with different stations responsible for generating different forms of fear-related behavior (20). In Gray's formulation, the system responds to signals of punishment by inhibiting ongoing behavior and producing an emotional state of fear or anxiety. It also increases cortical arousal and enhances attention, thereby facilitating the processing of the threatening signal. Individual differences in the reactivity of the behavioral inhibition system are thought to underlie dimensions related to neuroticism and neurotic introversion.

Theorists have suggested that children with ADHD may possess relatively weak inhibition systems (21,22). As a result, they are relatively insensitive to signals of punishment, and are less able to inhibit approach responses. At a behavioral level, deficits in inhibition could lead to the same types of problems as those arising from an overactive approach system; i.e., impulsive, short latency approach responses that are difficult to stop. In this case, however, the approach behavior would not necessarily be accompanied by positive emotion, but rather, by a relative absence of fear and anxiety.

Like the approach system, the anxiety-related system exerts influences upon attention that complement its behavioral functions. One influence is on orienting, with increased attention allocated to threatening stimuli so that they can be effectively evaluated. Our studies with college students indicate that anxious individuals have difficulty shifting from a threatening stimulus (7). Assuming that ADHD kids possess weak anxiety/inhibition systems, it would be relatively easy for them to disengage from signals of punishment or nonreward, thereby lessening the capacity for these stimuli to constrain their behavior. At conceptual levels, children with a weak anxiety system may also find it easy to shift attention and avoid ruminating on the negative consequences of their behavior.

The second reactive influence is on attentional focusing, with anxiety serving to concentrate attention on dominant or central perceptual stimuli. Presumably, such narrowing serves to facilitate the processing of local details that may be important in evaluating the stimulus and situation (8). If the anxiety system is weak, then important details that could constrain behavior may be overlooked. For example, the child may overlook certain aspects of another's facial expression or tone of voice, and thus continue with inappropriate behavior. At a more conceptual level, the child may have difficulty maintaining the "self-focused" attention related to anxiety,

and may thus have difficulty evaluating the appropriateness of their own behavior.

Many studies suggest that ADHD children are deficient in inhibiting responses. For example, they have difficulty inhibiting the initiation of response go/no-go tasks (15), suppressing an already-selected response in the stop-signal task (23,24), and stopping and changing a response in the change task (25). However, evidence that such inhibitory problems may be linked to an underreactive behavioral inhibition system (BIS) is lacking. For example, studies that manipulate incentives have not found insensitivity to punishment cues in ADHD children (15,26). In addition, the prediction that ADHD children should be low in anxiety is problematic. ADHD is often comorbid with anxiety disorders, suggesting an overreactive rather than underreactive BIS. Tannock (27) estimates that ADHD and anxiety disorders occur together in approximately 25% of cases. These and other problems for the weak-BIS approach to ADHD are well discussed by Nigg (28).

It may turn out that the individual differences in BIS reactivity will prove helpful in understanding the comorbid disorders accompanying ADHD. A weak BIS may exist in children where ADHD combines with conduct problems or undersocialized aggressive problems (21). Such children may have considerable difficulty in withholding approach responses because they fail to anticipate negative consequences. They may also fail to learn from their inappropriate behavior because their inattention to punishment makes it difficult to link it to their own behavior. In contrast, other ADHD children may possess a relatively strong BIS, making them vulnerable to comorbid anxiety. Compared to ADHD children with less anxiety, the more anxious children should show attenuated impulsive symptoms (29). They should be more attentive to potential punishments. Attentional orienting and focusing on threat should also make it easier for them to link actual punishments to their own inappropriate behaviors. As a result, anxious ADHD children should show better learning related to social and moral development.

So far we have described two types of motivational systems, one related to approach and the other to inhibition, which may contribute to ADHD. Both systems are capable of explaining some of the behavioral and attentional symptoms related to ADHD. These effects are primarily involuntary, a more or less reactive component of the overall pattern (i.e., behavioral, autonomic, attentional) of the motivational state. To better understand ADHD, however, it is necessary to consider a third system that allows for more voluntary control.

EXECUTIVE ATTENTIONAL PROCESSES

The systems responsible for voluntary control are thought to arise from "executive" attentional systems within the frontal lobe. Two of the most

influential models include Posner's "anterior attentional system" (6) and Shallice's "supervisory attentional system" (30). In addition, other theorists have discussed executive processes that go beyond attention, such as working memory and various forms of emotion regulation (31). Although much can be gained by studying these additional processes, we limit our present discussion to processes specified by Posner's "anterior attentional system." This circuitry is focused in the anterior cingulate cortex where it receives extensive inputs from motivational, perceptual, conceptual, response, and arousal systems. Based on this input, the anterior system provides voluntary control across the course of processing. For example, it regulates the posterior orienting system, thereby providing more flexible control over incoming perceptual content. When conceptual content is activated, the anterior system inhibits dominant conceptual associations, allowing control over highly automatized patterns of thought. It also inhibits dominant response tendencies, allowing more flexible response evaluation and selection. Finally, the anterior system is involved in detecting errors, allowing for corrections of responses and plans that go wrong (6,32). Children's differences in anterior system function have been investigated through Rothbart's construct of "effortful control" (33,34). Children scoring high on measures of effort control tend to show less negative emotion, which is consistent with the ideas that they can employ their attentional skills to cope with the impact of negative stimuli. In addition, effortful control is related to moral emotions such as empathy and guilt, and moreover, to the internalization of moral principles and the development of social competence (35–37).

Many symptoms related to ADHD may result from frontal deficits related to effortful control. Focusing on voluntary control of information access during response processing, we suggest that it involves attention to sensory events, alternative response options, and the affective outcomes associated with these responses. If the child's flexibility in attending to these three forms of information is impaired, then they will be at a disadvantage in controlling their behavior. Such inflexibility may in part arise from difficulties in disengaging attention of certain information in order to attend to other important sources (38).

During the initial selection of a response, children must often inhibit the dominant tendency and replace it with an alternative response. Rather than immediately reaching for a food item, for example, the child must suppress this tendency and obtain permission from the parent. This situation can be modeled as a simple conflict situation, where alternative responses have been associated with alternative outcomes. The impulsive act of reaching may be related to an immediate reward along with potential disapproval from the parents, whereas the alternative response of asking may be related to a slightly delayed reward along with potential approval from the parent. To the extent that the child is able to disengage attention from

stimuli that support the dominant tendency, such as the rewarding visual and taste cues, they should be better able to also attend to other information regarding the various outcomes. They can then weigh these outcomes and select the more optimal response. Such attentional flexibility may be impaired in ADHD children, leaving them at a disadvantage in inhibiting the dominant response. In many situations, effective behavior involves not only selecting a response, but setting up a plan or strategy involving a sequential set of responses. Although planning involves additional executive functions, attentional flexibility will play an important role. The most effective plans will be those that build with conditional response options, such that alternative actions can be executed depending on changing environmental events. Constructing such a plan requires that attention move flexibly among anticipated events, various response options, and their associated outcomes. If such flexibility is lacking, then the plan is likely to prove deficient. Recent studies have found deficits in strategy generation to be particularly severe in children with ADHD (39,40).

In other situations, a response or plan may be relatively easy to select, but must then be delayed in order to obtain a more optimal reward. Much research suggests that ADHD children have an aversion to delay. Although problems in delaying approach may reflect underlying motivational processes (41), they may also arise from attentional limitations. Mischel and his colleagues have shown that when presented with an attractive object and instructed to wait before approaching it, children who are successful in delaying gratification rely on a variety of attentional strategies (9,42). In general, these strategies involve disengaging from the rewarding aspects of the object (e.g., how good it might taste), and attending instead to "cooler" properties of the object (e.g., its color or shape) or to peripheral stimuli in the room. An inability to execute these types of distraction strategies may leave the ADHD child vulnerable to increased frustration as they attempt to wait, leading to a shorter period of delay.

Beyond distraction strategies, children acquire more complex cognitive strategies that support their self-control. We have recently suggested that children develop strategies of attending to conceptual and affective information that support their efforts for self-control (43). At a conceptual level, for example, the child can employ executive attention to engage various beliefs about what they "should" do (e.g., "I should be patient and calm") and what they "can" do (e.g., "I can resist this temptation"). At an affective level, the child may attend to representations of affective outcomes that might result from success (e.g., feelings of pride or self-satisfaction) and failure (e.g., feelings of guilt) in their attempts to control their behavior. As can be seen, these strategies can be complex and require considerable flexibility in shifting attention among different perceptual, conceptual, and affective content. If their executive attentional capacity is limited, children with ADHD may have difficulty in taking advantage of these strategies.

Once a response is initiated, another important executive function involves monitoring responses and correcting errors (32). Children with good attention may initiate a relatively impulsive response, but can still monitor the response and make adjustments if they are not getting closer to their goal. In addition, the child's impulsive responses may elicit negative responses from others, but they can shift to more acceptable responses. To the extent that executive attention is deficient in ADHD children, they may often lack the attentional flexibility to track rapidly changing outcomes and response options. Thus, their responses may tend to be ballistic and perseverative, and they may often find themselves frustrated or faced with disapproval from others.

After a response has failed, children with good attention are able to reflect on their failure and form a representation of the problematic behaviors and outcomes. Again, such reflection requires attentional flexibility in disengaging from the experienced frustration and reconsidering the individual actions and their relation to the unfolding negative events. A child with weak executive attention may have difficulty with such reflection, lacking the flexibility required for replaying, isolating, and linking the causal effects. In more extreme cases, some children may be virtually unable to disengage from their frustration, which functions to invigorate a dominant and ineffective follow-up response (18,19).

We have focused our discussion of executive functions primarily on limitations in attentional flexibility. The basic point is that the processing involved in selecting, executing, and reflecting on responses is complex, requiring attentional flexibility. If this flexibility is impaired, then the more dominant and often ineffective responses will tend to be favored, as is often the case in children with ADHD. It is important to understand, however, that this inflexibility may not always be solely due to the problems with executive attention. Rather, it may emerge from interactions between the voluntary attentional and more reactive motivational influences. In the final section, we consider several interactions between systems that seem relevant to ADHD.

INTERACTIONS BETWEEN MOTIVATIONAL AND ATTENTIONAL SYSTEMS

Perhaps the most obvious interaction involves children with a strong approach system accompanied by a relatively weak voluntary attentional capacity. There are several ways in which the strong approach system may tend to constrain the regulatory effects of voluntary attention. For example, some of the voluntary functions mentioned above (e.g., planning, reflection on failure) require time. If the approach motivation is too strong, then the child's impulse to act tends to short circuit the voluntary processes. In addition, with strong approach motivation, approach responses, especially

those associated with immediate reward, will be strongly potentiated and would be difficult to inhibit even with strong attentional capacity. Moreover, if the effect of strong approach motivation is to delay disengagement from a source of reward (7), then crucial attentional flexibility will be impaired. As can be seen, these reactive influences arising from strong approach motivation will only be controllable by strong executive abilities.

Similar, but not identical, effects might come about with another combination of temperamental characteristics, when strong approach is combined with low fear motivation. The lack of reactive behavioral inhibition would tend to disinhibit approach responses, often leaving insufficient time for more effortful processing (31). These children's thoughts could be dominated by immediate reward, along with a relative absence of information related to potential punishment. Because of this absence, it may prove difficult for such a child to voluntarily engage affective content that might support self-control (e.g., anticipated feelings of guilt or empathy), because such feelings are uncommon and thus not strongly stored as representations (44,45). In addition, the overly broad scope of their attention, resulting from an approach-related expansion in the absence of an anxiety-related narrowing, may make it difficult for them to focus on important details involved in planning and evaluating responses. Presumably, these limitations can be to some extent overcome if the child has good attentional control, but more effort and flexibility will be required.

As mentioned earlier, ADHD children with comorbid anxiety may actually benefit in several ways. For example, the strong anxiety may provide reactive control over dominant approach tendencies by inhibiting the selected response and allocating attention in favor of potential punishment. These reactive influences may actually prove beneficial to some executive functions. For example, increased attention to negative information may make it easier for the child to anticipate potential negative outcomes during planning, to detect and correct these outcomes during the execution phase, and to take better account of their mistakes in reflecting on their problematic behavior. At the same time, however, anxiety has other reactive effects that may impair executive functions. In particular, anxiety elicits an attentional narrowing along with enhanced attention to threat, both of which could easily undermine the flexibility required in controlling responses. The anxious ADHD child's strategies may prove effective in fairly simple situations, but in more complex situations substantial rigidity may characterize their behavior.

CONCLUSIONS

In this chapter we have considered ADHD as an outcome of reactive motivational processes and voluntary attentional processes. Although much evidence suggests an important role for executive processes, we have tried to

emphasize that the executive capacity will depend not only on frontal systems, but also on the subcortical motivational systems with which they interact. These subcortical systems exert reactive influences on behavior and attention, and it is within this reactive context that the executive mechanisms must operate. Thus, research needs to consider both types of processes. This can be most readily done by considering different types of executive processes set within motivational contexts that manipulate the child's reward- and punishment-related systems. Such an approach promises a broader and more integrated view of the functional deficits accomp anying ADHD.

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10

Where is the "Attention Deficit" in ADHD? Perspectives from Cognitive Neuroscience and Recommendations for Future Research

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INTRODUCTION

The suggestion that individuals with attention deficit hyperactivity disorder (ADHD) suffer from a subtle neurological dysfunction has existed throughout the history of modern clinical observations. However, after 100 years of observation and research, the identity of the primary mechanism(s) underlying this childhood disorder has yet to be conclusively resolved, as illustrated by the variety of neuropsychological theories covered in this edition. Whereas behavioral observations of "inattention" reliably distinguish children with ADHD from non-ADHD children (1), determination of whether inattention is a cognitive hallmark that identifies ADHD children from their non-ADHD counterparts has been more elusive. Clarification of this issue would allow for the development of more complete and accurate theoretical models of ADHD, aide in the etiological determination of the disorder, and inform cognitive neuroscience of the structure of attentional processes in normal and abnormal development. Clinically, such information would allow for more objective diagnostic procedures, earlier detection, and targeted therapies for rehabilitation.

The largest challenge to clinical research in this respect is to clearly define and accurately measure the multiple constructs of attention. Prior to

the advent of modern technologies that allow for improved control and measurement of component processes, clinical research more frequently relied upon face-valid definitions of "attention" and tasks of attention, rather than methodologies that tapped theoretically based and empirically supported attention structures. However, recent advances in cognitive neuroscience are providing new opportunities to examine the status of attention in ADHD. Due to the vast literature to be covered, this chapter will focus on only two of the more recent approaches to the study of attention in ADHD. The first of these is a distributed network model of visuospatial attentional orienting that Posner (2) and others' have extensively developed, and which has been applied to a variety of clinical populations. The second is a perceptual load model of selective attention that has garnered increasing excitement among cognitive neuroscientists since the mid-1990s (3). This model provides a unique perspective into the nature of selective attention, and may prove useful to the critique of previous findings and to the development of future studies of selective attention deficits in ADHD.

VISUOSPATIAL ATTENTIONAL ORIENTING

Although there is great variation in methodologies, the basic task is a simple target detection task in which reaction time (RT) is the main dependent variable. Participants are instructed to maintain fixation at a central point, and are cued to the location of a future target (i.e., right or left visual field) by an exogenous or endogenous cue. Figure 1 presents a schematic diagram of the paradigm. Exogenous cues orient attention automatically and appear

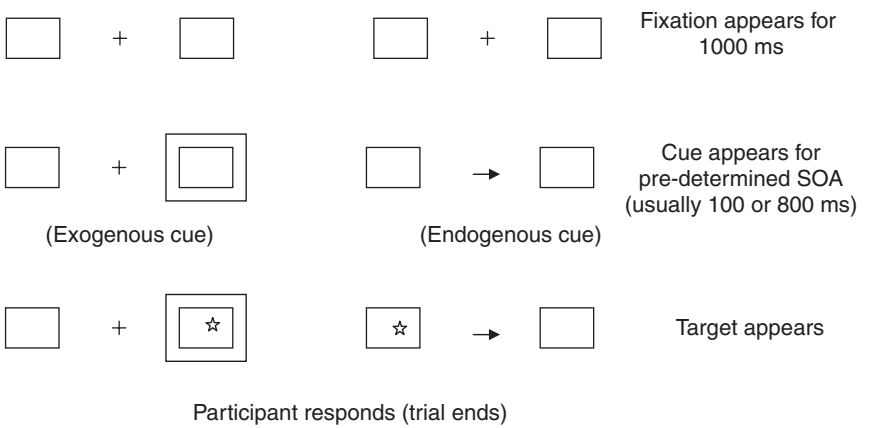

Figure 1 Diagram of the covert-orienting procedures for exogenous (right valid target) and endogenous (left invalid target) cueing conditions.

as a peripheral "brightening" in the right or left visual field. They are nonprobabilistic, that is only 50% of targets appear in a previously cued position. Endogenous cues, which are centrally located arrows, are probabilistic (typically 80% of targets appear in a previously cued location). Participants are therefore able to take advantage of the cueing probabilities to orient attention voluntarily for improved performance. Both cues decrease RT to detection at the cued location (benefits), with an accompanying increase in RT to targets appearing at the noncued position (costs).

Using this framework, Posner and colleagues have demonstrated that attentional control is derived from a network of at least three systems working together to orient visuospatial attention in a top-down goal-oriented manner, as well as a more data-driven automatic fashion. The posterior attention system (PAS), comprised of the superior parietal cortex, pulvinar, and superior colliculus, is responsible for automatically engaging, disengaging, and shifting attention in space. Thus, orientation to exogenous cues is believed to access the PAS. In contrast, the anterior attention system (AAS) is responsible for bringing targets into conscious awareness, for voluntary shifts of attention, and for decision-making. PET studies have found that midline frontal areas including the anterior cingulated gyrus and areas of the supplementary motor cortex are involved in detection (4–6). Orientation to endogenous cues accesses the AAS. The third network, the vigilance network, is responsible for maintaining sustained attention as well as for phasic alertness. This system is comprised of the noradrenergic system of the locus coeruleus, the cholinergic system of the basal forebrain, the intralaminar thalamic nuclei, and the right prefrontal cortex (7,8). The orienting paradigm was not optimally designed to evaluate the functioning of the vigilance network, but evidence for such a dysfunction could include slower RTs, increased variability of response, or specific performance deficits following neutral versus uncued targets in the experimental group (7,9,10).

This model has been validated by evidence from neuroimaging studies and studies of brain injured individuals (11–13). Accordingly, it has received extensive usage within clinical research for a wide range of disorders including Alzheimer's (14), Parkinson's disease (15), schizophrenia (16–18), brain injury, and collosotomy patients (19,20). Between 1990 and 2007, there have been 17 published studies of attentional orienting in ADHD utilizing Posner's model.

A review of that literature (21) found mixed evidence for a PAS deficit. That is, only 4 of 11 studies (22–25) found slower RTs for ADHD children (or their biological parents, as was the case in Nigg et al. (23)) to invalidly cued targets following exogenous cues. However, the affected visual field, and thus the affected hemisphere, did not replicate among the four. Poorer performance following invalid cues is associated with a deficit in the disengage operation, and has been found in individuals with documented right

parietal lobe lesions. Despite qualitative replication, quantitative meta-analytic review (of the nine studies providing enough data to be included in analyses) found homogeneously small effect sizes across studies (average $D = 0.26$), suggesting that any observed effects were too small for clinical relevance (21). Assuming population effects of that size, sample sizes of at least 112 for both the ADHD and non-ADHD controls would be needed for power $= 0.80$ in a two-way repeated measures design. None of the studies approached that n, which may help to explain the inconsistency in results among studies.

With respect to voluntary AAS processes, all four studies using endogenous cues found significant group differences, but no study finding replicated another (21). Due to incomplete data reporting, only two of the four endogenous studies could be analyzed quantitatively (26,27). However, their reported effect sizes were significantly heterogeneous to prevent an accurate summary of findings. That is, the average effect size for McDonald et al. (26) was 2.44 (due to atypically small standard deviation of RTs) in comparison to Pearson et al.'s (27) 0.13. Error rates, which may be indicators of AAS functioning, were modestly supportive of an AAS deficit. Seven of eight studies found more errors of commission in their ADHD group, but only three were significantly so (28–30). Two of four studies found greater omission errors, but only Swanson et al. (24) found significant group differences in the number of such errors.

And finally with respect to the vigilance network, 7 of 12 studies found slower RTs in the ADHD group, but only four of these were significant (23,25,26,31). Oberlin et al. (32), published after the 2003 meta-analysis, used a paradigm similar to the visuospatial cueing task (Attention Network Task), and found that adults with ADHD-C (but not ADHD-I) were generally slower to target detection following both spatial and alerting cues. The generalized slowness was corrected following administration of stimulant medications and results were interpreted as indicative of deficits in phasic alerting (32). As another potential index of vigilance system functionality, Huang-Pollock et al. (33), but not Novak et al. (29), found greater variability in RT for the combined but not inattentive subtype. However, effect sizes calculated from group mean RTs and standard deviations collapsed across cueing conditions were homogenous and small (average $D = 0.18$; Ref. 21).

None of the three studies that examined performance over time found performance to deteriorate at a greater rate than controls, supporting previous arguments against a sustained attention deficit in ADHD (34,35). However, the orienting paradigm was not optimally designed to measure sustained attention. To address this concern, Huang-Pollock et al. (36) collected data from 135 children with ADHD-C, ADHD-I, and non-ADHD controls using exogenous and endogenous cueing conditions to assess PAS and AAS functionality, respectively, but also evaluated the vigilance system

directly using a sustained attention paradigm (i.e., an A–X Continuous Performance test, CPT). There was no evidence of either PAS or AAS dysfunction in either ADHD subtype, but clear vigilance system deficits on the CPT emerged. Children with ADHD, regardless of subtype, had lower sensitivity (d), a highly activated response style ($\ln \beta$), and performance that decreased over time in a manner consistent with a sustained attention deficit. In a smaller ($N = 30$) sample of children with ADHD and non-ADHD controls, Barry et al. (37) found similar results that favored vigilance system involvement in the form of sustained attention deficits, but not AAS or PAS deficits.

Suggestions that ADHD may represent a right-lateralized deficit have been widely discussed (38–40). However, with respect to the orienting paradigm, five studies found evidence broadly consistent with right hemisphere dysfunction, one found evidence for a left hemisphere involvement, while four found no significant visual field effects. Thus, lateralized effects also did not strongly or consistently replicate across studies.

SUMMARY

Despite qualitative replication in favor for a PAS disengage deficit, suggestions of a nonspecific AAS deficit, and a possible alerting dysfunction in the vigilance system, quantitative meta-analytic review failed to find evidence for a clinically significant deficit in either the AAS or PAS attentional-orienting systems, or in the phasic response processes of the vigilance system. Of the three articles utilizing the Posner paradigm not included in the original 2003 meta-analytic review (36,37,41), none found significant group differences in performance that would indicate deficits in the PAS or AAS, supporting those initial interpretations. Sustained attention deficits as a function of the vigilance system remain an open possibility, but the orienting paradigm itself is not the best tool to test this hypothesis.

There are several reasons for the lack of strong findings, aside from the obvious interpretation that children with ADHD may not have deficits in the basic, low-level attentional processes needed to shift spatial attention. Comorbidity within study groups is one, but there were no consistent differences among studies that did (eight) or did not (five) control for comorbidity (21). Lack of homogeneity due to use of DSM-IIIR (42) criteria for the majority of studies reviewed, is another. However, consistent cognitive differences have yet to be demonstrated between the two subtypes (43), and some research suggests that it is the presence of inattention, rather than hyperactivity or impulsivity, which is associated with neuropsychological deficits in processing speed, vigilance, and inhibitory control (44). Huang-Pollock et al. (33,36) used DSM-IV (45) criteria to examine orienting in both the inattentive and the combined subtype of ADHD, and found no group differences in performance. Although Huang-Pollock et al. (33,36)

excluded children with either five symptoms of hyperactivity or inattention from analysis because subtype is difficult to determine in those cases (46), the issue of within-group heterogeneity even using DSM-IV criteria remains a general problem within the field of clinical research. Thus, subtle cognitive distinctions between subtypes may be obscured. Clarification of this question may require stricter control over groups (e.g., children presenting with fewer than four hyperactive symptoms, and who do not have comorbid oppositional or conduct problems), or consideration of additional symptoms (e.g., sluggish cognitive tempo, SCT) (47).

Low power due to small sample sizes may be another reason cumulative evidence for an orienting deficit has been elusive. The average group effect size across studies using exogenous cues was small, and required a total *N* of 224 for power to equal 0.80. Furthermore, the potential confounding effects of eye movements were not always controlled, and the paradigm itself may simply be less reliable in children than in adults.

Due to the large variability in methodologies (e.g., presence or absence of a "neutral" condition, forced-choice vs. simple detection tasks, and differences in visual angle or cue-target delays), it is recommended that future studies carefully weigh the potential benefits of information obtained from novel-orienting designs against the need for closer replication attempts. The common use of mixed cue types (e.g., predictive exogenous cues, or simultaneously appearing endogenous and exogenous cues) is also problematic. Such designs prevent clear interpretation of any group deficits as evidence for an AAS or PAS dysfunction. Due to the limited space available here, interested readers are directed to Huang-Pollock and Nigg (21) for a more thorough discussion of all these issues.

Although an accumulation of these methodological problems may contribute to the lack of significant findings for an orienting deficit, it is difficult to be persuaded that at least in the combined subtype of ADHD, an attentional-orienting dysfunction could be of sufficient magnitude to be of clinical relevance. However, further examination of performance in the primarily inattentive subtype, and of children with SCT, would be of interest given theoretical considerations of the disorder. Future investigators who want to pursue this are advised to attend to the issues of methodology specific to orienting outlined above, as well as to more general issues including attention to subtyping, comorbidity, and sample size. They are also advised to publish full tables of RT and standard deviations for each group in order to enable better estimation of meta-analytic effects.

The distributed network model of attention has gained wide usage not only because the neural structures it taps are well validated, but also because the computer-generated paradigm is well suited for research into cognitive processes. More generally, however, its popularity is evidence of a growing interest among clinical researchers in the application of cognitive neuroscience's theoretical advances for use in the study of clinical populations.

Such advances not only offer new avenues of research, but also provide a way to critique previous methods and results for their validity of approach. For example, there has long been the question of whether ADHD is represented by a *selective* attention deficit, and a recent model of selective attention may help address this issue.

PERCEPTUAL LOAD MODEL OF SELECTIVE ATTENTION

The perceptual load model of selective attention, like other capacity-based theories of attention, is founded on the assumption that humans possess a limited capacity for processing information. As such, it is necessary for an act of selection to occur so that only relevant items present in the perceptual world are selected for further processing, and irrelevant items are discarded. Whether this act of selection occurs early (48), prior to a full analysis of features, or late (49), after a considerable amount of processing has already taken place, has long been a matter of debate. Lavie (3) proposed that the locus of selection (i.e., early vs. late in the stream of information processing) is a function of the perceptual load on the attentional system. This model has been demonstrated in adults (3,50–52) as well as in children (53). When perceptual load is high, selection occurs "early," on the basis of the perceptual features such as color, form, and movement. In this situation, distracting task-irrelevant information is never processed, and the distractor's potential interference effect is small. However, when perceptual load is low, all stimuli are processed automatically regardless of their task relevance until capacity is exhausted. Selection in this case occurs "late," and is made on the basis of semantic identity. Thus, irrelevant distractors can subsequently cause significant interference in performance.

Lavie and Tsal (52) define perceptual load as consisting of two separate components: (i) the number of potentially task-relevant items in a display and (ii) the nature of the processing required for each item. High loads are those in which there are more task-relevant items on display, or when the display requires greater effort to process. Figure 2 presents examples of low and high loads. Early selection of perceptual features involves a posterior network of brain structures including regions of parietal and temporoparietal cortex (54–57). Late selection of semantic information (e.g., Stroop-like tasks; Ref. 58), involves a largely anterior network including the anterior cingulate gyrus and various regions of prefrontal cortex (59,60). Thus, when perceptual load is low, selective attention relies on anterior processes. But, when perceptual load is high, selective attention shifts and comes under the control of posterior network processes. Table 1 summarizes the perceptual load model of selective attention.

Readers will recognize that the neuroanatomical structures described here are similar to those associated with attentional orientation. Thus, a brief clarification of the relationship between selection and orientation is

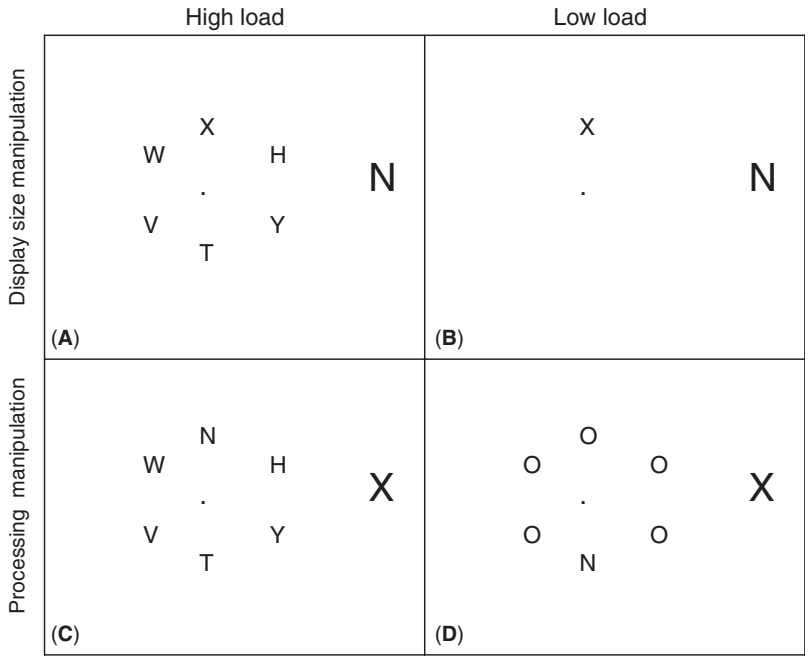

Figure 2 Example stimulus displays with high- and low-perceptual loads. The target, located in the circle of letters, can be either an "X" or and "N," thus requiring subjects to make a forced-choice response. The larger, peripheral letter represents the competing distractor. (**A**), (**B**): Manipulations of load by changing display sizes, with (**A**) representing a high load and (**B**) representing a low load. (**C**), (**D**): Manipulations of load by changing processing demands, with (**C**) representing a high load and (**D**) representing a low load.

required at this time. At its most basic, attentional orientation following an exogenous cue would be one example of an early selection process, because selection of a to-be-processed object is based on spatial location (i.e., the cue). In the orienting task, participants are instructed to maintain fixation at a central point. Automatic orientation to the peripheral cue occurs because the demands of maintaining fixation contribute only a low load to perceptual processes. Thus, there remains "extra" capacity available for the processing of the cue. Once oriented, information located within the cued region will receive facilitated processing in comparison to areas that are not selected, although automatic processing of irrelevant information would not be ruled out, assuming available capacity to process that information exists. Given that a particular spatial location will be attended, Lavie's (3) perceptual load model can be construed to ask: what determines future processing in that area? If the load is high, irrelevant information is more likely

Table 1 Summary of the Perceptual Load Model of Selective Attention

Locus of selection	Early	Late
Level of selection	External world	Internal representation
Selection based on	Perceptual features	Task demands
Perceptual load	High	Low
Automaticity	Automatic	Effortful
Neuroanatomical region	Largely posterior	Largely anterior

to be selected out of the stream of processing. If perceptual load is low, such information would continue to be processed along with relevant information.

One limitation to Lavie's (3) argument is that, at least in young adults, when participants are motivated to focus their attention to a discreet location in space, they are able to ignore distractors (i.e., abrupt visual onsets) (61). This occurs even when the perceptual load at the attended location is not sufficient to induce early selection. It may be that Lavie's (3) model of selection is optimal for situations in which individuals adopt a diffuse span of attention, or when they are unable to produce sufficient attentional focus (as in young children). That is, younger children whose anterior systems have not yet developed to sufficiently focus and maintain attention at fixed locations may depend more on older children or adults upon the automatic induction of early selection from heightened perceptual loads to limit interference from irrelevant information (53).

From the point of view of Lavie's (3) model, children with ADHD may be unable to shift from "late" to "early" selection to filter incoming stimuli from the environment, or, like younger children (53), they may require a greater perceptual load from their environment to engage this shift. Thus, the "beneficial" effects of high perceptual load to protect against distractor effects may be less evident in these children. Huang-Pollock et al. (62) examined both early and late selective attention using the perceptual load paradigm in children with DSM-IV ADHD combined and inattentive types, compared against non-ADHD controls. There were no significant differences in selective attention in either subtype. However, a subset of children with SCT demonstrated abnormal early selective attention deficits, and were unable to make the switch from late to early selection. Thus, it remains vitally important that future studies of selective attention or other cognitive processes in ADHD carefully attend to and reduce the group heterogeneity that arise from our current taxonomic classification. Consideration of SCT as well as stricter control over assignment to diagnostic subtypes is necessary to move the field forward in this respect.

Previous research has inconsistently supported a selective attention deficit in children with ADHD (63,64). However, when reinterpreted using Lavie's criteria, negative findings may be due to use of tasks that were not ideally suited to optimize the study of selective attention. That is, in order for early selective attention processes to be observed, a task must have (i) sufficient perceptual load to induce early selection (34,65,66) and (ii) the presence of a competing distractor that participants must suppress (67–70). Based on this model, future studies of selective attention in ADHD are also advised to attend to these two issues.

SUMMARY AND RECOMMENDATIONS FOR FUTURE RESEARCH

This chapter has reviewed and made specific recommendations for studies of visuospatial orienting and selective attention in ADHD. In summary, there appears to be little evidence for clinically significant deficits in the PAS or AAS as indexed by Posner's covert-orienting paradigm, in children with either the combined or primarily inattentive subtype of ADHD. Although lack of findings for PAS deficits is not entirely surprising, lack of evidence for AAS abnormalities is somewhat curious given theoretical explanations of the disorder. However, the executive construct is multicomponential (71), and these low-level early-developing voluntary attention processes may not be as impaired as those needed for higher level later-developing functions such as skill learning and attentional control. Some evidence for vigilance system deficits were found, but findings require replication among both of the primary DSM-IV subtypes. Only one study (62) has taken advantage of the perceptual load model of selective attention to examine early and late selective attention in ADHD. Results from that study found that children with ADHD and SCT demonstrated early selective attention deficits compared to children with ADHD without SCT or non-ADHD controls.

Regardless of the model of attention under investigation, future studies are advised to utilize models of attention processes that (i) target empirically validated attention structures and (ii) are capable of isolating component operations. Less-optimal functioning among a set of cognitive processes may in the end best describe the cognitive mechanisms that underlie ADHD. However, identifying which processes will require improved attempts at isolating and systematically combining component operations, allowing investigators to more accurately model, test, and describe the sequelae of such interactions.

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11

The Dual Pathway Hypothesis of ADHD: Retrospect and Prospect

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INTRODUCTION

The study of the psychopathophysiology of attention deficit hyperactivity disorder (ADHD) is at a wonderfully exciting phase in its development. Established ways of thinking about the condition are giving way to new ones: A paradigm shift is underway. We call it a paradigm shift because these changes relate to more than just a replacement of just one theory with another, but rather a fundamental shift in perspective—with one way of thinking about ADHD as a disorder giving way to another. Traditionally, ADHD researchers, influenced by assumptions within the classical disease model of psychiatric disorders (1), have attempted to isolate a common core deficit at the heart of ADHD. More recently there has been a growing acceptance that ADHD is a psychopathopsychologically heterogeneous disorder; with no particular pattern of impairment representing a necessary condition for the presence of the condition and with subgroups of children recognized each with a distinctive pattern of impairment (2). This has been a response to the inconclusive pattern found in studies of ADHD psychopathophysiology which are often contradictory and inconsistent and where replicated results are found, meta-analyses give pooled effect sizes in only the moderate range (i.e., Cohen's *d* .4–.6) (3). This shift in perspective has led to a different set of research questions being asked. Rather than asking; where is the core deficit responsible for ADHD? The question becomes: How many different profiles of impairment can be dissociated within the broader ADHD syndrome (4)?

In this chapter we give a brief overview of the development of the dual pathway model, first published in 2002. This model provides a useful starting point when thinking about heterogeneity in ADHD. The working hypothesis is that there are at least two dissociable pathways to ADHD which affect different subgroups of ADHD children. One pathway is predominantly cognitive and associated with executive/inhibitory dysfunction, and a second one predominantly motivational associated with a broad-based motivational style, delay aversion (5). Furthermore, we propose that (*i*) these pathways are underpinned at the neurobiological level by two functionally distinct, though anatomically proximate, dopamine modulated corticobasal-ganglia circuits (6) and (*ii*) follow different developmental pathways (7). In this chapter we review these developments and identify key question for future research and implications for clinical practice.

COGNITION AND MOTIVATION IN MODELS OF ADHD

Executive Dysfunction in ADHD

In the recent past ADHD has been seen as a disorder of dysregulation of cognition, action (8–10), and cognitive-energetic state (11,12) associated with the disruption of neurocognitive control systems (13–19). While nonexecutive processes have been implicated in the disorder (20), the most influential models could be called strong executive dysfunction models, in that they view brain-behavior relations as fully mediated by neuropsychological deficits in executive functions (8). Executive functions are higher order, top-down, cognitive processes that allow appropriate set maintenance and shift that facilitate the flexible pursuit of future goals. Deficits within the executive system in ADHD (21) have been consistently found with the strongest evidence existing in the area of response inhibition (8). Problems with working memory (15), planning, and set shift have also been identified (22). Executive dysfunction also disrupts the distribution of cognitive-energetic resources (i.e., effort) to those activation and arousal processes required to meet the changing demands of different situations and settings (9,11,12,23). Barkley (8) has argued that the general pattern of executive impairment associated with ADHD is grounded in more specific early appearing deficits in inhibition (24,25). Response inhibition refers to that ability to inhibit an inappropriate prepotent or dominant response in favor of a more appropriate alternative. Response inhibition is regarded as a necessary precondition for the establishment of self-control (26), emotional regulation (27), and cognitive flexibility (28). As a domain of competence, response inhibition appears to be fractionated into conceptually related clusters of functions with each cluster sharing elements of this common definition but being measured by different

neuropsychological tests (29). The most commonly used tests of children's inhibitory control include measures of response-conflict resolution such as the Stroop test (30) and the speed of inhibitory processes such as the stop signal paradigm (31).

At a neurobiological level, inhibitory control and other executive functions appear to be underpinned by one of a number of functionally segregated but neuroanatomically proximate brain circuits connecting cortical foci, basal ganglia, and thalamic nuclei (32–34). This circuit (i.e., the executive circuit) links the prefrontal cortex to the dorsal neostriatum (preferentially the caudate nucleus) with reciprocal excitatory connections back up to cortical regions via the dorsomedial sections of the thalamus. Data from neuroimaging studies (structural and functional) give some support to the idea that executive dysfunction in ADHD is associated with disturbances in this circuit (35–40). Dopamine, widely implicated in ADHD, is a key neuromodulator of the executive loop (41–44) with two branches specifically implicated. The mesocorticol branch originates in the ventral tegmental area of the rostral portion of the brainstem and terminates in the prefrontal cortex while the nigrastriatal branch originates in the substantia nigra and terminates in the dorsal striatum.

Despite the broad pattern of evidence linking ADHD to executive dysfunction it is becoming increasingly clear that executive dysfunction models of ADHD are only partially supported by empirical evidence. For instance, Nigg et al. (45) found that only a subpopulation of ADHD children had significant impairment on any one executive task and that the pattern of severe and pervasive impairment predicted by the sorts of strong executive theories of ADHD influential during the last 10 or so years (8), was present in only a very small minority of ADHD cases. This and other recent analyses have led to the question; If not executive dysfunction what is "causing" ADHD in these unaffected children?

Delay Aversion in ADHD

Motivationally based models, which shift the focus from inhibitory deficits to suboptimal reward processes, offer an alternative to inhibitory-based executive deficits as a basis for ADHD (46–48). The literature has been reviewed by Luman et al. (49). The review highlights the sheer range of motivational hypotheses that have been proposed. For instance, it has been hypothesized at different times by different people that ADHD children are undersensitive to rewards (50); have an underactive behavioral inhibition system and, are insensitive to nonreward or punishment (51) (52). Kollins et al. (53) and Tripp and Alsop (54) have hypothesized that ADHD children are less sensitive to changes in reinforcement contingencies and reinforcement history, respectively. Another promising domain relates to the so-called "hot"

executive processes implicated in decision-making about reward, risk, and punishment (55).

The most striking thing about the review is that despite the very broad range of deficits proposed, the evidence in support of any one is inconclusive—with initial positive findings followed by serial nonreplication. The one area that may be the exception relates to ADHD children's apparent sensitivity to delayed rewards. This is confirmed in a recent review (56). This phenomenon is at the heart of a number of models of ADHD (57) and can be seen most clearly in relation to ADHD children's choice of small immediate rewards (58–66; E. Willcutt, personal communication).

We have argued in the past that this pattern of preference is a hallmark of a broader motivational style called delay aversion (62). In one model (7) delay aversion is driven by fundamental impairments in the neural signaling of delayed rewards and associated increased reward discounting of delayed rewards (57); compounded by a pattern of delay-related negative affect acquired during development as the delay-impaired child learns to associate delay settings with censure and failure (5) and, expressed in different settings in different ways as a function of whether delay can be escaped or has to be tolerated and modified (5). Evidence for this broader motivational style comes from studies of ADHD children's levels of activity during delay (67); their response to the unexpected imposition of delay (68); the impact of delay on attention and perception (69,70); their performance on long and challenging tasks (71); their degree of reward discounting (72,73); their relative preference for reward immediacy over other reward parameters (74); and their response to slow event rates/sparse schedules (75,76). According to the delay aversion framework choices of small immediate rewards overlarge delayed rewards are motivated by two processes: (a) an unconditional preference for immediacy linked to deficits in signaling future rewards and (b) the desire to escape or avoid the negative delay-related affect. These effects add to each other to cause preference for immediacy over delay.

Interestingly the neurobiology of delay aversion and inhibitory deficits may share some common elements. It is likely that delay aversion is also related to alterations in one of the cortiobasal-ganglia circuits modulated by dopamine. However, in this case it is the reward circuit that is likely to play the dominant role. This links the ventral striatum (in particular the nucleus accumbens) to frontal regions (especially the anterior cingulate and orbitofrontal cortex), reciprocated via the ventral pallidum and related structures through the thalamus (77). The amygdala is also implicated in this system possibly playing a role in defining the motivational significance of incentives. Once again dopamine is a key neuromodulator. On this occasion, however, it is the mesolimbic branch of the dopamine system, originating in the ventral tegmental area and terminating in the nucleus accumbens and associated limbic foci, which is important. Studies point to a specific role for this circuit in signaling rewards, coding incentive value and regulating other

behavioral processes involved in the maintenance of responding under conditions of delayed reward (78–84). Lesions in the core of the accumbens reduced the ability of rats to wait for large delayed reward in a self-control paradigm (82). Animal models have highlighted the way in which alterations of dopamine activity within this structure may distort or reduce signals of delayed rewards (46,47,85–87).

Understanding the Relationship Between Delay Aversion and Inhibitory-Based Executive Dysfunction; Competing or Complimentary: Additive or Synergistic

In trying to understand the nature of psychopathophysiological heterogeneity in ADHD we have attempted to model the relationship between delay aversion and inhibitory-based executive deficits in ADHD. The first possibility, which can be dismissed on the basis of recent studies, is that delay aversion and inhibitory deficits in ADHD represent different facets of the same underlying impairment construct. That is they affect the same ADHD children. A head-to-head study (44) of delay aversion and inhibitory deficits in ADHD set out to provide a direct comparison of these two models. School-aged children with a diagnosis of combined-type ADHD performed the stop signal task (where a dominant response already initiated is inhibited following a "stop" signal) and a choice delay task in which children had to choose between a large delayed reward and a small immediate reward. There was no association between choices of the small immediate reward (delay aversion) and stop signal reaction time. This suggested that inhibitory deficits and delay aversion were independent characteristics. Furthermore, performance on both tasks was strongly associated with ADHD group membership—in combination the two measures allowed nearly 90% of ADHD children to be correctly classified. A subsequent reanalysis suggested that different subgroups of ADHD children with inhibitory deficits, delay aversion, both impairments and neither could be identified. In suggesting that delay aversion and inhibitory deficits were independently associated with ADHD, this study was consistent with a dual pathway model of ADHD. A similar pattern of associations has recently been found in a study of executive function and delay aversion in preschoolers (88). The independent association inhibitory-based executive dysfunction and delay aversion has been extended to other motivational systems such as "hot" cognition (55) and validated in animal models of impulsiveness and aggression (89).

On the basis of this data we have proposed a dual pathway hypothesis of ADHD (90). This hypothesis builds on the idea that alterations within the executive circuit modulated by mesocortical dopamine and the reward circuit modulated by mesolimbic dopamine constitute more or less

discrete neuropsychological bases for dissociable psychological processes leading to executive/inhibitory deficits and delay aversion, respectively. In initial models the two pathways were presented as independent factors acting additively (5) but more recent accounts have recognized the likelihood of synergistic interactions between motivational and cognitive factors. First, there is the suggestion that during development delay aversion can create the context for the development of executive dysfunction as this motivational style limits the opportunity for children to consolidate delay exploiting higher cognitive skills. At the same time executive dysfunction can lead to a learned helplessness and a motivation to avoid difficult and demanding and delay-rich tasks (6,7). At the same time there are likely to be synergies at the neurobiological level with cascading frontostriatal loops linking reward and cognitive processes (91). Taking a developmental perspective also highlights the possibility of the operation of compensatory mechanisms (7).

Finally, it must be recognized that a substantial minority of ADHD children may not be affected by either inhibitory-based executive dysfunction or delay aversion and that there are likely to be other operative pathways to ADHD (92). Candidate domains of dysfunction include: basic memory and perceptual deficits (2), state regulation and cognitive-energetic dysregulation (93), and altered timing processes operating in the millisecond range (94). Each represents a plausible putative ADHD psychopathophysiology and therefore may account for the condition in those ADHD children unaffected by executive dysfunction or delay aversion.

FUTURE DIRECTIONS FOR RESEARCH

While initial results are suggestive of the existence of independent delay aversion and executive pathways into ADHD further study of the relationship between these, and other candidate processes, is required to properly test this hypothesis. This research should employ multivariate approaches with large samples of children of different ages in longitudinal, genetically, and neurobiologically informative designs that would allow continuities and discontinuities between motivational and cognitive components of the disorder to be studied. It should also explore the interactions between motivational and cognitive features of the disorder, including at the neurobiological level and the possibility that ADHD children might develop compensatory skills and strategies. The implications for ADHD nosology and diagnosis need to be addressed. First, we need to identify the most diagnostically efficient and cost-effective test measures of delay aversion, executive dysfunction, and other key pathophysiologic markers. Second, the stability of these markers as dysfunctional traits needs to be established over time and context. Third, population norms for these

markers need to be established and algorithms for establishing clinical thresholds need to be determined. Fourth, the relationship between the markers and other disorders needs to be tested. Fifth, perhaps most significantly, the clinical significance of delay aversion, inhibitory deficits, and other markers need to be investigated in terms of comorbidity, long-term outcome, treatment response, and how this varies by disorder type. Finally, the significance of these markers needs to be validated by studying their functional neuroanatomy.

CLINICAL IMPLICATIONS

Multiple pathway models could alter the way we think about ADHD clinically. First, they will encourage the identification of different psychological subgroups, with different impairment profiles. These subgroupings may be specific to ADHD and meet the criteria for clinical subtypes—e.g., ADHD–EF type. Alternatively, they may be seen rather in terms of comorbidity between ADHD and a neuropsychological impairment—e.g., ADHD and comorbid executive dysfunction. In this latter case such comorbidities could be shared with children with other conditions such as oppositional-defiant disorder or pervasive developmental disorder. Either way this would encourage a move away from current phenomenological symptom-based approaches to diagnosis toward more theoretically informed models. Information about the context for symptom expression would become more significant with diagnostic criteria making increasing reference to contextual factors in order to distinguish between delay averse and disinhibited type ADHD children. For instance, symptoms of inattention and overactivity only displayed in delay-rich settings may be indicative of a delay averse type of problem while more pervasive expressions might reflect more fundamental cognitive deficits associated with inhibitory deficits. Neuropsychological testing may also take on a greater significance. While at present evidence for the diagnostic value of laboratory tests is lacking it is possible that tests of inhibitory deficits and delay aversion may play a key role in the more precise definition of the clinical phenotype. Second, once the psychological subtypes have been identified it may be possible to better match them to particular treatment options. This applies equally to pharmacological and nonpharmacological interventions. Agents that target specific frontostriatal circuits are likely to be differentially effective in treating the inhibitory and delay averse subtypes. There may also be potential to tailor nonpharmacological treatments to psychological subtypes. For instance, shaping and fading of delay tolerance leading to desensitization to delay may be useful for the delay averse children while attention and cognitive training may be valuable for dysexecutive children.

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12

Cortical Excitability in ADHD as Measured by Transcranial Magnetic Stimulation

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INTRODUCTION

All rating scales for attention deficit hyperactive disorder (ADHD) include items that inquire to evaluate motor hyperactivity. Although these ratings can be confounded by aggression, oppositionality, and reduced impulse control, the motor aspect of ADHD is an important one, since a general motor hyperactivity is the most apparent symptom of ADHD in young children. Further, the working group of Gillberg described as DAMP syndrome a group of children with deficits in attention, motor control, and perception (1). This combination is often found in ADHD children, particularly of the combined subtype. The motor activity in children with ADHD is not only quantitatively increased compared to healthy children but, especially in waiting situations (2), movements start earlier compared to their peers and this movement is disorganized, poorly modulated, shows problems in goal direction and cannot

be inhibited properly (3). Also, some studies found that children with ADHD are not only more active during daytime than age-matched controls but even during sleep (4–6) indicating that locomotor hyperactivity is a primary symptom. Further, Rothenberger (7) and Yordanova et al. (8) demonstrated that ADHD children (registration of brain electrical activity using event-related potentials) seem to have a deficit of motor control in the primary motor cortex as well as of the frontal lobe. This view is supported by Mostofsky et al. (9) who, on the basis of MRI findings, suggested that the clinical picture of ADHD encompasses dysfunctions attributable to anomalous development of both premotor and prefrontal cortices. ADHD children do not regulate the neuronal networks responsible for voluntary motion with selective activation and sufficient precision. This possibly applies even more for spontaneous movements, which are poorly under voluntary control in ADHD children. Hence, as one example, their tendency for associative mirror movements may be better clarified by using specific experimental tasks such as transcranial magnetic stimulation (TMS). Unfortunately, in a preliminary study, Barker et al. (10) did not find a significant correlation between mirror movements and the ipsilateral silent period evoked by TMS, although they could show an abnormal transcallosal inhibition in children with ADHD.

Thus, more general neuronal processes should be investigated, since neurophysiological studies could help to determine that the disturbance in motor control processes is attributable to (1) a lack of selective neuronal ability to choose adequate motor programs, (2) to energetic deficits in the early information processing steps which translate these programs into the intended movements, and/or (3) to basic neuronal problems with excitability within the motor system. Surprisingly, such a fundamental issue remains unresolved, although nearly all attempts to produce animal models of ADHD begin with locomotor hyperactivity (11), which may be associated with both hypodopaminergic and hyperdopaminergic status in animals, which might indicate that either dopaminergic extreme can produce behavioral and cognitive dysregulation (12).

Hence, it is a great advantage that recently the noninvasive method of TMS gives us the opportunity to investigate the basic neuronal problems with excitability within the motor loops of ADHD children.

TRANSCRANIAL MAGNETIC STIMULATION

Neuroimaging techniques such as positron emission tomography (PET), single-positron emission computer tomography (SPECT), or functional magnetic resonance imaging (fMRI) offer considerable potential for studying the developing human brain; e.g., developmental changes in the efficiency of brain circuitries invoked by cognitive tasks (13). However, the activation seen in functional imaging studies probably results from excitation rather than

inhibition (14). Therefore, direct conclusions concerning the significance of inhibitory neuronal processes, which are central to current theories of psychopathology (e.g., ADHD), have not been tested by using these methods. Further, the time window of these neuroimaging techniques is much broader compared to electrophysiological methods such as stimulus-evoked changes of electrical brain activity.

TMS allows investigation of activation as well as inhibition of neuronal systems. TMS uses very short (about 200 μsec), strong magnetic fields (e.g., 2 T) inducing an electric current in circumscribed brain regions (15). This method combines excellent time resolution with acceptable spatial discrimination and enables the investigation and modification of different brain functions in humans [e.g., visual system, language, memory; for review see (16–18)].[a] Stimulation of the motor cortex, and thus the cortico-striato-pallido-thalamo-cortical motor loop (19) elicits muscle twitches or suppresses ongoing voluntary movements. These effects can be assessed and quantified by measuring changes in the induced motor-evoked potentials (MEPs).

Applying single- or paired-pulse magnetic stimuli over the motor cortex, there can be derived parameters of motor system excitability such as the motor threshold (MS), the cortical silent period (CSP), and the extent of intracortical inhibition or facilitation (ICI and ICF) (20).

The MS allows determination of excitability at the level of the neuronal membrane, which is regulated by the permeability of ionic channels (21). Based on the CSP, which also depends to a limited degree on peripheral (spinal) inhibitory processes, the total magnitude of inhibitory effects on the sensorimotor system can be measured (22). By measuring ICI and ICF it is possible to draw conclusions concerning the extent of inhibitory and excitatory processes within the motor cortex itself (23).

Typically, to measure these parameters, the child sits in a comfortable chair. A magnetic coil (flat 70-mm butterfly coil) is laid on the left side of the head to evoke a muscle twitch at the (mostly) dominant right hand. By applying magnetic stimuli over the hand region of the motor cortex a transsynaptic activation of corticospinal neurons is produced. As a result of this activation, a MEP can be measured electromyographically using surface electrodes on the target muscle, in our case the abductor digiti minimi of the right hand. Three measurements can be derived:

- MS
- CSP
- ICI and ICF

[a] Due to ethical reason, only single- and paired-pulse TMS over the motor cortex have been applied in children so far. Because seizure elicitation is the major safety issue linked to repeated rhythmic TMS (rTMS) and little information is available about its long-term effects (19), this innovative approach should presently be restricted to adults.

For details of TMS measurement, see Ziemann et al. (24) and Moll et al. (20).

By studying the normal development of these parameters, it could be shown, that for the MS there is a significant reduction (i.e., it becomes easier to excite neuronal membranes) from 8 to 16 years (25).

A similar statistically significant age dependence was found for the duration of the CSP. This became longer with increasing age, so that an increase in the inhibitory mechanisms in the motor system may be assumed.

No age dependence could be established for the measures expressing intracortical excitability. This indicates that both inhibitory and excitatory interneurons in the motor cortex have already reached a mature functional state in prepubertal children.

DEFICITS IN MOTOR CONTROL IN CHILDREN WITH ADHD

As one of the possible neurobiological bases for ADHD, a disturbance in the control and/or regulation of motor processes has been discussed (26). The role of the sensorimotor system and its individual parts, in particular the motor cortex, which until recently has hardly been considered in proposed pathological models (in contrast to the prefrontal or parietal cortex), is still largely unclear. For this reason, it was necessary to use TMS to measure neuronal excitability in the sensorimotor system in children with ADHD in comparison with healthy children in order to test "close to the substrate" the idea of a "motor response regulation deficit" in ADHD. The hypothesis to be tested was that children with ADHD would show deficient inhibitory processes compared to healthy children. For this reason we measured and compared the neurophysiological parameters of motor system excitability of 18 children with ADHD and 18 healthy children, aged from 8 to 12 years (27).

Both for the MS and, unexpectedly, for the CSP, we could not find any differences between children with ADHD and healthy children. While there was no difference in the parameter of ICF, the children with ADHD showed a statistically significant reduction in ICI in comparison with healthy children. Because the paired stimulus paradigm used allows separate activation of inhibitory and excitatory interneurons projecting onto the motor neurons (21,23), this finding suggests a diminished expression of inhibitory processes in the region of the motor cortex in ADHD children.

Functional imaging studies can show indirect (general) differences in neuronal activity between healthy subjects and patients with ADHD, but direct conclusions concerning the significance of inhibitory neuronal processes have not been possible using these methods. Since a general deficit in behavioral inhibition is assumed to be fundamental to ADHD (28), and deficits in motor inhibition have repeatedly been described (11), the TMS method offers a means of measuring the postulated inhibitory deficit.

The normal MS found in children with ADHD gives no indication for hyperexcitability at the membrane level of cortical neurons in the

motor system. Unexpectedly, children with ADHD showed normal duration of the CSP. The latter suggests in contrast to shorter CSP in children with tic disorders (20), no evidence for a generalized deficit of inhibitory processes in the sensorimotor system.

Although the deficit of ICI in ADHD was demonstrated only at the motor cortex, the TMS results could reflect a generalized inhibitory deficit in cortical areas in children with ADHD, also accounting for the attention-related abnormalities and dysfunctions in the prefrontal and parietal neuronal systems described in the literature. This explanation only partly corresponds with a model of a generally inadequate behavioral inhibition as the basis for ADHD (28), because inhibition can be found only for certain aspects (e.g., motor function) and is nonspecific for the disorder (3,20,29,30).

DEFICITS IN MOTOR CONTROL IN CHILDREN WITH COMORBID ADHD AND TIC DISORDER[b]

The two "hypermotoric syndromes" of GTS and ADHD show clinical overlap. Around 50% to 60% of children with a tic disorder show hyperkinetic signs, and about 30% of children with ADHD also have a tic disorder (31). Previous studies at several levels (e.g., morphology, neuropsychology, and neurophysiology) in children with comorbid ADHD and tic disorder compared with children with only one of these disorders have produced partly equivocal results concerning the assumption of an additive effect at all levels of investigation (7,32). For this reason the question of comorbidity, particularly concerning the excitability of the motor system (additive vs. nonadditive effects) needs to be further investigated. We wanted to test the hypothesis that in the motor system of children with comorbid ADHD and tic disorder both TMS abnormalities, i.e., shortened CSP and reduced ICI, would be present. To test this hypothesis we compared in a 2×2 factorial design the neurophysiological parameters of motor system excitability of a group of 16 children with comorbid ADHD and tic disorder (chronic motor tic disorder or Tourette's syndrome; ADHD + TIC) with that of 16 children with only ADHD (ADHD only), 16 children with only tic disorder (TS only), and 16 healthy children, aged 8 to 15 years (33).

In children comorbid with both disorders—ADHD plus tic disorder—both TMS abnormalities could be found in comparison with healthy children, i.e., both a significantly reduced ICI (ADHD factor) and a significantly shortened CSP (tic disorder factor) (Fig. 1).

[b] For most recent evidence based knowledge on ADHD plus TD comorbidity see Rothenberger A, Rocmner V, Banaschewstri T, Leckman J (eds., 2007) Co-existence of tic disorders and attention-deficit, hyperactivity disorder-recent advances in understanding and treatment European Child and Adolascent Psychiatry 16: Supplements.

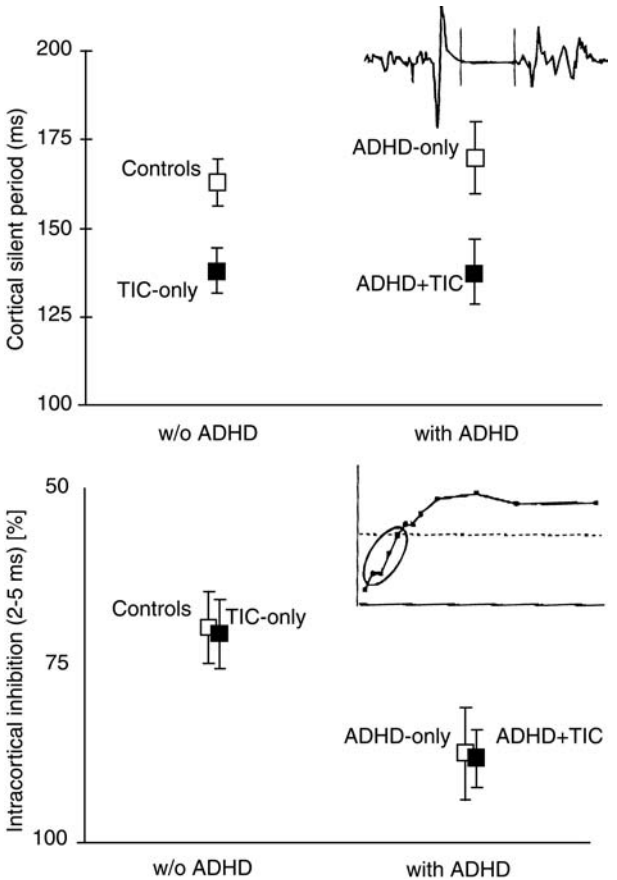

Figure 1 Additive inhibitory deficits in the sensomotor system cortical silent period (*above*) and intracortical inhibition (*below*) in children with comorbid ADHD and tic disorder. For each group mean ± mean standard error is presented. □ no tic disorer; ■: with tic disorder.

Because children with comorbid ADHD and tic disorder showed both a shortened CSP and also reduced ICI, we may assume a purely additive effect. Concerning different kinds of comorbidities in ADHD, such an additive effect could not be found in neuropathological studies of volume changes in the region of the basal ganglia (32), nor in neurophysiological studies on cognitive task-related cortical information processing (34–38). The additive effect demonstrated with TMS can therefore only be related to the excitability of the motor system.

The demonstration of both inhibitory deficits, which can be differentiated with TMS in the motor system of children with comorbid motor

hyperactivity disorders—shortened CSP as evidence for inhibitory deficits probably at the level of the basal ganglia (tic disorder factor) and reduced ICI as evidence for inhibitory deficits in the region of the motor cortex (ADHD factor) corresponds phenomenologically with the simultaneous presence of both features of motor processes (pattern related in TD and general motor hyperactivity in ADHD). This finding also corresponds with the effectiveness of specific therapeutic interventions to improve the inhibitory deficits in the motor system, i.e., dopamine receptor antagonists in patients with tic disorders and methylphenidate (MPH) in patients with ADHD (39).

MPH AND INTRACORTICAL EXCITABILITY IN ADHD AND NORMALS

We know that MPH ameliorates motor problems of hyperactive children. For this reason, in children with ADHD who had not yet received any medication and where MPH treatment was indicated, we carried out a TMS study to test the acute effects of 10 mg MPH on their motor system excitability measured by TMS parameters (20). Comparison between the two TMS measurements showed (as the only statistically significant difference) an increase in ICI after MPH treatment; i.e., a tendency of normalization of their basically reduced ICI (Fig. 2).

The reported increase in inhibition in the motor system of ADHD after MPH intake shown with TMS cannot be considered as a disorder or symptom-specific phenomenon in children with ADHD, since it is not only the motor control, but the whole spectrum of ADHD symptoms—inattentiveness, impulsivity, and motor hyperactivity—that is improved. Consistent with this, the extent of motor inhibition measured using purely overt behavioral stop-signal tasks, was increased by MPH in children with ADHD (40), but attentional capacity and the overt neurophysiological parameters corresponding to information processing functions were also improved in an unspecific and more general manner (41–43).

In summary, we have a significant enhancement in ICI but no effects on ICF in children with ADHD. Since psychostimulants such as MPH lead to similar behavioral effects even in healthy children (44), and there is no developmental effect in ICI and ICF we expected a similar TMS result in healthy adults taking MPH. Hence, we investigated in healthy adults the effect of MPH on cortical excitability (29). We could demonstrate that an acute administration of a standard dose of 10 mg MPH had a pronounced effect on intracortical excitability. MPH significantly enhanced ICF. This was an unexpected observation because dopaminergic effects of MPH directly at the cortical level could explain the enhancement of the ICI but not ICF, since dopamine may act as an inhibitory agent at the level of the neocortex (45). Alternatively, MPH may also act by D2-receptor activation in the striatum via the striato-thalamo-cortical sensorimotor circuit, since the excitability of the cortical neurons is altered via the ascending synaptic input (46).

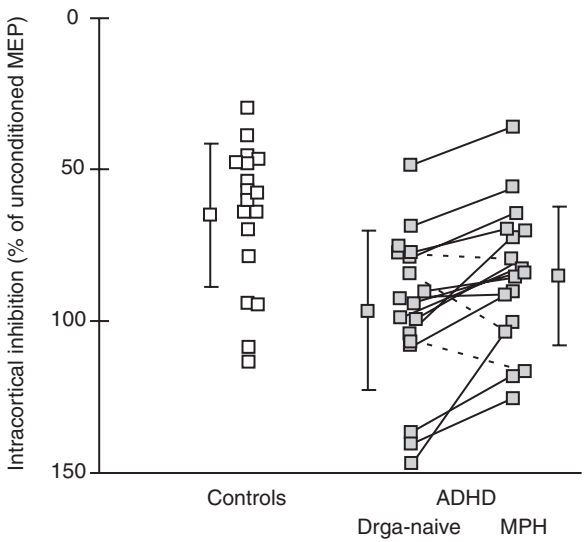

Figure 2 Intracortical inhibition [as percentage of unconditioned motor evoked potential (MEP) mean value over interstimulus intervals (ISI) 2–5 ms] in 18 drug-naive children with attention-deficit hyperactivity disorder (ADHD) aged 8–12 years compared to 18 age-matched healthy children. For each ADHD child, the effect of 10 mg methylphenidate (MP) on intracortical inhibition is also depicted. The group's mean values and standard deviations are plotted beside each group and condition, respectively. The insert shows MEPs of a representative ADHD patient (drug-naive, thick line; MP, thin line) to the test stimulus alone (upper trace) and conditioned by a subthreshold stimulus at ISI 13 ms ($\hat{=}$ inhibitory interval, lower traces).

In contrast to ICI the enhancement of ICF by MPH in healthy adults cannot readily be explained by the activation of D2-like receptors, because other D2-agonists such as bromocriptine do not significantly enhance the ICF (24). On the other hand, noradrenergic projections (such as those from locus coeruleus) are widely distributed in the neocortex, and studies from other authors indicate that norepinephrine modulates excitatory neuronal transmission (47). Further, intake of 40 but not 20 mg yohimbine, a central norepinephrine enhancing drug has been shown to increase ICF (48). Hence, it may be speculated whether MPH enhances ICF by increasing the excitatory neurotransmission via indirect noradrenergic neurons, similar to-amphetamine (49).

It is unclear, whether the acute effects of MPH in ADHD treatment results from drug-induced catecholamine changes at presynaptic and/or postsynaptic sites (50). Nevertheless, an increased striatal dopamine transporter availability was reported in adult patients with ADHD compared with healthy controls using SPECT (51,52). Therefore, a different status of dopaminergic innervation (the different level in ADHD may be

"functionally normalized" by MPH) might contribute to opposite effects of MPH on intracortical excitability in ADHD compared to healthy subjects (29). In this context, it should be noted that changes in ICI and ICF may also be due to other reasons which are not related to intracortical effects (33). Therefore, not only different dosage effects, but also input–output curves of MEP with and without MPH as well as direct measures of spinal motor neuron excitability are required to substantiate these findings. Moreover, also adult patients with ADHD need to be examined, although it seems unlikely that the observed opposite effects of MPH depend on a developmental process, since no age-dependent changes could be found in intracortical excitability during adolescence (25).

CONCLUSION

With these TMS studies on motor system excitability in children and adolescents with ADHD we have been able to obtain substantial new information to further support the notion that motor excitability plays an important role in ADHD. Further insight into the pathophysiological background of child psychiatric disorders may be expected by combining TMS with brain electrical methods and neuroimaging techniques, especially fMRI.

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Section IV: Management

13

Assessment and Remediation of Organizational Skills Deficits in Children with ADHD

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INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) affects about 6% of the school age population, and is the most prevalent disorder in child psychiatric clinics. It is characterized by age inappropriate inattention, motor activity, and impulsivity, to the point of causing meaningful impairment in the child's function. In addition to the cardinal signs of ADHD, it is generally recognized that other clinical features affect children's function. Among these other features are problems in organizing tasks and activities, with disorganized work habits, and a tendency to scatter, lose, or carelessly mishandle materials necessary for tasks (1). These characteristics have been conceptualized as reflecting deficits in executive function (EF). A prominent model of ADHD (2,3) posits that deficits in EF represent the underlying pathological process in ADHD. Although this view has been influential, it has not been translated into therapeutic action. Multiple psychosocial strategies have been developed for the management of children with ADHD (4,5), but none has incorporated the reversal of organizational deficits as a key component. The relative lack of attention paid to the organizational, time management, and planning (OTMP) skills in ADHD is noteworthy, given that ineffective OTMP skills compromise school success, and also result in family conflict, and decreased work performance.

We have attempted to address this neglected clinical issue through the development of a treatment approach specifically designed to ameliorate

deficits in time management, organizational, and planning skills in elementary school-aged children with ADHD. This chapter provides an overview of an intervention we developed and evaluated with the support of an NIMH R21 Treatment Development grant.

BACKGROUND

There is converging theoretical, clinical, and empirical consensus that an essential element of ADHD is poor organization of materials, time, and actions, and that these deficits play a critical role in the adjustment and functioning of individuals with ADHD. Recent models of the core cognitive and behavioral characteristics of ADHD (2,3), and findings on the adult adjustment of ADHD children highlight the impact that poor skills in organization of time, activity and materials, have on ultimate functioning (6–8). Barkley's theoretical model suggests that EF, including deficits in the capacity to plan actions into the future and organize actions for current situations is at the core of the disorder (2,3). Although this model is perhaps best formulated by Barkley, others as well have discussed the importance of EF deficits in ADHD (9,10). These formulations imply that weak executive functioning accounts not only for overt behavioral problems of impulsivity and unfocused restlessness, but also for poor attention to details, for poor time management, and for deficient planning of future actions, all characteristics of ADHD. These OTMP deficits have negative repercussions on multiple aspects of youngsters' function, including academic performance. For example, poor organizational skills result in misplacing or losing materials at school and home, forgetting to bring home materials needed for school assignments, losing or forgetting to bring completed homework to school, etc. Further, a poor sense of time (11,12) and deficiencies in time management, coupled with procrastination and inefficient planning add to the difficulty ADHD children have in starting and completing daily, as well as long-term academic assignments. Not surprisingly, these related difficulties lead not only to suboptimal academic work, which impacts negatively on the children's scholastic performance and grades, but also frequent conflicts with parents and teachers. Moreover, children's OTMP deficits affect social functioning. Lateness, and losing or misplacing materials needed for games and sports, impact negatively on peer relationships.

Of note, OTMP difficulties typically continue into adolescence and adulthood, and adversely affect work performance and occupational status. Follow-up studies of ADHD children grown-up indicate significant problems with fulfilling work expectations, working independently, and completing tasks (13). Moreover, in a norms adult ADHD rating scale (14,15), the factor that best distinguishes ADHD and nonimpaired adults is "inattention/memory problems," which consists almost entirely of items that reflect OTMP behaviors (e.g., "disorganized," "lose things I need," "don't plan ahead,"

"absent-minded," "misjudge time," etc.). These findings are consistent with the clinical description of ADHD in the DSM-IV.

Despite recognition of the salience of organizational skills in ADHD, there are neither comprehensive assessment measures of OTMP skills in children nor have there been efforts to develop and test interventions that specifically target OTMP deficits in ADHD. The Adolescent Subcommittee of Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD) Public and Professional Education Committee developed the classroom performance survey in 1995 (16). However, the instrument evaluates only a handful of OTMP relevant behaviors, and lacks normative data. Relatedly, the revised Conners scales, among the most widely used ADHD assessment and outcome measures, have a limited item pool for OTMP behaviors (two items on the teacher scale, and four on the parent scale). The Child Organization Hyperactivity Index (17), a 26-item parent scale includes items about organization of materials and time, but the 8-item subscale that has shown discriminative utility assesses a restricted range of OTMP behaviors. The Behavior Rating Inventory of Executive Function (BRIEF) (18), a measure for teachers and parents with representative norms for children and adolescents, has two clusters that assess aspects of organization of materials and planning and organization and appears useful in screening children for disturbances in some OTMP behaviors. Children with ADHD, learning disorders, and brain injury were more impaired than nondisordered children on these item clusters and on a general factor (Metacognitive Index) (18–20). However, the scale has numerous repetitions and non-specific items. Items overlap considerably with core symptoms of ADHD. As a result, the BRIEF does not provide a profile specific to deficits in organization, or details of OTMP behaviors necessary to develop interventions and monitor progress.

There is a similar dearth of validated OTMP skills intervention programs. In lieu of empirically based programs, there are published guides for teachers that highlight the need to instruct ADHD students in management of materials and schedules (21–23). Levine (23) has provided several guidelines for helping children with "persistent organizational failure." Remediation recommendations include strategies to: (1) provide children with assistance in managing their notebooks, (2) monitor their study areas to be free from distractions and clutter, and (3) develop awareness of time demands. These recommendations, though creative in addressing the needs of students with deficient OTMP skills, have not been put to the test.

Cognitive remediation for individuals with acquired brain damage has focused on the facilitation of OTMP skills. Many patients with brain injuries experience deficits in executive skills, including disturbances in planning and organization (24,25). Although some remedial training has focused on these deficits (26), efforts have primarily emphasized assistance to adults with loss of function. There are efforts underway in youngsters with sequelae from

injury, or CNS radiation or chemotherapy treatments, but their application to children with developmental disorders is unclear and effectiveness has not been established to date (27).

Classroom interventions in ADHD typically focus on improving on-task and related behaviors (28–30). Treatment studies rarely evaluate students' responses to the organizational demands in school settings, even though "persistent organizational failure" is recognized as a major problem (23). To our knowledge, no empirical studies have assessed the impact of OTMP interventions, which, if they exist at all, are small components of a larger treatment program (30,31). For example, a brief organizational skills treatment module was developed for the multimodal treatment of attention deficit hyperactivity disorder (MTA) school-based psychosocial treatment component (32). The behavioral strategies in this module integrated a variety of procedures, including prompting, external reinforcement (including contingency management and token economies), self-monitoring and self-reinforcement, all of which were intended to modify and improve organizational skills. Targeted behaviors included general organization of the child's desk and materials, organization of homework-related behaviors, and planning of long-term assignments. Additionally, in consultation with the children's teachers, MTA therapist–consultants reviewed the teachers' organizational skills and how they impacted on classroom functioning. The program allowed for flexibility in teachers' presentation of assignments and management of classroom materials in response to individual children's needs. However the organizational skills module was only a minor component of the MTA psychosocial intervention package. Moreover, because the MTA was not designed for component analyses, determination of the clinical efficacy of the organizational skills module was not possible.

Although there is an extensive literature regarding the effects of stimulant medication on the core symptoms of ADHD, there is a dearth of controlled studies that have evaluated medication's impact on children's organizational skills. A recent placebo (PL) controlled crossover study evaluated methylphenidate (MPH) effects on OTMP behaviors in nineteen 8–13 year old stimulant naïve youngsters with ADHD and organizational skills deficits. These deficits were ascertained via the Children's Organizational Skills Scale (COSS), a measure developed in conjunction with our training program (described in the following sections). Although children's OTMP scores were significantly improved with MPH compared to PL, 61% of children had COSS scores that were not normalized with MPH, and these youngsters continued to meet the study entry criteria for impaired OTMP skills (33).

In summary, although there has been increasing awareness of the deficits in EF among children with ADHD, there has been little systematic assessment of "real-world" functionally relevant organizational, time management,

and planning skills of children with ADHD. There have been even fewer efforts to develop treatments specifically designed to target these skills and to ascertain the utility of the intervention to ameliorate OTMP deficits, maintain improvements, and enable children to generalize treatment gains to new functional domains. In recognition of the dearth of OTMP assessment measures and interventions, our research efforts have focused on three interrelated activities: (1) instrument development, (2) treatment development, and (3) pilot intervention testing. These efforts are described in the following sections.

ASSESSMENT OF OTMP BEHAVIORS

In light of the paucity of OTMP behavioral measures, we considered the development of such measures an essential component of treatment development and evaluation. Thus, the first goal was to develop "real-life" measures of OTMP skills to (1) inform the development of the training program, including the content and focus of treatment; (2) identify each child's specific areas of impairment, and (3) assess treatment outcome. To this end, we developed parent, teacher, and child self-rating scales to determine children's OTMP skills, and to identify specific problem areas in these domains.

Children's Organizational Skills Scales

Development of the scales was conducted through consultation with clinicians, teachers, and parents to obtain behaviors that reflected the day-to-day organizational difficulties that children with ADHD demonstrate. Lists were composed, critically evaluated by parents and teachers, revised to alter reading level, and compiled into versions that were used to gather data on a normal sample of children in the New York Metropolitan Region. Ratings of children by teachers, parents, and children were obtained. A sample of over 900 third to eighth grade children was rated by teachers and a separate sample of 137 children was rated by parents and themselves. Analysis of the teacher ratings (using principal components factor analysis with varimax rotation) yielded a three-factor solution: "organized behaviors" consists of 11 items that describe actions that facilitate school efforts, the effective use of organizational tools such as folders and calendars, and neat results (e.g., "This student is organized"; "This student makes lists, schedules, and reminders to keep him/herself organized"); "lapses in memory and materials management" consists of 11 items reflecting problems in forgetting assignments, forgetting the materials needed for those assignments, and losing, misplacing, or poorly organizing materials for assignments (e.g., "This student has trouble finding school supplies when they are needed"; "This student loses things at school"); and "task planning," which consists of 6 items that reflect actions related to time management and steps needed to complete a plan (e.g., "This student seems

to run out of time before assignments are finished"; "When this student has a big project to do, he/she doesn't know where to begin"). In addition, a "cross-factor cluster" consisting of 7 items that load on more than one factor was retained because the items reflect important functional concerns that have implications for day-to-day functioning (e.g. "The child's backpack is messy"). A 41-item version of the measure, which includes 6 items that assess the degree of impairment associated with these skills deficits, is used to provide the clinical profile for intervention and ranking on the factors. The measure has been found effective in distinguishing children who receive supplemental special educational services from those that do not and in distinguishing girls from boys in the normative sample. Children who obtain special educational services and boys were rated as less effective on all factors. An independent sample of clinically diagnosed children with ADHD has been found to be significantly more impaired on all factors and the cross-cluster items (34).

Smaller sample sizes have prevented the completion of a factor analysis of the parent and child versions. Thus far, only a Total summary score has been utilized with the parent version. Significantly, a sample of children with ADHD has a lower total score on the parent COSS, reflecting less effective organization. Arrangements to obtain a nationally representative sample are under way. All three versions of the COSS will be used to obtain multiple-rater information on each child in the sample. Analytic strategies for this sample include reliability studies, validity studies, confirmatory factor analysis on the teacher version, and initial factor analysis on the parent and child versions of the scale.

OTMP INTERVENTION PROGRAM

Rationale

The intervention program was developed for 8- to 11-year-old children with ADHD, in grades 3–5. This age group was selected to reflect the elementary school grades in which demands for independent function become salient. The program attempts to ameliorate OTMP deficits through the use of child-focused behaviorally based skills training facilitated via the involvement of parents and teachers. Skills training that incorporates important adults in the child's environment has been shown to be an appropriate behavioral treatment strategy for ADHD children (30,35). It is not assumed that the intervention directly affects the putative deficits in EF theorized to underlie ADHD symptomatology. Rather, our position is that children can be taught to minimize their functional consequences. If proven effective, the treatment is intended to serve as an important adjunct to other validated treatments such as pharmacotherapy and parent management training, and not as a stand-alone intervention for the treatment of ADHD.

Overview of Treatment Principles and Features

The 10-week, 20-session manualized, flexible individual intervention program consists of a number of integrated procedures that are intended to maximize the development and appropriate use of OTMP skills in children with ADHD. There are several key principles and assumptions upon which the intervention is based. These are described in the following sections.

Treatment Tailoring

There has been increasing recognition of the need to incorporate tailored treatment strategies in ADHD interventions (36–38). The training program consists of modules that focus on specific OTMP skills (e.g., management of materials, planning for short and long-term projects, use of organizational aids, and time management). Although all children are exposed to all training modules, the emphasis placed on each module is individualized for each child. A needs assessment approach is used to identify each child's relative OTMP strengths and deficits so that tailoring procedures can target OTMP skills that have been determined to be especially salient for each child.

Needs assessment is ascertained via consideration of information from several sources. Each child's OTMP domain scores on the teacher, parent, and child versions of the COSS are compared to each other and to normative levels to determine the child's relative deficits in the OTMP skills domains targeted in the training program. Additionally, discussions with the teacher, parent and child are used to confirm the initial interpretation of the child's OTMP scores and to better clarify the specific nature of each child's difficulties.

As per procedures implemented in the MTA school consultation program (32), teacher interventions are individualized as well. Careful attention is paid to establishing a relationship with the teacher and assessing his/her current classroom behavioral and environmental procedures relevant to OTMP behaviors (e.g., use of homework assignment sheets, side-of-desk folders for each academic subject, etc.). Rather than foisting an inflexible protocol on teachers, clinicians assist teachers to use whatever strategies from the OTMP intervention protocol are feasible. In addition, teachers are involved in decision-making processes to assure that behaviors selected for intervention are socially valid (i.e., important to the teacher, and therefore likely to be reinforced by the teacher).

Skills Acquisition

The intervention program is based on the assumption that children with ADHD are more likely to use skills appropriately if they have demonstrated a high level of skills acquisition. Thus, shaping and successive

approximation procedures are used early on in each training module to facilitate the initial stages of skills acquisition. This is followed by multiple opportunities to practice and master target skills during and in-between clinic-based sessions. The behavioral skills training approach integrates a number of behavior therapy strategies, including verbal instruction, modeling, behavioral rehearsal with feedback, cueing and use of lists, behavior prompting and reward, self-monitoring, as well as guided and rewarded practice between sessions.

Generalization

To be successful, ADHD intervention programs that target broad functional domains, such as social skills, require that the children learn and/or hone these skills in training and use them appropriately in a host of complex, multidimensional interpersonal situations and contexts. Unfortunately, these programs have been relatively unsuccessful. We considered possible reasons for their limited effectiveness. By their very nature, such training programs, whether they occur in the clinic or in specialized treatment settings, restrict the opportunities to provide training and practice in the exact interpersonal situations that a youngster confronts in daily life. Consequently, to use these broad functional skills appropriately, a child must demonstrate generalization skills in an extremely wide-range of heterogeneous social situations. That is, the child must recognize that the situation (s)he is confronting is a variant of the situation encountered in training (stimulus generalization), and then engage in social behaviors that are often a variant of the specific social behaviors focused on during training (response generalization). The disappointing results of social skills training programs (39) attest to the difficulty in achieving generalization effects.

In contrast, the OTMP skills targeted for intervention in this program focus on a somewhat circumscribed set of behaviors and recurring situations (e.g., getting ready for school, leaving school, initiating and completing homework). As such, there is an opportunity to target a relatively delimited number of skills and settings. Because these specific skills are typically required in real-world settings that do not vary much from day-to-day, the child has the opportunity to practice and refine these specific skills on a regular basis.

Notwithstanding the relatively limited range of situations requiring the use of OTMP skills, the intervention program incorporates systematic approaches throughout training to facilitate and evaluate generalization effects. Included here are efforts to involve parents and teachers via training in prompting, cueing and reinforcement procedures to be used with the child throughout the training program. Between-session practice and homework assignments are also included as generalization aids. Numerous exemplars are used in training to facilitate generalization, including the use of the child's own school-related assignments and materials.

Reinforcement

To facilitate learning of new OTMP skills and increase the children's motivation to use these skills outside of training, reinforcement procedures are used throughout the training program. During clinic-based sessions as well as between training sessions, a variety of contingency-based reward procedures are implemented. For example, to facilitate tracking and monitoring of assignments, tests and managing materials, children are taught to use a daily assignment record (DAR). By using step-wise training procedures, children learn to use the DAR to write down homework assignments for each subject, their due dates, and the exact materials that are needed to complete this assignment. The teachers provide feedback (by signing the DAR) in accord with the specific step(s) focused on in training. Teacher feedback is backed up with reinforcements provided by parents at home. Eventually, with the inclusion of cues (e.g., a small "reminder" card attached to the child's book bag zipper), at the end of each school day the youngster self-monitors whether all the necessary homework-related materials are in the book bag. Similar procedures regarding materials management are used at home.

Maintenance

A primary intervention goal is to facilitate OTMP skills maintenance after the completion of training. To this end, maintenance probes are conducted throughout the program. These probes, which rely on parent, teacher and child ratings and reports, are intended to evaluate whether learned skills, no longer targeted directly in clinic sessions, continue to be used appropriately outside of training. Problems regarding maintenance of specific skills are followed-up by reexposure to and reinforcement of these skills in and outside the clinic. Additionally, at the end of treatment parents are provided with an owner's guide, which provides a summary of training procedures and copies of key forms used in treatment. Therapists discuss with parents how they can make use of the guide once treatment has ended.

Engagement

Children function as collaborators in the treatment process. The tone of treatment emphasizes the mutual efforts that the child, therapists, parents, and teachers are making to overcome the impact of ADHD on the child's life. In the process, training exercises, although understood as having a serious intent, are playful and interactions with the child are informal. Also, to foster an alliance with the child and to facilitate engagement in the goal, children are presented with a rationale for overcoming the effects of ADHD so that the disorder does not interfere with their success. Similar to successful efforts used to help children overcome anxiety disorders utilized by Kendall in his Coping Cat procedure (40) and March

and Mülle (41) in their method to "Run OCD Off My Land," we describe the child's and helpers' goal as "Controlling the glitches" that interfere with: keeping track of materials, remembering items and events, managing time, and planning steps. We use drawings to convert the "glitches" into characters that reside in the minds of people. We also provide children with workbooks that help them keep another aspect of their mind, the "mastermind," as active as possible in controlling the glitches. Our methods are intended to enhance success by objectifying the disorder's impact, by making the treatment "child-friendly" (42), by creating a collaborative team, and by converting the conflicts often encountered by the child when he or she fails to remain organized into fun exercises that can be incorporated into new habits.

Overview of OTMP Program

Treatment consists of 20 sessions, which occur twice weekly for 10 weeks. The content of the sessions includes: (1) parent and child Orientation; (2) parent guidance in building new skills through behavior modification; (3) module for keeping track of assignments; (4) module for organizing materials and papers; (5) module for time management; (6) module for planning tasks; (7) module on transfer of skills to other typical activities; (8) maintenance module; (9) phone contact and coaching; (10) graduation ceremony and a child's video-taped summary of skills learned and skills to be kept.

Parents and children are oriented to the program to help them understand the model of training utilized so that they are invested in the process. Participants are informed that evidence suggests that persons with ADHD learn new behaviors (even those that seem easy to carry out) most effectively when those responses are prompted in detail, when the responses are monitored carefully, and when the responses are praised and rewarded. Repetitive practice of small behavior chains is described as a necessary step for building skills, leading to skills mastery. This strategy is considered a viable means of increasing the likelihood that the behaviors will become embedded in the child's habitual response to situations that call for OTMP skills. Each training session integrates behavior therapy procedures to build skills through psychoeducation, modeling, guided practice, prompting and practice with reward in several situations, and use of home exercises to utilize the skill in the child's usual routine. Teachers as well receive training in the use of prompting and labeled praise. Teachers are asked to monitor the results of the child's efforts on the DAR, to be sent home each day. Graduated privileges are provided to the child based on the success indicated by the DAR. Thus, prompting, reinforcement with rewards in several settings, and repetitive practices are used to facilitate skill development.

Generalization Procedures

Overview: We adhere to a specific model to monitor and train for generalization in the main training modules (i.e., materials management, time management, and planning). First, training is conducted in the clinic setting for a specific task, and ratings of how well the child completes that task at home and at school are gathered. The task is practiced in the clinic session with a number of trials. The trials involve situations that are similar to the child's day-to-day circumstances. However, to facilitate generalization and recognition of the steps involved, a "fantasy" situation is also presented. Next, children explain the skill steps to parents and parents are educated to prompt and praise the use of those skills at home on a daily basis. Third, prompting and praise for use of the steps in school is fostered through the use of teacher consultation procedures used in previous clinical trials (32,43). Fourth, other situations that require the same skills are monitored and rated by parents and teachers to determine generalization across tasks.

Training Example: For example, when working on space and materials management as applied to a desk work area, children are presented with steps to review as they prepare to complete work. They are trained to determine what materials are needed for the task, what materials are present on the desk, what materials need to be added to the supplies present, and what materials need to be put away because they are unnecessary and may be distracting. They are presented with a task involving writing, a task involving taking notes from a book, a task to construct a 3D model, and a task to complete math problems using a ruler and calculator. As a generalization "fantasy" task, they may be asked to use the steps to prepare a work area for mapping a rocket ship course to Mars. Additionally, parents are trained to prompt and monitor the steps as the child completes daily homework. Teachers as well are asked to monitor the child's material and space management for select times during the school day. Parents and teachers rate the child's use of skills and the end result in-between training sessions. If the child has a low rating at home, the clinic setting is used to simulate home situations and practice continues until parents report an effective transfer of skills to the home setting. Meanwhile, teachers report on the school desk. The DAR provides information for monitoring by the treating clinician. Training in the clinic setting that simulates the school desk is or is not conducted depending on the teacher's report. Thus, application of the skills in several settings is monitored and addressed as needed to facilitate generalization across situations.

For task generalization, parents monitor the child's organization of his/her school book bag or backpack. How well the child puts in necessary items and keeps out unnecessary items are tracked. This information is used

to determine how effectively skills are applied to similar tasks. Specific training is utilized in this task if transfer is not documented. For further extension, children's use of other bags for sports equipment, for example, is reviewed and trained if necessary.

Recognizing Where and When to Use OTMP Skills: In addition to using multiple exemplars, a procedure recommended to facilitate generalization, other key generalization training procedures are implemented to help children learn to recognize when and in what situations OTMP skills can be used in their day-to-day activities. The recognition procedures include the use of between-session diaries where children list situations in which they believe that OTMP skills would be useful. Children are also asked to develop a label for each skill and are asked to list when they used the varied skills. Relatedly, parents are asked to keep a separate diary of episodes in which they observe their children using OTMP skills. Finally, children are directed to review their upcoming schedule and anticipate when OTMP skills could be used in those activities.

Maintenance Procedures

A systematic sequence to fade prompts and rewards is followed to facilitate maintenance in the natural environment. As a first step, the number of steps prompted to complete a task is decreased in a planned way. For example, when space management for the work area is the task, prompts to place materials into groups and to leave a clear area for writing may be faded to the single prompt: "Please straighten out your work area." Rewards are provided for the end goal. Eventually, all prompts are faded and children are monitored and rewarded. Rewards are eventually faded to an intermittent schedule. Initially, praise and rewards are available as the task is ongoing; subsequently, they are faded to task completion, and then to daily, weekly, and longer time periods. Following fading, subsequent "maintenance probes" are used to determine if behavior has become embedded in the child's repertoire. Behaviors that are not demonstrated appropriately receive additional training.

Treatment Adherence and Fidelity

Measures of treatment adherence are implemented throughout the training program to ascertain the degree to which children, parents, and teachers carry out requisite treatment activities. Tracking adherence includes monitoring children's between-session "home exercises," including completion of calendars and school-assignment planners, parents' record sheets of behavioral procedures implemented at home, and teachers' completion of the DAR. Similarly, in-clinic sessions are monitored to track treatment fidelity and integrity.

Manuals Features

The treatment manual ("Organizational Skills Training"; OST) consists of specific instructions for each session.

Session Guidelines: Each session contains descriptions of the session goal and target skills, an overview, rationale, tasks, and the materials required. Detailed descriptions of the content of each session are presented, including the behavioral procedures to be implemented in the session tasks. Specific guidelines for in-clinic, home, and school activities are provided. Between-session "home exercises" are specified for the child, parent, and teacher.

Treatment Monitoring Forms: Each session contains treatment adherence, treatment fidelity, and performance forms. Treatment adherence forms track the degree to which the previous session's assignments were carried out; treatment fidelity forms track how much and which components of the session were completed during the session; session performance forms assess how well the child performed the session tasks.

Pilot Study of Intervention

The OST program was evaluated for feasibility and effectiveness in an open pilot study in 20 children with ADHD and organizational skills deficits. The youngsters were in grades 3–5; 60% had a diagnosis of ADHD Inattentive type and 40% Combined type; 50% were receiving stimulant treatment in the community and the remainder was medication free. Treatment was delivered by behaviorally trained Ph.D. clinical psychologists. The findings were positive and provided a signal of the intervention's effectiveness. Significant pre-post improvements were found on: teacher and parent ratings on the COSS ($p < 0.01$); parent ratings of homework problems ($p < 0.05$); and children's performance on an academic planning task ($p < 0.001$). Improvements were not related to children's medication status or type of ADHD. No children dropped out of the program, and there was a high level of attendance, with all youngsters completing at least 17 sessions. Further, both parents' and teachers' ratings indicated satisfaction with the program.

Future Directions

We are currently evaluating the efficacy of the OST intervention in the context of a dual-site randomized controlled trial. The study design includes a wait-list group to control for the effects of repeated assessments and time, and an active treatment comparator. The latter, entitled "Parents and Teachers Helping Kids get Organized" (PATHKO), excludes any skills training with the child. Rather, it utilizes contingency management procedures, implemented by parents and to a lesser extent teachers, to target the end results of behavior

chains that are likely to require effective OTMP behaviors (e.g., bringing home school assignments, handing in work on time), and reinforces children for engaging in relevant OTMP identified "end behaviors."

In addition to comparing the impact of skills versus performance-based interventions on children's organizational and academic functioning, the study is designed to evaluate maintenance and moderator effects. To this end, children's functioning is evaluated during the school year following their participation in treatment, and the moderating effects of parental ADHD on outcome are assessed as well.

Finally, the study includes children with OTMP deficits, regardless of their medication status. This sample will enable us to explore whether medicated children, whose OTMP deficits presumably reflect a skills rather than performance deficit, show greater improvement with OST than PATHKO, Such findings would have important implications for tailoring treatment interventions based on the nature of children's OTMP impairments.

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14

School Consultation for the Mental Health Professional Working with ADHD

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RATIONALE FOR SCHOOL CONSULTATION BY THE MENTAL HEALTH PROFESSIONAL

For a mental health professional trained in traditional approaches to therapy with children and adolescents, it may be tempting to follow a practice of primarily conducting individual therapy with the youngster, additionally conferring with the parents. However, therapists with current knowledge of attention deficit hyperactivity disorder (ADHD) treatment will be far more likely to conduct behaviorally oriented family therapy to address the primary and secondary behavioral concerns often associated with ADHD. This includes creating structure within the home that facilitates follow-through with instructions, reducing oppositional behavior, alleviating "homework hassles," and establishing rules and contingencies to prevent and deal with problems. While these strategies will address difficulties occurring within the family, they will not be sufficient to address the youngster's difficulties at school. Improvements at home likely will not generalize to the school setting, and similar approaches will need to be employed there (1). Ideally, the school personnel will be well-trained in working with youngsters with ADHD, and perhaps school-wide interventions, or at least strategies to assist the particular youngster, are already in place. Often, however, this is not the case. The main point of this chapter is that mental health professionals treating youngsters with ADHD need to be proficient in school consultation skills. Such consultations typically involve visits to the school to develop strategies and to assist with their

implementation. When assessing problems or requesting that particular strategies be implemented, mental health professionals should not rely exclusively on written contact with the school, telephone calls, or using the parents or the youngster him/herself as a conduit.

For several reasons, the mental health professional is the ideal person to assist the school with interventions for ADHD. First, he or she knows the youngster and family. Youngsters with ADHD may have depression, anxiety, troubled families, poverty, and any of the other mental health problems and psychosocial stressors endured by those without ADHD. The youngster's ADHD or that of another family member also may predispose the youngster to any of these conditions (2). The mental health professional often is the individual most aware of these issues in a child's life, and is in an ideal position to interpret these issues to school personnel. Second, the mental health professional usually has expertise with medications for ADHD and is in the best position to facilitate treatment that maximizes the effects of both medication and classroom interventions, possibly even making it possible to reduce medication doses (3). Third, he or she can facilitate communication between the school and home, and reduce the tendency for these interactions to become adversarial.

CONSIDERATION OF RESEARCH IN SELECTING INTERVENTIONS

Interventions selected should be supported by research. They should be feasible for the setting and acceptable to those who will be involved in implementing them, as well as to the youngster him/herself. Mental health professionals who are abreast of the literature pertaining to the treatment of ADHD may have concerns about the recently published MTA results suggesting that psychosocial interventions, including school consultation and school-based behavioral strategies, do not offer an incremental benefit over stimulant medication in the treatment of ADHD (4). While this interpretation of the MTA results is accurate when interpreting the effects of the treatments on ADHD symptoms in the overall study sample, mental health professionals should be cautioned that the issue is far more complicated, and any implications of the MTA for community practice are unclear. First, not all youngsters with ADHD receive stimulant medication, for reasons that include parent and/or student preference and adverse side effects. Second, the abundant literature on the management of disruptive behavior in the school setting informs the practice of ADHD intervention in the school setting. Medicated or not, a youngster's disruptive behavior must be dealt with. Third, youngsters with ADHD, medicated or not, typically exhibit disorganization and inattention, both of which can be fatal to school success. While research targeting these behaviors is less extensive than research targeting disruptive behavior, well-documented

strategies do exist, and work is continually being done to expand this area. Fourth, the medication protocol followed in the MTA was far more meticulous than that typically employed in community practice, and it is logical to infer that benefits accruing from medication will be more variable than those attained in the MTA (5). Fifth, the MTA children who had both comorbid conduct problems and anxiety responded best to the condition that combined psychosocial intervention and medication (6).

STEPS IN PROVIDING SCHOOL CONSULTATION

Prior to conducting a school consultation, it is important to gather relevant information. Comparable to the information gathered in the process of assessing for ADHD, this should include an in-depth history of the child, including family, school and home behavior, health, social, and academic. It is helpful to know what school interventions have been particularly helpful for this youngster in the past. In addition to checklists that assess for the presence of ADHD-related behaviors, behavior rating scales that assess for social or emotional difficulties and atypical behavior should be obtained from all teachers presently involved with the youngster. Having this information in advance of the school visit enables the mental health specialist to consider the teachers' concerns while observing.

The next step should be a planned observation of the youngster in the school setting. There are published methodologies for conducting the observation (7), or the observation may be informal, but it is important to observe the youngster in as many as possible of the settings where he or she reported to be experiencing difficulties. The key here is that the manifestation of ADHD-related behaviors in any particular setting should be viewed as a function not only of the ADHD, but also of the characteristics. Ultimately, it may prove easier to modify aspects of the setting than to change the ADHD itself. For the observation, relevant characteristics include, but certainly are not limited to:

- teaching style (enthusiasm, clarity, warmth, confidence, etc.),
- teacher's typical responses to off-task or disruptive behavior exhibited by any student,
- degree to which distractions are present,
- aspects of the classroom organization such as seat arrangement and placement of shared materials,
- extent to which a clear time limit is imposed for completion of individual tasks,
- interest level of instruction and other tasks, and
- degree to which youngster possesses the academic and organizational skills needed to comply with teacher's expectations.

The next step is to meet with the teacher(s) and any other relevant personnel. To facilitate communication and cooperation among all those helping the youngster, it is most helpful to invite the parents to this meeting, and often the youngster as well, particularly at the high school level. Involvement by members of the student support team (SST) can be very helpful in the process of generating ideas, as SST members ultimately will be involved in the implementation of interventions and in the process of maintaining those interventions as the youngster moves to the next grade. Interventions should be designed collaboratively, along with a plan for ongoing evaluation of their success. They should target specific behaviors of concern and strategies should be specific, along with procedures to monitor their effectiveness. The roles of the mental health professional, teachers, and others should be spelled out.

Finally, follow-up should be systematic. Subsequent visits to the school may be necessary, or phone contacts with key personnel may suffice. Behavior rating scales should be used at regular intervals to assess the extent of remaining problems, just as they are used for medication monitoring. Often, follow-up can be accomplished through office visits to the mental health professional and phone calls to the school, but when school difficulties persist, or when issues change, successive visits may be needed.

TECHNIQUES THAT CAN BE APPROPRIATE OUTCOMES FOLLOWING CONSULTATION

Techniques based on contingency management—systematic positive reinforcement of appropriate behavior and systematic ignoring and punishment of inappropriate behaviors—can be highly effective. Systematic verbal feedback by the teacher has been demonstrated to be a powerful consequence in classroom management. In particular, reprimands that are firm, delivered in a neutral as opposed to emotional manner, brief, and as immediate as possible following the onset of off-task behavior have been shown to be a key component of successful management of off-task and disruptive classroom behavior (8). To initially establish their maximum effectiveness, the teacher should pair reprimands with back-up consequences, generally loss of a privilege, as needed. Besides teacher feedback, one of the best supported interventions is home-based contingencies, also referred to as a daily report card, or DRC for short. With this procedure, the teacher rates several specific behaviors on a checklist that the child brings home daily. Parents can provide praise and other positive consequences contingent on a positive report; sometimes loss of points or a privilege are made contingent on a negative report or failure to bring the DRC home (9). Other strategies include systematic use by the teacher of positive reinforcement, including points toward tangible rewards and privileges; response cost, involving loss of points or direct loss of privileges; and extinction

(ignoring) of minor inappropriate behaviors. Relatively simple yet sophisticated systems utilizing these approaches can be tailored using individualized checklists for particular youngsters or implemented as classroom-wide strategies (8). Peer-mediated interventions, where the teacher enlists peers to withhold attention from the youngster's inappropriate behavior and where the whole group benefits from supporting his or her appropriate behavior, can also be very useful. Peer-mediated strategies have an advantage over exclusive use of direct contingent reinforcement administered by the teacher, in that they can dramatically reduce the amount of peer reinforcement of inappropriate behavior that is competing with teacher-administered reinforcers, thereby decreasing not only the amount of teacher effort expended on counteracting peer attention, but also lessening the need for punishment (8).

In addition to strategies based on principles of contingency management, and particularly to address behaviors primarily reflecting inattention and disorganization, the mental health professional may suggest modifications of the classroom environment, the way tasks or instructions are provided, or the nature of the tasks themselves. Excellent resources are available that list suggest modifications along these lines (10,11). Some commonly recommended strategies include shortening the length of tasks, providing more frequent feedback to youngsters as they work independently, varying the type of activity to reduce boredom, and providing the youngster with a quiet area shielded from classroom stimulation. However, in the author's experience, such recommendations are best offered, and tailored to the youngster, following an observation that focuses on the specifics of a particular classroom and teaching style.

SPECIAL CONSIDERATIONS FOR SECONDARY STUDENTS

Managing ADHD within middle schools and high schools is challenging. These settings demand a high level of organization with respect to assignments and materials, and youngsters with ADHD often need ongoing assistance. Securing consistency between teachers in applying systems involving contingency management or organizational strategies is challenging. Finding relevant reinforcers and negative consequences becomes far more complicated for older students. Several consultation techniques can be useful in addressing these challenges. First, the mental health professional should try to involve a central person through such as the team leader (middle school) or guidance counselor (high school) for obtaining rating scales from teachers, scheduling the visit, and coordinating the meeting that follows. This is more effective than the mental health professional's trying to communicate individually with teachers. Second, secondary teachers may be reluctant to provide accommodations, particularly because ADHD is an "invisible" disability whose

symptoms they may attribute to poor motivation or disinterest. This issue must be addressed forthrightly, and the follow-up meeting is an ideal forum in which to do that. Often, some members of the school team are quite enlightened regarding ADHD and the need for accommodations, while other members are not. The consultation meeting can provide an ideal forum for less enlightened teachers to hear from their peers about strategies they use to assist youngsters with ADHD, and considerable attitude change may result from this discussion. Third, the youngster him/herself often can be included in meetings whose goal it is to establish accommodations. With the support of the mental health professional, the student can become skilled in communicating with his/her teachers about his/her needs. This can have the added benefit of helping the youngster be seen by his/her teachers as positively involved, rather than unmotivated or oppositional.

When working with teens with ADHD, the mental health professional often is addressing issues of depression, struggles with peer relationships, academic failure, planning for the future, and temptations regarding substance use, among others. As compared with school personnel, the mental health professional often is better positioned to integrate information from all available sources including school, parents, and the youngster, as well as knowledge about educational and vocational choices that can capitalize on the youngster's strengths and avoid pitfalls. The information gleaned through therapy with the teen and his/her parents should be shared as needed (and as requested by the family) with the school, in support of a genuine team effort to address the ADHD and the related concerns.

FORMALIZED SPECIAL SERVICES

Many youngsters with ADHD exhibit considerable residual symptomatology despite good efforts at treatment. In such cases it is often advisable to formalize the intervention plan via an individualized educational program (IEP). This plan serves as a guarantee that the necessary services will be provided, specifies personnel and amount of service, and indicates goals and objectives for academic and behavioral targets. For ADHD, the two primary avenues to obtaining an IEP are special education eligibility under the 2004 revision of the Individuals with Disabilities Education Act (IDEA) and Section 504 of the Americans with Disabilities Act. Any mental health professional working with youngsters with ADHD who wants to conduct meaningful school consultation should be familiar with the provisions of both, including the circumstances under which it is advisable to request that the youngster's eligibility for either be considered by the school. Depending on the presentation of the youngster's issues, one or the other may be the more appropriate avenue to pursue. In general, it is more difficult for a youngster to qualify for an IEP under IDEA than 504.

Within IDEA, ADHD falls in the category other health impairment (OHI). When other difficulties besides ADHD are present, such as significant behavioral or learning problems, the OHI eligibility can be preferable, as the IEP process includes a broader range of services and guarantees than is involved with 504 plans, which involve only accommodations. For example, under IDEA the IEP specifies any additional "related services" for which the youngster is eligible, such as speech and language therapy or occupational therapy. There is also a section that specifies a behavior intervention plan for the youngster. Further, the IDEA IEP provides for any academic support for which the youngster qualifies, such as the services of a learning disabilities specialist.

In contrast to IDEA, IEPs written under 504 are designed only to specify accommodations made necessary by the youngster's condition, in this case ADHD. Typical accommodations include additional time or a quiet place in which to take tests, a reminder system for homework assignments, class notes supplied to the student, extra time for completion of work, and notification to parents of both due and uncompleted assignments. Accommodations such as these are commonly included in IEPs written as part of OHI eligibility as well.

An important provision of IDEA is that it mandates a SST, sometimes known by other names such as "child study team," at each school. This team evolves into the eligibility committee that considers the question of special services, and then into the committee that designs the IEP. Membership changes as appropriate, but includes both regular and special education teachers, an individual qualified to supervise special education services, the school psychologist, others such as the guidance counselor, and the parents. This team meets regularly to discuss all youngsters who are experiencing difficulties at school, provide teachers with strategies to address these, and evaluate the success of these strategies. The SST manages the process of determining whether a youngster should be evaluated for special education support under IDEA, or for accommodations under Section 504. Mental health professionals should become comfortable attending SST meetings when their input is needed, and likely will find that communicating with SST members as needed can facilitate the consistent provision of services to the youngster. Often the mental health professional must play an advocacy role in order to facilitate the process of having the youngster found eligible for services, seeing that the necessary services are written into the IEP, and ensuring that the school follows through with the provision of the services.

CONCLUSION

School psychologists and other school personnel, including teachers, guidance counselors, and administrators, have increasingly taken up the

challenge of providing the necessary services to youngsters with ADHD. It has been the author's experience that school personnel are increasingly aware of empirically supported interventions. With this trend, the primary responsibility of the mental health professional in the school consultation process can shift from that of educating school personnel about ADHD to one of collaborating with the school to provide smart, sophisticated interventions that hone in on the youngster's difficulties without being excessively burdensome to teachers. No matter how great a youngster's need may be for school intervention, the mental health professional should remain keenly aware of the amount of responsibility teachers carry for large numbers of students. Interventions should not overburden teachers. Just as the mental health professional must advocate for services for youngsters, they should also urge support for the teachers who must implement those services. Mental health professionals involved in school consultation should look for opportunities to influence policies—Federal, state and local—that impact services provided to youngsters with ADHD.

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Daily Report Cards

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HOME-BASED TREATMENT FOR ACADEMIC AND BEHAVIOR PROBLEMS IN THE CLASSROOM

Barkley (1) stresses the importance of parent involvement in the management of the academic performance of attention deficit hyperactivity disorder (ADHD) in children. Home-based behavioral interventions include teaching parents how to deliver time-out, the use of token economies, and contingent attention (2). Academic interventions in the home include homework routines, goal setting and contingency contracting for homework (3), and response cost and positive reinforcement contingent on academic performance (4,5). Grolnick and colleagues (6) note that parents' involvement in their children's academic career is associated with children's success in school. Parents have an important role in their children's education, and home–school communication has been shown to lead to better educational outcomes (7). One way to facilitate such a relationship is to involve both parent and teacher in home-based interventions for classroom problems.

ADVANTAGES OF DAILY REPORT CARDS

A daily report card is a home-based classroom intervention that allows parents to receive frequent feedback about their child's classroom behavior. The reports are completed and sent home daily by the teacher. The notes contain information rating the student's performance on that day. Parents are responsible for providing rewards for the child's appropriate behavior. Home-based intervention has many advantages over school-based intervention.

Daily report cards, also known as school-home notes, provide increased communication between parent and teacher and encourage greater parent involvement. This is a vast improvement over the more common practice of parents receiving intermittent, negative feedback from the school when children misbehave. School-home notes allow parents to offer powerful reinforcers that may not be available to teachers at school. Also, daily report cards are a quick and simple intervention, making them more likely to be utilized by teachers. The use of the note relieves teachers of the duties to discover effective reinforcers for the students and to spend time providing consequences. The note puts these responsibilities on the parents of each individual student. The simplicity, ease, and non-time-consuming nature of daily report cards are valuable advantages of this home-based intervention (8).

DECIDING TO UTILIZE A DAILY REPORT CARD AND DEFINING TARGET BEHAVIORS

Daily report cards may be individually tailored to suit a wide variety of students with a range of classroom problems. Children as young as preschool and as old as high school may receive treatment benefits from school-home notes. They have proven effective in reducing behaviors such as talking in class, leaving the desk without permission, and other disruptive behaviors. Daily report cards also have been used to increase positive behaviors such as paying attention, completing positive social behaviors, and following teacher instructions. Although positive changes in classroom behavior are often accompanied by improved grades, specific academic behaviors may also be targeted, including completing and properly turning in classwork and homework. School-home notes have also been utilized as a treatment component for strengthening appropriate behaviors that are inhibited by anxiety. Targets may include working without crying for school-phobic children and talking in a loud voice for shy or selectively mute children. However, much of the literature on the efficacy of daily report cards has focused on externalizing behavior problems and students with ADHD.

Another consideration in the design of the note itself is its comprehensiveness. Students may be evaluated during multiple intervals throughout the day, such as every class period or before and after lunch, or at one specific time of day, such as lunchtime or math class.

Essential to the success of daily report cards are parents' willingness and commitment to review the note daily and provide contracted consequences consistently. It is also necessary for teachers to consistently and fairly complete the report card. It is important that the child is able to perform the behaviors defined by the note. For example, a student with a learning disability may not be capable of completing class assignments

without additional help. Such a case may be better treated with an academic intervention plan.

After deciding to implement a school-home note, parents and teachers, as well as a consultant if available, should collaborate in determining the behaviors to be targeted by the note. They should include socially valid behaviors important to the child's academic success, such as "completed classwork" and "followed directions." Conduct behaviors including "kept hands to self" and "talked only with permission" may also be included. It is essential to define each behavior as operationally as possible in order to decrease the subjectivity of its ratings. Also, the target behaviors should be stated positively, as behaviors to increase rather to decrease. For instance, if a student is perpetually leaving his seat in the classroom, the behavior to be rated by his teacher on his school-home note should read "stayed in seat" rather than "left seat without permission."

HOW TO IMPLEMENT A DAILY REPORT CARD

Kelley (8) offers general guidelines for the use of school-home notes. Parents and teachers should be trained in the use of basic contingency management procedures. The note should evaluate the target behaviors during several different time intervals throughout the day, giving frequent, time-specific feedback about student performance. Parents, students, and teachers should collaborate when developing performance goals and appropriate reinforcement. They should all be involved in constructing a "contract" outlining what constitutes appropriate behavior and, in turn, a "good note" worthy of positive consequences.

The majority of daily report card interventions require parents to positively reinforce any acceptable notes brought home with either tangibles or activities that the child may enjoy that day after school. Praise alone does not appear to be adequate. Typically, parents are not instructed which specific reinforcers to utilize, but common suggestions in the literature include: special snacks, TV time, late bedtime, verbal praise, and freedom from chores (9–11). The daily behavioral criteria for earning rewards are spelled out in the contract. For example, one child's criteria for an acceptable note may be 8 of 10 behaviors rated by the teacher as good or fair and only 2 or less rated as bad. The school-home note contract should also include specific rewards that may be earned based on the performance ratings. Many home-based reward programs include more valuable weekly rewards in addition to smaller daily rewards.

The daily report card should be reviewed by the parent with the child each day. Parents should attempt to focus equal time on the positive and negative ratings received by the child. After proceeding through the entire note from the beginning of the child's day to the end, parents are

encouraged to provide the contracted consequences as soon as possible. The reward given should be recorded in order to document treatment integrity.

RESEARCH ON TREATMENT OUTCOME

Ayllon et al. (12) used a "good behavior" daily report card targeting disruptive behaviors including out-of-seat, vocalizations, and any motor activity that interfered with the other students' studying in a third-grade classroom of 23 children. Parents provided appropriate rewards on days the child's behavior warranted a "good behavior" letter. The average level of disruption decreased from 90% during baseline to zero during the treatment phase. In another study, Blechman et al. (13) used a "good news note" to decrease inconsistency of math classwork in a group of elementary students with inconsistent math performance. Teachers sent a note home on days the student's math performance equaled or exceeded performance during baseline. Parents delivered positive reinforcement on days the child received a "good news note." The note significantly increased consistency in math performance.

ADDING NEGATIVE CONSEQUENCES

Research has consistently shown, however, that positive consequences alone are not sufficient to maintain the desired behavior of ADHD children (14–17). These studies suggest that both positive and negative consequences are necessary to achieve optimal levels of appropriate classroom behavior. Response cost is a behavior modification technique that may be incorporated into a daily report card so that a child's classroom behavior may earn positive or negative consequences. Response cost has been defined as a punishment procedure which involves the loss of positive reinforcement (privileges, points, rewards) contingent on misbehavior or failure to meet specified behavioral or academic criteria (18). In the case of a school-home note, a child may be instructed by the teacher to cross off a smiley face from his note contingent upon inappropriate behavior. The loss of the smiley face decreases the child's chance of bringing home a "good note" for the day and earning a reward.

McCain and Kelley (19) compared the effectiveness of a school-home note with and without response cost in improving the classroom performance of three fourth-grade boys in a public school. A multiple-baseline design with alternating treatments was used. On-task (oriented toward work), off-task (not oriented toward work), and disruptive behaviors (out of seat, making noise, other teacher disapproved behaviors) were recorded. Parents were instructed to reward good notes with positive reinforcement according to a contract that outlined contingencies for reinforcement. In addition, the school-home notes with response cost required parents to

provide consequences contingent on satisfactory on-task behavior and minimal loss of response cost points. The addition of response cost increased the effectiveness of the intervention beyond the traditional school-home note without response cost. That is, all three students showed decreases in off-task behavior and exhibited low, stabilized levels of disruptive behavior during the response cost intervention as compared to the traditional school-home note.

Kelley and McCain (20) found similar results in a study that compared the effectiveness of a school-home note with and without response cost for increasing academic productivity and appropriate classroom behavior in five elementary-aged children. Both notes included the target behaviors "completed classwork satisfactorily" and "used classtime well." Teachers rated each behavior as "yes," "so-so," or "no." Notes were taken home and parents provided rewards contingent upon satisfactory behavior. The note used during the response cost condition had the addition of five smiley faces on the page. Teachers instructed students to mark off a smiley face every time they were off-task or behaved disruptively. Notes were taken home and rewards were provided contingent upon satisfactory behavior ratings as well as minimal loss of smiley faces. Both appropriate classroom behavior and academic productivity increased in all five children with the use of school-home notes. In three of the subjects, the inclusion of the response cost component lead to significantly greater improvement over the traditional school-home note.

More recently, Jurbergs (21) compared the effectiveness of similar school-home notes with and without response cost in improving the classroom performance of six, minority, first- and second-grade students with ADHD. A reversal design with alternating treatments was utilized. On- and off-task behavior was measured using direct observation. Academic productivity was measured in percentage complete and percentage correct during each phase. Again, both on-task classroom behavior and academic productivity increased in all participants during treatment phases. Also, accurate classwork completion increased substantially. However, no consistent added benefits of the response cost component were found. The school-home note with response cost was more effective in increasing on-task behavior for two of the subjects, while the no response cost note was more effective for one of the subjects. The other three subjects, however, showed no difference in levels of on-task behavior between the two notes.

TREATMENT ACCEPTABILITY

The same study also examined treatment acceptability of daily report cards. The interview data collected after the conclusion of the study indicated that both notes were highly acceptable to all teachers, parents, and students involved.

Although no differences in treatment efficacy were demonstrated, all participants reported finding the response cost note more acceptable.

In summary, school-home notes have been shown to be effective in the classroom management of children with ADHD (5,10,12,13,19–21). Various aspects of school-home notes such as target behaviors, consequences, and age of subjects have been varied in the literature without diminishing effectiveness. Home-based contingency interventions have been effective in increasing both academic performance and appropriate classroom behavior. Such techniques have also been described as very highly acceptable by parents, teachers, and students. These findings as well as the advantages of parent involvement in their children's classroom behavior make daily report cards an important behavior modification intervention for use in educational settings.

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Tailoring Psychosocial Treatment for ADHD-Inattentive Type

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Despite the prevalence and significant impairment associated with attention deficit hyperactivity disorder-predominantly inattentive type (ADHD-I), treatment studies of this subtype are lacking, partially because the field has focused on the combined type of ADHD (ADHD-C), and also because the specification of ADHD-I as a distinct condition only occurred in 1994 (1). The critical lack of any treatment studies of ADHD-I was noted in the NIH Consensus Development Conference on ADHD (2) with the recommendation that more systematized treatment strategies be developed and evaluated for ADHD-I.

Stimulant treatment (ST) and behavioral interventions are both evidence-based treatments for the combined type of ADHD and it stands to reason that these interventions also would be helpful for ADHD-I. Findings from recent studies (6) show that many children with ADHD-I can benefit from ST. However, psychosocial interventions (PST) may be especially important for those with ADHD-I based on reports that medication may be somewhat less helpful for this subtype (3,4), that the social impairment in ADHD-I (e.g., social passivity, withdrawal, lack of social knowledge) may be more amenable to PST than ST (5), and that even in cases showing a positive response to ST, normalized functioning is often not achieved and the inclusion of PST may be necessary to produce "excellent" treatment response. Also, acceptability of treatments is an important factor to be considered in the selection of treatments. Parents show a significant

preference for behavioral treatments over pharmacological treatment alone (7), and there is growing concern among the public and government over the proliferation of ST with children. This chapter will describe the characteristics of ADHD-I important for targeting in psychosocial intervention and a new multicomponent psychosocial intervention for this subtype of ADHD.

TAILORING PSYCHOSOCIAL TREATMENT TO ADHD-I

The evidence-based psychosocial interventions developed for ADHD-C appear to be appropriate for addressing the needs of ADHD-I. These include training parents in behavioral strategies and classroom accommodations and consulting with teachers to implement behavioral strategies at school (including daily report cards) (8). In addition, social-interaction training provided in the context of a behavior modification program and parent involvement may be helpful for improving social skill deficits (9,10).

Unique characteristics of ADHD-I, however, suggest the need to tailor these interventions. Evidence is emerging that the cognitive/attentional deficits of ADHD-I overlap only partially with those of ADHD-C. Several studies suggest that children with ADHD-I show more severe alertness/orientation problems or sluggish cognitive tempo than those with ADHD-C (11–13). Both ADHD-I and ADHD-C share deficits on tests of frontal lobe functions, but slowness in perceptual motor speed and automatic information processing may be specific to the attention-deficit disorder (ADD) without H group (14–17). It is also worth noting that the "sluggish cognitive tempo" and excessive passivity aspects of ADHD-I bear similarities to impairments seen in patients with mild traumatic brain injury (TBI). Adults with mild TBI often exhibit a reduced level of alertness and a reduced ability to initiate behavioral sequences (18,19). Rehabilitation psychologists and psychiatrists use a broad array of techniques to help these patients, ranging from behavior modification, cognitive rehabilitation and other neuropsychological approaches, mnemonics, and ecological supports. Psychosocial treatment for ADHD-I would likewise do well to emphasize adaptive skills, functional competence, and compensatory strategies. Specific teaching strategies used with TBI also are likely to be helpful with ADHD-I. These include use of cues and prompts, routinization of recurring problem situations, increased rehearsal of information used in daily life, and metacognitive strategies such as self-identification of off-task cognitive states and self-redirection to task. On the other hand, there is no evidence that cognitive remediation emphasizing computer-based practice/learning of deficient cognitive skills, often used with TBI, would be helpful for ADHD-I. Even for TBI, the efficacy of these approaches is less recognized than that of compensatory-substitutive approaches (20), and task-specific training appears to provide greater benefit than more generalized training (21).

Academic impairment appears to be especially pronounced, relative to other problems, in children with ADHD-I. They show considerable impairment in academic functioning including underachievement, underproductivity, and learning disabilities (22–24). Homework problems are ubiquitous (25). These serious academic concerns necessitate close involvement with the school and direct intervention for homework.

Recent findings suggest that ADHD-I is associated with a pattern of low motivation for learning, less interest in challenging tasks, less persistence and being more easily discouraged (26). Although children with ADHD-C also have motivational deficits (particularly during low interest activities without external reinforcement), Booth et al. (26) report differences between the two subtypes. Children with ADHD-I were found to prefer a cooperative work setting relative to those with ADHD-C who tended to prefer a more competitive environment. Also, children with ADHD-I seemed to be more motivated to perform well to please the teacher and make good grades rather than for their own curiosity, interest, or internal drive. Perhaps, as the authors speculated, this is due to a more passive approach to academic work. In contrast, those with ADHD-C were significantly more likely to value being perceived as high performing and successful than those with ADHD-I. Recently Huang-Pollock et al. (27) reported subtype differences in motivation on a reward-based variation of the stop-signal paradigm, whereby children with ADHD-I tended to give up more easily than those with ADHD-C when rewards were not as available.

The findings of relatively slow cognitive processing, low levels of curiosity, interest, and enjoyment of learning, preference for less challenging tasks, preference for cooperative work environments, and greater reliance on external criteria for determining success all need to be considered in planning optimal learning environments at school and at home. Those that emphasize noncompetitive external rewards for meeting specific goals and accommodations to tasks and assignments to address slow work style appear indicated.

Social impairment is also marked in ADHD-I, but is distinct from ADHD-C. Those with ADHD-I tend to be unpopular and socially withdrawn (23) and have social skill deficits rather than only performance problems (28,29). Children with ADHD-I receive more peer nominations of being very shy and being teased and left out than those with ADHD-C (who receive nominations for fighting and arguing). Teachers and parents report that those with ADHD-I are more socially passive (28) and they have been observed to be more socially withdrawn during play groups—engaging in solitary play to a greater degree and having less sustained interaction (30). Their attentional problems may lead to poor tracking and processing of social cues and faulty timing during interpersonal interactions (31). Recently, Mikami et al. (27) reported further evidence for unique social deficits in ADHD-I on a computer-based chat room task: those with

ADHD-I were more disengaged and had poorer memory for social conversation than those with ADHD-C. The social difficulties of ADHD-I youth including passivity, withdrawal, lack of skill, and inaccurate processing of social cues point to the need to carefully teach and practice specific skills, and provide opportunities and reinforcement for approaching and interacting with peers. Interventions to help parents with programming social activities in cases where a child's proclivity is to select passive, nonsocial activities would seem important. Likewise, daily living skills are also deficient, pointing to the need to increase levels of independence in completing daily tasks, most efficiently done with parent monitoring and reinforcement.

In addition, children with ADHD-I are known to have fewer disruptive behavior problems. Children with ADHD-I exhibit less aggression, fewer oppositional problems, and are less likely to meet criteria for oppositional-defiant disorder or conduct disorder than children with ADHD-C (32,33). As a result, limit setting strategies, such as time-out, are likely to be less useful with these children than they are for ADHD-C where behavioral control is so important. Instead, positive reinforcement targeting specific goals and routines may be especially helpful as noted above.

THE CHILD LIFE AND ATTENTION SKILLS PROGRAM FOR ADHD-I

We have developed a multicomponent package of integrated behavioral and cognitive-behavioral interventions to address the unique impairments of ADHD-I, described above. The package includes three components: teacher consultation, parenting skills, and child life skills training. The teacher and parent components are designed to facilitate generalization and maintenance of strategies taught directly to children during the child training. The teacher and parent components are expected to exert effects on core ADHD-I problems (e.g., disorganization, failure to sustain attention to task, forgetfulness) and related impairments (e.g., academic underproductivity, social withdrawal, homework problems, lack of independence in self-care and daily activities) by structuring school and home environments to enhance functioning in these areas. To accomplish this, the parent and teacher interventions specifically target these areas in contingency management programs and by altering environmental "antecedents" (e.g., by establishing routines, using organizational lists and plans, using assignment books, simplifying tasks, using strategic reminders). The child skills component provides children with instruction and practice in strategies for improving attention to task, work productivity and organization at school and home, and for improving interpersonal relationships (with adults and peers). The child groups provide direct instruction in strategies to remediate skill deficits (e.g., how to enter peer groups, complete work, keep work space organized, track homework) and provide practice (behavioral rehearsal) to

remediate skill performance deficits. The program also integrates cognitive-behavioral components (e.g., problem solving, self-monitoring/self-evaluation) with the behavioral approaches based on published work suggesting this combination is beneficial (10,34).

The program includes 8 to 10 concurrent group sessions of 90 min (one for the parents and one for the children), up to 5 individual family sessions and up to 5 meetings between the teacher, therapist, parent, and child over a 12-week period. It is important to note that these interventions, although manualized, are individualized for each family. For example, target behaviors, rewards, and negative consequences are based on the specific needs and proclivities of the child and family and strategies are tailored to the child's cognitive functioning. This individualization occurs during each group session and is a specific focus of the individual family sessions and teacher consultation meetings. Thus, this plan begins with group-based interventions that target needs that virtually all ADHD-I cases have, followed by distribution of intensive problem-focused treatment where and when it is needed.

Teacher Consultation Component

This component is intended to provide the teacher with consultation in behavioral interventions and classroom accommodations, with a focus on development and implementation of an individualized daily home–school report card and classroom accommodations specific to concerns of each child. Interventions for this component are based on numerous studies documenting efficacy of classroom behavior modification and teacher consultation for children having ADHD (8,35). Consultation consists of an orientation meeting providing an overview of behavioral interventions and classroom-based accommodations for working with children having ADHD-I (1 hr), followed by up to four meetings of teacher, parent, child, and therapist. In the first two of these meetings, a school-home daily report card (classroom challenge, CC) is designed and implemented. The CC is intended to provide the needed structure and reinforcement to support improvement on school-based tasks. Target behaviors are individualized based on the needs of the child and typically include common problem areas for ADHD-I including: academic work (e.g., completion of assigned work, completion and return of homework, accuracy of completed work), work behavior/study skills (e.g., following directions, having necessary materials to begin work, getting started on work, staying on-task), and social interactions (e.g., entering peer groups, accepting consequences, being a good sport, using assertive behavior). Skills taught in the child group are shared with teachers so that the child's use of these skills can be reinforced (often by including as a target on the CC) in the naturalistic environment of the school. During the remaining two meetings, the program is reviewed

using the "Challenge Review" script to ensure that all critical points are covered and to help parents develop a set of transferable skills for working with their child's teachers. The therapist may model use of the script, but the parent is shaped into taking the lead role in the teacher meetings. In addition to the daily report card, the therapist may also suggest environmental or academic accommodations (e.g., additional time or "time challenges" to complete work, preferential seating, reduction in workload, use of assignment book, use of completed work folder, time limits) depending on the needs of the child and the teacher's overall teaching style.

Parent Skills Component

Our approach to teaching parenting skills is similar to the approaches used in a number of studies of parent training (36–39), but adapted to more fully address the concerns facing ADHD-I. These include an increased emphasis on improving homework routines (bringing home materials, completing assignment, returning it back to class), improving independence, self-care skills, and follow through to parent requests, increasing organizational and time-management skills, and facilitating peer interactions. The program begins with an overview of ADHD-I and the social learning model. Thereafter, a set of strategies is presented over the course of the 8–10 group sessions. Strategies covered include: use of attending, rewards, and other positive consequences; establishing effective routines for the morning, for homework, and for the evening; planning activities, giving directions and commands, and using prudent negative consequences, to promote attention and adaptive functioning. Parents also are taught communication skills for interacting effectively with teachers and are introduced to the school-home note (CC, the primary school-based intervention described in the teacher consultation component above). Additionally, the modules covered in the children's groups (see below) are reviewed each week and parents are taught methods to promote and reinforce their child's use of skills taught during these sessions (e.g., independence skills, positive social interactions).

Child Skills Component

The child program is divided into modules that teach children skills to be independent at school and home (academic, study and organization skills, self-care and daily living skills), and modules to improve social interactions and increase social competence. These modules address both skill knowledge deficits and performance problems through didactic instruction, behavior rehearsal and in vivo practice in the context of a dense, reward-based contingency management program. Self-management of alertness is supported by group-reinforced "attention checks" (40) during which time children are prompted to repeat back the last comment made or activity that occurred. In addition to the behavioral interventions, children are taught

cognitive-behavioral strategies (e.g., problem-solving steps, how to use cues/verbal mediation strategies to stay on-task and focused, use of reminder lists of activities to be completed) including skills for self-monitoring and self-evaluation (e.g., "Match Game") in light of studies supporting their use with ADHD youth (10,34). The social skills modules are based on a previous treatment study for ADHD (10) and include the following: being a good sport, accepting consequences, assertion, ignoring provocation, problem-solving, friendship-making skills, and emotion management. Additional focus on friendship-making skills and planning playdates is included due to the specific deficits in these areas associated with ADHD-I. Modules focused on independence include the following: homework/study skills, self-care skills (e.g., getting ready for school) and getting chores done independently. Role-plays of common problem scenarios for ADHD-I are covered as a part of each module (e.g., joining a game, being teased, being left out of an activity, "spaciness" during a game, staying on-task during homework, staying focused when getting ready in the morning) and solutions are practiced until success is achieved. Children also practice new skills during play activities and mock school/home routines with high doses of positive reinforcement. The module focused on homework/academic skills is reinforced by having children and parents participate in "mock" homework sessions during which time they are coached in strategies to improve homework success. During the last 15 minutes of group, parents and children meet together to go over the "skill of the week" and plan homework for the upcoming week.

RESULTS OF RANDOMIZED-CONTROLLED TRIAL OF THE CHILD LIFE AND ATTENTION SKILLS PROGRAM

With funding from the National Institute of Mental Health, we completed a randomized-controlled trial of this intervention with children between 7 and 11 years of age (41,42). Sixty-nine children were randomized to the intervention (Child Life and Attention Skills Program) or to a control group which did not receive the intervention. Our findings reveal significant treatment-related improvement on the number and severity of DSM-IV inattention symptoms and symptoms of sluggish cognitive tempo as well as on functional impairment associated with ADHD-I including organizational skills, homework problems, and social skills. These findings were maintained into the next school year. Our program was well-received by parents, teachers, and children. Feedback from the teachers suggests that the school component is suitable for implementation in general education classrooms (where most students with ADHD-I are taught). The fact that gains were sustained after treatment was completed (which is often not the case in treatment studies with ADHD-C), is consistent with theories (29) that ADHD-I may be more associated with remediable skills deficits and less associated with disinhibition compared to ADHD-C. We attribute the

efficacy of our program to the focus on specific areas of impairment for this subtype and the integrated approach that puts parents, teachers, and the children themselves on the same game plan. This integrated approach appears to improve functioning for children with ADHD-I to a greater extent, and for longer period of time, than the sum of the individual treatment effects would suggest.

NEXT STEPS

Continued development and evaluation of psychosocial treatments for ADHD-I are in order. Our results suggest behavioral approaches integrated between home and school can have a significant impact, but more needs to be known about the moderating and mediating mechanisms underlying treatment response to allow for more refined tailoring of intervention. Future studies should also evaluate when and how psychosocial interventions may best be combined with medication for optimal response. Equally important will be studies on how best to disseminate these treatments in the community.

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Social Skills Training

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Difficulties in peer relations plague many, if not most, youth with attention deficit hyperactivity disorder (ADHD). These problems can be extremely debilitating and can cascade into a variety of serious outcomes, including academic failure, school dropout, substance abuse, other mental health issues, and legal problems (1,2). Not only are social problems enduring, among the most impairing issues for those with ADHD and often the reason for referral to mental health clinics, they are difficult to treat (3). This chapter summarizes the social profile of youth with ADHD and social skills training programs that have been developed to address the problems.

SOCIAL PROFILES OF ADHD YOUTH

While most youth with ADHD exhibit considerable impairment in the social arena, these problems are not uniform across subtypes and also seem to be influenced by the presence of comorbid disorders. The literature on peer relations in ADHD is based on studies of children with the "classic" triad of symptoms of ADHD: inattention, hyperactivity, and impulsivity, now referred to as ADHD-Combined Type. In some ways, the behavior of those with ADHD-Combined Type is not different from their non-ADHD counterparts. They tend to exhibit similar rates of positive behaviors and neutral verbal interchanges (3). However, negative behaviors, often a result of high activity levels and impulsivity, are excessive. Parent and teacher reports and observations of children in classrooms and on the playground, indicate that youth with ADHD are more dominating, controlling, and aggressive (3,4). They issue more commands, grab desired objects from

others, cut in line, and quickly change the rules of a game (or cheat) when the rules do not suit them (5). Their tendency to blurt out comments is often disruptive in a classroom and annoys other children who are trying to concentrate on their work. Often the comments are insensitive or insulting, and even though unintentional, can be hurtful to peers. Recently, Mikami et al. (6) also reported this pattern on a computer chat room task: children with ADHD-C were far more likely to be off-task and hostile in their responses to computerized peers compared to comparison children. Children with ADHD-C also have a pattern of emotional dysregulation characterized by intense emotional reactions, which they have difficulty adjusting to the changing demands of social situations (7). They frequently do not recognize the physical boundaries of others, touching or poking them or otherwise "getting in their space." Excessive physical activity, over-exuberance, and talkativeness are often bothersome to peers. To add to their problems, they are often unaware of the negative impact of their behavior on others (8).

Although much less is known about social functioning in ADHD-I, existing data suggest that these children are less disruptive than those with ADHD-C but still exhibit social problems. In several studies, both boys and girls with ADHD-I were rated as being passive and socially withdrawn relative to those with ADHD-C and to comparison children (7,9–11). In a recent observational study, those with ADHD-I, relative to ADHD-C and nonclinical controls, engaged in more solitary play and spent more time as onlookers of their peer's activities (10). When they did play with other children, it was for shorter periods of time relative to those with ADHD-C and nonclinical controls. Similarly, Mikami et al. (6) found that while children with ADHD-I were equally off-topic as those with ADHD-C during a computerized chat room interaction, they were far less engaged and had poorer memory of the chat room conversation relative to children with ADHD-C.

The peer status of youth with ADHD is, not surprisingly, compromised. Peer status, like peer interactions, appears to differ by type of ADHD. Boys and girls with hyperactivity and impulsivity (both the combined and hyperactive-impulsive types) are more often openly rejected by their peer group and rarely receive positive nominations from their peers. Children with only attentional problems also have low popularity, but they tend to have less extreme ratings of rejection (although still elevated), and seem to show more evidence of being neglected (12). The more withdrawn disposition of youth with ADHD-I may make them less visible to peers. However, they are not completely overlooked since they are often rated as being very shy, teased, and left out. Hodgens et al. (10) posit that their withdrawn behavior may be what leads to the low levels of peer acceptance.

Recent research has also begun to evaluate friendships in youth with ADHD. Dyadic friendships, being characterized by reciprocity and mutual

affection, are distinct from general acceptance by peer groups and appear to contribute independently to mental health (13). Few studies have investigated friendships among children with ADHD, but those that have show that ADHD children have fewer friends than others and are seen as less desirable friends (13). Lack of friendships may be particularly deleterious in girls. During a summer camp experience, girls with ADHD were found to have fewer friendships than comparison girls—due to having either fewer multiple friends or no friends at all. The stability and quality of the friendships were compromised for girls of both subtypes (9).

Comorbid aggression, oppositional or antisocial behavior exacerbates the social problems of children with ADHD to the extent that this combination of problems leads to the worst social outcomes. Boys with ADHD and these comorbidities exhibit more aggressive verbal (e.g., yelling, teasing) and nonverbal (e.g., pushing, hitting) behavior than boys with only ADHD and they are least preferred by peers (4). While girls, in general, exhibit less physical aggression than boys, girls with ADHD-C show more overt aggression than those without and such aggression is linked to fewer nominations from peers as being "liked most" and more nominations of being "liked least" (14). A more common form of aggression for girls has been termed "relational aggression." This type of aggression includes a range of behaviors (e.g., social exclusion, spreading rumors, teasing) intended to hurt another child's friendships or peer status (15). Similar to physical aggression, high levels of relational aggression have been shown to adversely affect the quality of friendships and overall social acceptance (9,14). These studies found that girls with ADHD (especially the combined type) exhibited greater conflict and relational aggression than those without ADHD and that those with high levels of relational aggression also had the most compromised peer status and friendships.

MECHANISMS UNDERLYING SOCIAL PROBLEMS

These behavioral descriptions provide important information about what children with ADHD might be doing that contributes to their peer problems. Theories regarding why these problems occur are also important for development of effective intervention programs. A number of studies suggest underlying problems of affect regulation, behavioral intensity, cognitive distortions, and lack of skills (4). Barkley's theory of self-control of ADHD implicates the lack of behavioral inhibition as a key mechanism underlying social impairment (16). Based on this theory, difficulties with the executive functions of nonverbal working memory, internalized self-speech, affective and motivational self-regulation and reconstitution occur and markedly affect the ability to self-regulate social interactions. These factors might account for the excessive behavioral intensity, affect dysregulation, and aberrant social information processing often seen in these children.

They seem to take insufficient time to process and evaluate social information, fail to attend to important information, not talk themselves through potential responses, overreact to emotional factors, and/or fail to evaluate the appropriateness of their behaviors.

Social information processing deficits may also underlie the peer relationship problems among youth with ADHD. Encoding deficits have been found such that children with ADHD tend to form decisions about a situation utilizing less information than those without ADHD (17). Furthermore, they are less able to utilize the social cues they do observe to appropriately modulate their behavior in different situations. Social problem-solving skills also are deficient in that they generate less friendly, more assertive and impulsive, and less effective solutions (5). Other social information processing abnormalities appear to underlie the aggressive behavior of youth with ADHD. These include: overattributions of hostile intent in the behavior of peers, social agendas that prioritize troublemaking and having fun at the expense of breaking rules and teasing kids, and greater confidence in one's ability to succeed with aggression (4).

Recent theorizing by Wheeler and Carlson (7) suggests that the extent to which skill knowledge or performance problems account for social problems may differ by subtype of ADHD. Those with the hyperactive-impulsive component may be more likely to exhibit performance problems rather than skill deficits. That is, when asked, they know what they should be doing, but in actual practice they do not exhibit those behaviors. Performance problems may be due to excessive negative behaviors (e.g., grabbing, interrupting, breaking rules) or too few prosocial behaviors (attending to another child, initiating an interaction). In either case, motivational factors or lack of behavioral inhibition is thought to underlie the performance problems. Skill deficits may be a relatively stronger mechanism in ADHD-I. Children with this subtype may simply not know what to do in various social situations. In addition, their attentional problems may lead to poor tracking and processing of social cues from other people, apparent disinterest in carrying on a conversation, and faulty timing during interpersonal interactions. These problems may be particularly impairing for girls with ADHD due to their greater focus on verbal communication. Based on findings of Blachman and Hinshaw (9), they may have specific difficulty balancing multiple friendships, perhaps due to their lack of active engagement and focus.

Given the complexity of the problem, it is likely that differences in subtype are relative rather than absolute, and that children with ADHD will vary in the degree to which skill remediation or performance motivation is beneficial. The challenge of modifying these problems is complicated by data showing youth with ADHD lack awareness of their social ineptitude and tend not to take responsibility for their transgressions (8). The lack of

accurate self-appraisal limits their ability to learn how to modulate their behavior to different circumstances (13).

SOCIAL SKILLS TRAINING TO REMEDIATE PEER PROBLEMS IN ADHD

Historically, social skills training has been used to treat children identified as being rejected or neglected by peers and also to treat children with aggression and conduct problems (18–20). A number of studies report improvement in social behaviors as a result of the training, however, the involvement of parents and teachers was necessary to support their use of the social skills outside of the therapy setting (21). Social skills training programs were first systematically investigated with youth having ADHD in the early 1980s. In one of the first studies of social skills training (SST) with ADHD, Pelham and Bender (22) applied a variant of the program developed for socially isolated youth. The concepts of cooperation, communication, participation, and validation-support were taught in small groups via direct instruction, modeling, role-playing, and coaching. SST alone did not lead to improvement, although when positive reinforcement was added for prosocial behavior, improvement was observed. Over the next decade or so, several other studies attempted to improve social interactions via self-instruction training in which children were taught to modify their self-talk in order to self-regulate their behavior. Short-term beneficial effects were found for impulsive children (23), but this approach has not been shown to be effective for ADHD. During this time, commercially available social skills training programs proliferated and became quite popular (24).

Clearly, there is intuitive appeal for the idea of training children in skills to improve their social relations. However, reviews of the SST literature provided little evidence that such training changed the way children behaved or were received in the natural environments of home and school (24,25). The typical approach to training referred to as "train and hope," wherein children are taught skills in an office (or other contrived) setting via didactics and modeling and without explicit programming for generalization outside of the training setting, showed little effect.

Since then, several well-controlled studies of SST tailored to the needs of ADHD and incorporating strategies to address the generalization problems have shown beneficial effects. Pfiffner and McBurnett (26) evaluated a broad-based SST program for ADHD children with the goals of teaching skills of social significance, using motivational systems to reduce performance problems, increasing awareness and understanding of verbal and nonverbal social cues, and promoting generalization and maintenance by incorporating significant others (parent and teachers) in treatment. The SST program included eight 90-min group sessions covering the following modules: good sportsmanship, accepting consequences, assertiveness,

ignoring mild provocation, problem-solving, and recognizing and dealing with feelings. Didactic instruction, modeling, role-plays, and a variety of games were used to teach the skills. Children were taught to evaluate their own performance each week. A token reinforcement system was implemented to reinforce skill use during sessions. Children were randomly assigned to three groups: SST only, SST plus parent generalization training, or a wait-list control group. Parents in the parent generalization group were taught methods for supporting their child's use of the skills at home and also worked with their child's teacher to set up systems for reinforcing their child's use of the skills at school. The token system used in the group was also used at home by parents and at school by the teachers. At the end of treatment both the SST groups resulted in gains in child social skill knowledge and in parent report of improvement in social interactions and home behavior problems with the gains maintaining for 3–4 months following treatment. Some generalization to the school setting was also found for the parent generalization group only.

Frankel et al. (27) also found positive effects of their 12-week SST program focused on training in conversational skills, group entry, handling teasing and rejection, negotiation skills for changing activities and praising others. At posttreatment, parents rated significant reductions in social skills deficits relative to a wait-list control group. Children without oppositional defiant disorder (ODD) showed significant drops in teacher-rated aggression and withdrawal. In a subsequent study in which they added modules for addressing disruptive classroom behavior and aggression and also trained parents in homework compliance, methods for working with teachers to decrease disruptive behavior at school and methods for coaching their child in peer interactions significant gains also were made for children with ODD (28). In another study, concurrent parent and child behavioral skills groups resulted in reductions in ADHD symptoms and improvement in parenting at home for medicated children in an outpatient primary care clinic (29). The efficacy of SST with young (age 4–8 year olds) children having conduct problems has been demonstrated recently with equivalent benefit for the subgroup with ADHD. Here too, treatment included direct involvement of parents and teachers for facilitating generalization of skills to home and school (30). While the greatest improvement seems to occur from programs that actively include parents and/or teachers in the treatment, SST has shown some effect with minimal parent involvement. Antshel and Remer (31) implemented an 8-week SST program with medicated youth having ADHD (ages 8–12) focused on training in a variety of social skills (e.g., cooperation, problem-solving, recognizing and controlling anger, assertiveness, conversations, and accepting consequences) and included several informational sessions for parents. Both parents and children reported significant improvement in assertiveness at posttreatment relative to a wait-list control group.

As these studies indicate, there is accumulating evidence to support use of SST with ADHD youth. The positive effects are seen on parent and teacher ratings of social behaviors; whether training effects extend to observations of the children's actual interactions with peers or peer acceptance requires further study. To maximize positive effects of SST, the following factors are important:

1. The curriculum should be based on problems exhibited by ADHD. For ADHD-C this means addressing problems such as intrusiveness, impulsivity, and emotional dysregulation. For ADHD-I this means addressing problems such as disengagement, social withdrawal, and passivity (32). For both subtypes, it means learning to adjust their behavior to the nuances of the social environment. It follows then that treatment should be tailored to the specific social-cognitive deficits associated with ADHD. For example, to address attentional problems, children can be taught how to be better observers of other children; to address lack of social problem-solving skills, children can be supplied with a range of effective solutions for a variety of problems; to address the lack of self-appraisal or insight into their own behavior and consequences, treatments may incorporate strategies such as Match Game (33) wherein children are taught and reinforced for accurate self-appraisals. Another approach may involve having children view and evaluate videotaped samples of their own interactions with peers. Attributional problems may also be remedied by using specific cognitive strategies and behavioral rehearsal (34).
2. Strategies to decrease aggressive behavior, be it physical or relational, need to be in place. This should include contingency management and other behavioral interventions to manage aggression as well as methods for altering the aggressive social agendas, distorted cognitive appraisals, and poor social problem-solving skills characteristic of those with comorbid aggression. Programs such as those developed by Lochman and Lenhart (19) for aggressive children may be useful models.
3. SST is best implemented in the context of a group in order to facilitate peer modeling and practice of skills. However, if a group is not available, individual training may be effective if adequate opportunity for peer interaction is provided. For example, Colton and Sheridan (35) successfully trained several individual children via individualized coaching, role-plays, prompts for skill use ("friendship cards"), self-monitoring of recess behaviors, and a home–school communication system with positive reinforcement at home for school success. Importantly, parents and teachers also were encouraged to provide ample monitoring and feedback of the children's social behavior.
4. A behavior management component is necessary to handle behavior excesses in group, particularly for ADHD-Combined Type (28).

Without this component, the attention and focus needed from children to learn new skills will be limited.

5. A generalization component needs to be in place since children do not usually transfer the skills they learn in SST on their own to their interactions with peers (26,28). The greatest gains result from programs where parents and teachers are actively involved in reinforcing the social skills taught during SST. In classrooms, playgrounds or families where negative, coercive behaviors are prominent, this may require altering the environmental milieu so that prosocial behavior becomes desirable and the norm among all individuals.
6. Even after children learn new skills and modify their behavior, peers may not alter their negative assessment of them. Reputational biases may be addressed by making treatment class-wide, incorporating cooperative play activities, and making sure the skills taught are of value to peers (13). In some cases, reputations may be virtually impossible to change; switching classes or schools may be the best solution for these children.
7. SST should not be considered a sole treatment for the social problems accompanying ADHD. Parent training and classroom-based interventions, the primary evidence-based psychosocial treatments for ADHD, are necessary to help supervising adults develop needed skills for monitoring, prompting and reinforcing prosocial behaviors, and decreasing aggressive behaviors. Stimulant medication also has been shown to improve peer interactions and in conjunction with SST and other psychosocial interventions leads to optimal effects, especially in moderate to severe cases of ADHD. The combination of medication and behavioral interventions is recommended due to their effects on different underlying processes of social impairment with medication affecting inhibitory processes and SST affecting skill, social cognition, and judgment (4).

IMPROVING PEER INTERVENTIONS

Although SST shows benefit, the intensive environmental support needed for optimal maintenance and generalization of treatment gains is often difficult to accomplish, making the need for further development of peer interventions a priority. One area usually not addressed in SST is the development of dyadic friendships. Based on a number of studies indicating that good friendships may compensate for the negative impact of peer rejection and seem to predict better adjustment later in life, greater focus on developing dyadic friendships is important. One promising approach has been developed by Hoza et al. (36). The focus of this intervention is on developing a positive relationship with one specific peer rather than

improving peer relations in general. The program was implemented in the context of an intensive, camp-like behavioral treatment program which included SST. It involved pairing children with one buddy based on interests, competencies, and practical considerations (how close the families lived to one another). Buddy pairs were scheduled to spend more time together, received special privileges as a pair, and were evaluated and rewarded for good friendships. The children's parents were encouraged to have the children get together during playdates outside of the program to promote the friendship. Buddy coaches helped work out problems between the buddies while at the treatment program. Initial results show that frequent playdates significantly contributed to the quality of the friendships. Also, children paired with less disruptive/antisocial children showed the most benefit. The positive effects of the playdates appear dependent on control of disruptive and aggressive behavior of the buddies by supervising adults. The actual efficacy of the intervention requires further study due to the lack of a comparison group not receiving the intervention. However, strategies focused on developing dyadic friendships appear readily integrated into traditional SST programs via prescribed playdates and training for parents to support these interactions and friendships (32,37,38). They also may be integrated into classrooms (13). The focus on dyadic friendships may be especially helpful to address the social withdrawal often seen in the inattentive type.

Environmental accommodations to improve the fit between the child and the demands of the environment are an additional method for augmenting social skills or friendship interventions. In the classroom, accommodations to assignments, seating, instructional format, etc., are routinely implemented to improve classroom behavior and academic functioning. However, accommodations to the environment are less often emphasized for improving peer relations, but may be effective for reducing unfocused, impulsive, or disruptive behavior. For example, during playdates this may include having a structured play activity planned in advance, keeping the activity brief and relatively fast-paced, having play activities in the child's areas of interest and rotating these activities to maintain motivation. For after-school activities, small peer groups with close adult supervision are advisable and activities should allow the child to be active and involved most of the time.

Peer tutoring in social interaction skills also may be of benefit as it has been for academic skills (39). Such tutoring may involve pairing children and having them work together on cooperative tasks for successful outcomes during recess and lunch. A variant of this concept is the student-mediated conflict resolution program developed by Cunningham and Cunningham (40). This program involves teams of older children, trained as mediators, helping peers solve interpersonal conflicts when they occur such as during recess or lunch. The mediators help negotiate resolutions and plan

strategies for preventing future problems. Initial outcomes of this program have been quite positive with evidence for reduced conflicts of the type often experienced by children with ADHD. Although not specifically evaluated for effects with ADHD, training in mediation skills and serving as a mediator could offer significant benefits for the child with ADHD including improvements in one's reputation among peers, and acquisition of skills in perspective-taking, self-awareness, and resolving conflicts.

CONCLUSION

Recent advances in SST suggest that this form of treatment shows promise for treating the social difficulties of youth with ADHD. However, positive effects are limited to programs that address the specific social problems of children with ADHD and those that actively program generalization via involvement of parents and/or teachers. Further development of SST should incorporate greater focus on development of dyadic friendships and environmental accommodations to promote successful peer interactions. Additionally, peer-mediated conflict resolution programs show promise for addressing conflict in the natural environment.

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Parent Training in the Treatment of ADHD

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Attention deficit hyperactivity disorder (ADHD) is a chronic and impairing disorder of childhood, adolescence, and adulthood and is characterized by primary symptoms of inattention, impulsivity, and overactivity (1). In addition, ADHD is usually associated with one or more comorbid conditions, associated features, and functional deficits, or combination of these, which add to the impairment picture and complicate treatment planning. Oppositional defiant disorder (ODD) is the most common comorbid condition with 35% to 60% of ADHD children also meeting criteria for an ODD diagnosis (2,3). Conduct disorder (CD), another significant comorbid condition occurs in 30% to 50% of ADHD cases. Among the functional impairments, difficulties within the family and parenting domains are prominent.

The primary difficulties with inattention, impulsivity, and overactivity present parenting challenges to the mothers and fathers of ADHD children. Inattentive children have a difficult time sustaining attention and completing tasks as they move through the structured activities of the day. The impulsivity of these children often results in verbal or even physical aggression directed toward siblings or other family members as well as other social disruptions that require parent intervention (e.g., grabbing toys away from siblings; inability to wait to take one's turn; loud verbal outbursts that are annoying to others; etc.). Overactivity can produce behaviors that are very disruptive or require constant intervention by parents (e.g., running around the table at mealtime; inability to sit still and play quietly while parents are occupied).

Within the parenting and family domain, the parent–child interactions of ADHD children and adolescents with their mothers and fathers are frequently disturbed and conflictual. Parents of ADHD children display more negative reactivity, more commanding, directive behavior, and less positive responsivity to ADHD children than do parents of normal children (4–6). While disrupted parent–child interaction is probably not etiologic in ADHD, it may have a primary causal role in the development, escalation and maintenance of the oppositional and aggressive behavior that is characteristic of ODD and CD.

These comorbid conditions (ODD and CD) also carry implications for parent training interventions. Research has documented that the presence of ODD is associated with much of the parent–child interactional conflicts in ADHD families (7,8). Nevertheless, parental intrusiveness and overstimulation in the infant–child relationship are significant early antecedents of later hyperactivity in kindergarten (9) and parents and children with ADHD alone still display interactions that deviate from normal (6,8). This suggests that intervening in parent–child interactions may be important not just with ADHD comorbid with ODD and CD but with pure ADHD.

For all of these reasons, parent training interventions have developed and been utilized as one of the primary psychosocial treatment strategies in the armamentarium of clinicians working with ADHD children. Parent training may be used as a frontline treatment but is often used in conjunction with stimulant medication therapy and school interventions for those children who have significant difficulties in the school environment.

Although a number of clinical researchers have employed Parent Training programs with families of children with behavior problems, the investigators most associated with this approach for use with ADHD populations are Barkley (10) and Wells and colleagues (11,12). Barkley adapted an 8–10 session intervention for use with ADHD children from the Parent Training program first developed by Constance Hanf. Wells and colleagues developed an extended Parent Training program that incorporated many of Barkley's adaptations, but embellished and extended the basic program to include attention to school and other parent factors that are often issues in ADHD families. Each of these will be described briefly.

In Barkley's version of parent training for ADHD, treatment begins with a review of information on ADHD as well as causes of oppositional and defiant behavior, including diagnosis, theories of etiology, and principles of social learning theory that are relevant to parent–child interactions. Once this background has been discussed with parents, presentation of parent management skills begins, starting first with increasing positive parental attention to children during a 10–20 min "special time" every day. Once parent attention has been established as a reinforcer, parents are next taught how to apply their positive attention to two critical target behaviors

for ADHD children; compliance to parent instructions and independent play. Parents are taught to "catch the child being good" (i.e., compliant) and also to attend and praise the child when the child is playing independently while the parent is engaged in some other activity (such as working or cooking).

Compliance to parental instructions is felt to be a critical target behavior to increase in ADHD children. Noncompliance is the keystone characteristic of ODD and decreasing this comorbidity is important in the clinical management of these children. However, even in children with pure ADHD, improving compliance to parental instructions is often the key if parents are to assist the child with managing his/her inattentive, impulsive, and overactive behaviors. That is, management of these behaviors can only be accomplished via parental instructions to the child (e.g., "sit down at the table and don't get up again until dinner is finished") and establishment of house rules (e.g., "grabbing your sister's toys without asking is not permitted"). If the child cannot or will not follow these instructions and house rules, then the parent will be unsuccessful in assisting the child with his overactive and impulsive behaviors. Likewise, independent play is felt to be a critical target behavior in these children since staying "on task" for an age-appropriate amount of time is a frequent, primary problem behavior.

For young children improving parent positive attention may be sufficient. For older children, the next step is establishing a home token economy which sets up a reward system for compliance as well as an expanded array of target behaviors, such as social behaviors related to impulsivity (e.g., hitting, swearing, etc.), age-appropriate chores and other responsibilities. Later, parents are taught a "time-out" procedure to use as a mild punishment procedure for decreasing noncompliance and later, other disruptive behaviors that may still be occurring (violations of house rules, etc.).

In the final stage of the basic Parent Training program, attention is paid to establishing generalization of treatment effects across settings and time. Parents are taught procedures for managing disruptive behavior in public places and at school [using the home-school daily report card (DRC) system]; as well as strategies for managing future behavior problems. A booster session is then held 1 month after the final intensive phase session, to review treatment goals and consolidate treatment gains.

The Parent Training program developed by Wells and colleagues (11,12) was used in the MTA study of multimodal treatment of ADHD. This program is a 27-session treatment program that incorporates adaptations of the 8–12 session program described above, but extends well beyond the basic program. It provides more discussion of clinical nuances that arise in treatment of ADHD families, and more step-by-step instructions of basic procedures. However, beyond embellishments to the basic program, the Parent Training program of Wells et al. (11) was designed more intensively

and comprehensively to address multiple settings and domains of child and family functioning in ADHD. First, great emphasis is placed on intervention in the school setting, since most ADHD children display considerable difficulties related to primary ADHD symptoms in school. Many sessions are devoted to discussing, modeling, and role-playing with parents, both in therapy sessions as well as in visits to the school, parent advocacy, and teacher consultation skills. Other innovations include training parents in cognitive strategies for changing their own maladaptive cognitions and attributions related to parenting a child with ADHD (e.g., "my child is bad; I must be a very bad parent"), as well as stress management strategies, including calming "self-talk" and relaxation skills, to use in disciplinary encounters with the child. These innovations were added to address findings from empirical research that have shown that parents of ADHD children experience more parenting stress, anger, and irritability and a decreased sense of parenting self-competence compared to other parents (13–15).

Since 1980, there have been several controlled studies in the published literature that have examined Parent Training as a single treatment or as a component of a clinical behavior therapy package for youth with ADHD. These studies have shown that parent training produces reductions in inattention and overactivity (16–18) in child noncompliance and conduct problems (18–20) and in child aggression (16). As would be expected, improvements in parenting skills (19,21) also have been found. Some studies also have reported reductions in parent stress, and improvements in parent self-esteem with parent training (16,18,21). Effect sizes for parent training for ADHD of 1.2 have been reported on ADHD symptoms. Anastopoulos et al. reported that 64% of their sample demonstrated clinically significant changes in terms of percentage of children no longer in the clinical range on ADHD Rating Scale with Parent Training compared with 27% for a waitlist control group.

Other studies have examined multicomponent behavior therapy programs of which Parent Training is one component. The most typical combination involves Parent Training plus Teacher Consultation. In Teacher Consultation, the therapist works with the teacher to set up a DRC focusing on classroom behavior and academic performance and may also consult with the teacher on classroom-wide behavior management strategies as well. Several studies have combined Parent Training and Teacher Consultation (22–24) and compared them to medication, with results generally showing that the combination of Parent Training plus Teacher Consultation results in significant improvement in children's home and school behavior. Even greater improvements are noted when Parent Training and Teacher Consultation are combined with stimulant medications (24).

The two large-scale randomized clinical trials in the published literature each included Parent Training as one component of comprehensive behavior therapy programs, and compared behavior therapy to medication

alone and their combination (25–27). While the effects of Parent Training alone can not be elucidated from these studies, they are instructive when considering the best multimodal treatment for ADHD children. In both studies, medication outperformed behavior therapy alone on several measures of ADHD children's functioning. However, on some measures, the combination of medication and behavior therapy resulted in greater improvement than medication alone (25), or than community-treated controls whereas medication alone did not result in greater improvement than community-treated controls (26). Full normalization on objective classroom measures was only achieved with combination treatment (25) and parents were more satisfied with behavior therapy alone and with combination treatment than with medication alone (26). These results suggest that a comprehensive behavior therapy approach that includes Parent Training will be most effective (on some but not all symptoms) and result in greater normalization of ADHD children. All of these studies confirm that Parent Training is and will remain an important component of the treatment armamentarium for the families of children with ADHD and should be considered to be an essential "leg" in the three-legged stool comprising treatment of these children (i.e., stimulant medication, Parent Training, and School Intervention).

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Summer Treatment Programs for Children with ADHD

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OVERVIEW AND DESCRIPTION

For more than 20 years, the summer treatment program (STP) has been used to treat children with attention deficit hyperactivity disorder (ADHD). The STP was first implemented by the senior author (WEP) at Florida State University in 1980. The program has been continually developed and expanded since that time and has been used in over 20 locations throughout North America. The STP was included as a key component of psychosocial treatment in the Multimodal Treatment Study of Children with ADHD, which was the largest study ever conducted to evaluate treatment of ADHD or any other child mental health problem (1).

The STP takes place in the summer, typically for 8 weeks. Children attend weekdays for approximately 9 hr/day (8 a.m. to 5 p.m.). Children spend 3 hr each day in education settings (art classroom, academic classroom), which are conducted by a teacher (usually a special education teacher) and an aide. The remainder of the day is spent in recreational activities. The STP provides treatment to children with ADHD in a summer camp-like setting. From the children's point of view, they are participating in a summer camp; they play soccer, softball, and basketball; go swimming; do arts and crafts; work on computers; and have free time. They participate in these activities in groups that consist of 12 age-matched children and five counselors (undergraduate and graduate students). The same children and

counselors stay together all summer so that children have a chance to make new friends and keep them for a number of weeks (a novel experience for some campers) and so that counselors gain detailed knowledge of the nature and extent of the children's psychosocial difficulties. Each group of children and counselors is under the supervision of senior level staff, typically psychiatrists and/or psychologists, who monitor and evaluate the children's treatment response, as well the counselors' delivery of treatment, throughout the summer (2).

In the context of these activities, numerous empirically supported treatments are delivered, including: a comprehensive token economy (i.e., a point system), sports skills training and practice, group problem-solving training and practice, social skills training and practice, group and individualized parent education, ubiquitous positive reinforcement, time-out, daily report cards (DRCs), and academic training and practice. These interventions are adapted or supplemented with other, individualized treatments when necessary, and individualized medication assessments are also employed when appropriate. In addition, all staff members are taught to use positive reinforcement to encourage adaptive behavior and to avoid positive reinforcement following maladaptive behavior. Commands are issued in a manner that maximizes the likelihood of compliance. Consistency is emphasized by having children follow the same schedule each day, with rules for each activity repeatedly rehearsed, to help ensure that children know where they are supposed to be and what they are supposed to be doing. All of these interventions are implemented at a developmentally appropriate level for each child. They are also integrated into the context of the ongoing activities such that for both the children and the counselors these treatments become an integral part of the child's day at summer camp.

These interventions are the means through which the STP attempts to achieve six treatment goals: (1) developing children's problem-solving skills, social skills, and the social awareness necessary to enable them to get along better with other children; (2) improving the children's learning skills and academic achievement; (3) developing the children's abilities to follow through with instructions, to complete tasks that they commonly fail to finish, and to comply with adults' requests; (4) improving children's self-esteem by developing competencies in areas necessary for daily life functioning (e.g., interpersonal, recreational, academic) and other task-related areas; (5) teaching the children's parents how to develop, reinforce, and maintain these positive changes; and (6) evaluating the effects of medication on the child's academic and social functioning in a natural setting. These treatment goals represent the areas that research and clinical experience suggests are typical among most impaired in children with ADHD. They are also the areas that are of most concern to their parents and teachers.

THEORETICAL RATIONALE

The pervasive impairment experienced by a child with ADHD across important functional domains (e.g., academic functioning, peer and adult relationships, self-esteem, parenting) cannot be treated in an office setting, and it is impractical to think such profound impairments could be treated through periodic counseling visits. The STP is notable in that it explicitly targets the maladaptive behaviors (e.g., aggression, noncompliance), functional impairments (e.g., peer relationship problems, academic problems), and weak competencies (e.g., poor knowledge of sports rules and skills) that are hypothesized to be important predictors of long-term outcome. For example, because children receive treatment in the context of peer group activities, peer relationship problems are direct targets of interventions in the STP. There is considerable evidence that children with ADHD often have seriously impaired relationships with their peers (3,4). In fact, a number of recent studies suggest that peer problems may be more highly associated with the features of ADHD than with the features of other disruptive behavior problems, such as aggression (5–9). This is noteworthy in light of evidence that problems with peer relationships tend to be stable over time (10), and strongly predictive of poor developmental outcome (11), and may thus mediate the poor long-term outcome experienced by many children with ADHD (12). Typically used treatments, including outpatient behavior therapy and psychostimulant medication, have been largely unsuccessful in ameliorating problems with peers (4,13–15). One explanation for this lack of success is that typical treatments are not able to directly target peer relationships. The STP overcomes this weakness by providing treatment in the context of ongoing peer relationships in real-world situations (sports, classroom activities).

Second, the treatment approach in the STP is intensive. The STP takes place during the summer, when children are able to attend full time without interfering with their participation in school. By providing full-time treatment, children receive at least 360 hr of intensive treatment in a very short period of time—more intervention time than a child would receive in 6 years of typical outpatient treatment. This fact is especially compelling when one considers that alternative summer activities (often unsupervised, unstructured activities) may result in a decline in behavior. By offering intensive treatment over a considerable period of time, the STP is able to overcome some of the most common problems of implementing behavior therapy. For example, it is sometimes the case that children will show an initial negative reaction to behavioral interventions, exhibiting higher rates or degrees of the undesired behavior after introducing treatment. This is a well-known, widely studied phenomenon known as an extinction burst (16) and it is usually followed by a dramatic reduction in undesired behavior. Unfortunately, parents and teachers will often stop the new treatment in response to an

extinction burst, thereby reinforcing the child's higher rate of negative behavior. The STP helps avoid this problem by providing treatment that is of sufficient duration and intensity to overcome an extinction burst, allowing for subsequent improvements that parents and teachers can then maintain.

Third, the treatment in the STP is multimodal and multicomponent. The STP uses numerous specific interventions (behavior, cognitive-behavioral, social skills, recreation therapy, and medication) to assist the children with ADHD, as well as their parents and schools. The parenting components include daily meetings between the child's counselors and parents to discuss the child's daily progress, weekly parent education and support meetings, and individualized meetings between parents and a clinician. The school components include not only the classroom interventions in the STP, but also the development and implementation of a daily home-school note. By developing a home-school note in the STP, the family can easily adapt the goals and reward procedures when the child returns to the normal school setting. Finally, we provide recommendations and consultation to each child's teacher in the fall to set up the daily home-school note and other programs to maintain treatment gains.

Fourth, the STP provides excellent motivation for children to change. Throughout the STP, children's behavior is carefully and systematically measured and recorded. This allows counselors the opportunity to give the children specific and immediate feedback and reinforcement. For example, children have the opportunity to earn playtime, which most children enjoy, twice per day if they achieve specific, individualized treatment goals. Similarly, children have the opportunity to earn a fun activity on Friday afternoons if they achieve their weekly treatment goals. Alternatively, children who have an exceptionally poor week, showing a decrease in adaptive behavior, receive minor negative consequences, such as having to do light chores or serve "detention" for a short period of time instead of going on a field trip. These procedures are in place to provide the children maximal motivation to change their behavior in an adaptive fashion, as well as to teach them the important lesson that what they do influences what happens to them. It is also likely that children are motivated to do well in the STP because they find the STP enjoyable and like spending time with the counselors.

EMPIRICAL SUPPORT

As noted above, the STP includes many different types of treatments that are interwoven in the context of summer camp activities. Hundreds of studies have evaluated these individual components and have found them to be effective. One review of treatments for ADHD found more than 100 studies supporting the efficacy of behavior modification (including 48 examining

classroom situations and 80 examining parenting programs), hundreds supporting the efficacy of psychostimulant medication, and 10 supporting a combined (i.e., both behavior modification and stimulant medication) treatment approach. These same treatments are provided in the STP, providing some support for the STP.

At the same time, it cannot be assumed that combined interventions have the same effects as their component parts (17). Indeed, there are multiple ways that treatments may combine, some of which result in more positive treatment effects and some of which result in a reduction of treatment effects (18). Therefore, it is important to empirically examine combined treatment approaches such as the STP, and recent research has begun to do so.

One review of nearly 500 families that attended an STP (19) found that nearly 100% of them anonymously rated the STP as at least somewhat beneficial to themselves and their child, with the vast majority (80%) rating the STP as very beneficial. Moreover, 95% of parents indicated that their child enjoyed the STP. Ratings from the STP staff followed the same pattern, with 95% of children rated as at least somewhat improved by the STP. Finally, the authors found that less than 5% of families who started treatment failed to finish treatment. This is remarkable when one considers that the failure rate for typical treatments of ADHD are estimated closer to 50% (20,21).

The authors also examined whether ratings of children's behavior and impairment improve as a result of participating in the STP. Parent ratings of ADHD, oppositional defiant disorder (ODD), and conduct disorder (CD) symptoms showed a 24% improvement after the STP as compared to before the STP, and an 18% improvement in parent ratings of overall problems (19). In another study (22), teacher ratings of hyperactive-impulsive and ODD symptoms, conflict with the teacher, and dependency on the teacher all improved significantly after the STP as compared to before the STP. The change in ODD symptoms and conflict with the teacher are especially noteworthy because children were rated as significantly different from normal controls prior to the STP but were not significantly different after the STP, suggesting that they were "normalized" after participating in the STP.

An add-on to the Multimodal Treatment Study of Children with ADHD examined the effects of the STP by comparing children who received only the STP to those who received both the STP and medication (23). Results showed that children who received both the STP and medication were superior to children who received only the STP on five measures, whereas groups did not differ on the remaining 30 measures, with both groups showing a similarly positive response to the STP. This study also replicated the high satisfaction ratings and improvement ratings reported by Pelham and Hoza (19).

A recent series of investigations is providing a wealth of evidence for the efficacy of the STP treatment package as a whole, compared with a no-treatment condition (24–27). In a study of a 2-day withdrawal of the STP procedures (26), the withdrawal produced immediate and significant deterioration in behavior with very large effect sizes—regardless of whether or not children were receiving a medication regimen. A subsequent investigation removed the behavioral treatment for 2 weeks in a BABAB design (24,27) and again showed large and significant effects of the STP treatment.

These results have recently been replicated and extended in a program of research that examined the unimodal and interactive effects of behavior modification and stimulant medication by manipulating the intensity of the two treatments as administered in an STP setting The first published study in this program of research examined the classroom behavior of 44 boys and 4 girls (5–12 years old) who participated in a 9-week STP (28). Throughout the STP, children were administered different doses of treatment. Each child received a placebo, low dose (0.15 mg/kg), medium dose (0.30 mg/kg), or high dose (0.60 mg/kg) of immediate release methylphenidate in the morning, at noon, and in the midafternoon each day. These doses were randomly assigned across days in the program. At the same time, each group participated in a 3-week block of no behavior modification (NBM) treatment, low behavior modification treatment (LBM), and high behavior modification treatment (HBM). In the NBM treatment, classes were structured like a general education class—children received adult feedback in response to rule violations, and were asked to leave the classroom for severely disruptive behavior. In LBM treatment, children had a DRC that targeted academic and classroom behaviors, could earn weekly home and camp rewards for meeting DRC goals throughout the week, and staff were trained to provide high rates of praise and social reinforcement for meeting classroom goals. The HBM condition included a DRC that was backed by daily home and camp rewards for meeting DRC goals, a token economy point system linked to camp rewards and privileges, high rates of praise and social reinforcement delivered by staff, and individualized behavior modification programs as needed.

Results of the study supported the effectiveness of behavior modification, stimulant medication, and their combination in the classroom setting. LBM and HBM procedures were generally effective for classroom behavior and seatwork completion. For medication, a low dose resulted in a substantial increase in work completed, with modest increases obtained with increasing doses. Specifically, results showed that half (i.e., 0.15 mg/kg) of the standard dose used in most studies (i.e., 0.3 mg/kg) was effective. When behavior modification and medication were compared, LBM and HBM conditions alone were as good as or better than low, medium, and high doses of medication alone on measures of classroom rule violations. When medication and behavior modification were combined, many interactive

effects were observed. For example, LBM combined with a low dose of medication was equivalent to a high dose of medication or high behavior modification alone. Similar results were found for recreational (29) and home (30) settings.

In summary, there is now clear evidence that the STP intervention is effective compared to an attention-control condition consisting of a summer camp where minimal or no treatment is provided. Further, there is now clear evidence that the blended treatment components offered in the STP result in significant improvement across domains, raters, and measures.

FUTURE DIRECTIONS

Although we have shown that the STP produces significant improvements in the behavior of children with ADHD, additional research will help to answer specific questions regarding the STP. One question concerns the mechanism(s) of action through which the STP has its effects. It has long been known that peer relationships are impaired in children with ADHD, and it has been speculated that peer problems may be a mediator of long-term functioning. It would be interesting to evaluate how the STP impacts peer relationships in children with ADHD and whether this influences the long-term outcome of children with ADHD. Similarly, recent theories of ADHD argue that cognitive impairments play a central role in ADHD (31,32). It would be useful to evaluate whether the STP impacts these purported deficits. It is likely that there are complementary effects of the different types of interventions offered in the STP. For example, the social interventions may help children get along better with peers and adults, whereas time-out procedures may improve children's levels of aggression, and the classroom intervention may improve children's ability to stay on task. In fact, a recent investigation (33) found that the time-out component of the STP produced significant improvement in noncompliant and aggressive behavior beyond the improvement induced by the point system and other treatment components of the STP, lending credence to the hypothesis that it is the combination of the component treatments that provide maximal benefit.

Second, just as with most other treatments, there is a need for more research on how to generalize treatment effects beyond the treatment setting. Many aspects of the STP are implemented to help ensure that the STP is the first step of a long-term intervention to help the child. Parents are included in the child's treatment as much as possible through daily meetings with the child's counselors and weekly parenting meetings that they are required to attend. Similarly, a DRC is developed for each child that can be easily adapted to the child's natural classroom after that STP. Further, we offer children's teachers considerable information about the STP (including a free tour of the STP) to increase the chance that the children's teachers

implement effective behavioral treatments routinely in their classroom. In addition, many of the treatments provided in the STP (e.g., social reinforcement, time-out, point systems, etc.) are widely employed in home and school settings and therefore immediately generalize to these settings. The STP provides parents and teachers an excellent opportunity to refine the procedures they use when implementing these treatments. Further evaluation of these efforts in helping children maintain treatment gains that result from the STP would be both interesting and useful.

Finally, evaluation of the cost-effectiveness of the STP would be useful. A key consideration in implementing any intensive treatment such as the STP is whether it offers sufficient supplemental effectiveness (beyond more traditional interventions) to justify its use. The costs of conducting the STP, including comprehensive follow up for 1 year, ranges from US $ 3000 to US $ 5000 (in U.S. dollars) per child (19). This is roughly the same cost as 1 year of weekly individual outpatient therapy sessions. For the same cost, we believe that available evidence strongly supports the effectiveness of the STP over traditional outpatient therapy. Further, if the STP is effective in partially or wholly ameliorating the long-term negative outcomes associated with ADHD, the cost of the STP will be more than justified. Indeed, the incremental costs associated with ADHD have been conservatively estimated at US $ 14,576 per year (34). If participation in the STP leads to less use of special education services, less contact with the juvenile justice system, less use of medication, or less use of residential treatment services, then these costs would be considerably reduced. In light of these arguments, further examination of the cost-effectiveness of the STP seems warranted.

SUMMARY

Intensive summer day treatment is an effective approach for treating children with ADHD. Children are treated in their natural environments using a variety of interventions that have been demonstrated to be effective for children with ADHD and other disruptive behavior problems. Data from the STP suggests that children and families are likely to stay in treatment, are satisfied at the end of treatment, and show significant improvement on symptoms of ADHD and related impairments. Such effects are unique among treatments for child psychopathology and indicate that the STP approach to treating ADHD is one of the most effective available.

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ADHD: Organizing and Financing Services

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Mental disorders among children and adolescents constitute a serious public health and public policy problem in the United States. One in five children and adolescents has some level of impairment associated with a specific diagnosis, and the majority of these young people receive no mental health care (1). The delivery of mental health services to children and adolescents is complicated by the range of settings, including schools, juvenile justice, social welfare, and primary care, in which these youth may access and receive care. The most commonly diagnosed childhood psychiatric disorder is attention deficit hyperactivity disorder (ADHD), which is estimated to affect 3–5% of school age children (1–3). ADHD receives relatively more public attention than other mental disorders among children in part because it is more prevalent, in part because of well-publicized treatment controversies regarding the use of stimulants, and in part because of the impact of ADHD on the broader education and primary healthcare systems. This chapter examines the financing and organization of services to children and adolescents with ADHD from the perspective of current trends in children's mental health services research.

SYSTEMIC REFORMS AND EMPIRICALLY SUPPORTED TREATMENTS

Research on the organization, financing, and delivery of children's mental health services is currently dominated by two movements (4): (*i*) The systems of care philosophy and approach to service delivery (5) and (*ii*) The

implementation and development of evidence-based or evidence-supported practices (6,7). Although these two sets of approaches developed independently out of different traditions, methods, and philosophies, they are increasingly becoming interrelated for scientific, pragmatic, and political purposes. The systems of care approach focuses largely on how to more effectively organize and finance services for youth who have severe emotional disturbance often involving multiple diagnosis (5), including ADHD as one of the more prevalent primary or secondary diagnoses (8). The system of care approach is, at its core, a systemic, policy-oriented change in the structure and delivery of services. Systems of care place a special emphasis on linkages between child-serving agencies such as mental health, juvenile justice, social welfare, and education, on community-based care in lieu of restrictive placements, on developing a continuum of services, and, in some cases, on measuring the costs and outcomes of care.

The term "systems of care" is part of the child, and often now adult, mental health lexicon, used both with and without any particular meanings or definitions in many states and localities to describe service systems and sometimes even programs or practice approaches. The growth in systems of care is remarkable and can only be considered a tremendous success in terms of its popularity across the United States. This growth occurred even in the context of equivocal findings regarding the effectiveness of these reforms (1,9,10).

Unlike systems of care, empirically based and supported treatments grew out of academic research centers and professional organizations. Empirically supported treatments (ESTs) exist predominantly at the practice level of service delivery. The American Academy of Pediatrics (11) and the American Academy of Child and Adolescent Psychiatry (12) followed the medical pharmaceutical (MP) model (13) utilizing efficacy treatment outcome findings and the consensus conference model (researchers and practitioners meetings to deliberate best practices) to reach agreement on practice guidelines and parameters.

Treatments are first developed in a university laboratory to assess the efficacy of the intervention and later implemented in the field to assess the effectiveness or public health impact. Using randomized controlled trials (RCTs), researchers work to isolate the utility of a treatment in direct comparison to an alternative treatment approach. RCTs can afford a unique opportunity to determine the efficacy of a treatment, the probability that the intervention will generate positive change under ideal circumstances (14). Treatments evaluated as efficacious within the context of an RCT earn the labels, "evidence-based practice" or EST. Pharmacological, psychosocial, and multimodal (15) treatments, which combine pharmacological and psychosocial interventions, have been studied using the MP model with regard to ADHD. Evidence-based or supported treatments constitute the backbone of academic research in mental health service delivery, though they

traditionally have not been particularly popular methods of service delivery in community settings. This situation is rapidly changing, however, as NIH and other funding sources began to lay out roadmaps for bridging science, practice, and translational research (16).

Research on children with ADHD tends to focus largely in the arena of empirically based and supported treatments and their efficacy and effectiveness, with less attention to the questions of access or equity and efficiency or cost that constitute a primary focus of the systems of care approach. Although there is a growing body of research evidence for diagnosis based and increasingly sophisticated treatment approaches for ADHD, significant barriers to service delivery clearly exist. There is only the most limited information pertaining to how services can best be financed and organized to provide efficient and equitable services to youth with ADHD.

FINANCING SERVICES FOR ADHD

The U.S. Surgeon General (1) placed the overall cost of mental illness at $ 69 billion in 1996. Costs of childhood-specific disorders are not well documented; however Hinshaw et al. (17) place the estimated costs for ADHD treatment for children diagnosed with ADHD to be about 3.5 to 4.0 billion dollars. The researchers note that this figure is likely a low estimate as it only accounts for children eligible for special education services. Based on Medicaid data, the average reimbursement for total treatment costs of a child with ADHD in 1999 was estimated at $ 1795 and this disorder was the most common diagnosis for privately insured children. To date, the direct and indirect cost to society for ADHD has not been calculated. There is only limited research regarding the cost of ADHD to individuals, systems (e.g., education, foster care, health care, juvenile justice), or society (e.g., employment loss, disruption to families).

Estimating the treatment costs for ADHD is made more difficult due to the complexity of public and private mental health coverage and ongoing changes in how services are financed. Private health insurance remains problematic with regard to funding children's mental health services. Private health insurance is usually limited and will not cover long-term or more intensive treatment needs and typically limits access to mental health services. An increasing emphasis on managed care has resulted in attempts at "cost-effective" services by reducing inpatient hospitalizations and increased use of short-term therapies.

Within the public sector, access to and availability of services varies by location and type of payer. The federal Medicaid program is the primary mechanism for funding public mental health services to children and adolescents. In 1989 opportunities for accessing the federal Medicaid program increased significantly through the expansion of the Early Periodic

Screening, Diagnosis and Treatment (EPSDT) program (Omnibus Budget Reconciliation Act of 1989 [PL 101-239]). Most states have expanded their Medicaid Services through EPSDT; however, rules and regulations regarding EPSDT and Medicaid remain complicated and also are subject to change. In addition, states must provide matching funds to Medicaid, effectively limiting the degree to which states choose to participate in the program.

Accessing other public funds outside of Medicaid to provide mental health services is often possible; though doing so requires joint planning and may require federal waivers. Child welfare entitlement funds, for example, including Title IV-A, IV-B, and IV-E can be utilized to provide mental health services, particularly those who are at risk for separation from their families through out-of-home placement. Many states have become creative in utilizing a range of public funding sources to provide mental health services because of limitations to Medicaid funding and the joint public responsibility across public agencies of many youth with behavioral disorders. Nonetheless, funding restrictions in the public sector along with limited mental health coverage in the private sector lead to large numbers of youth not receiving mental health services as well as considerable variability across states with regard to access.

Historically, the schools have been considered a primary potential arena for providing mental health services, particularly for youth with ADHD which has a direct negative impact on educational attainment. Many children do receive services as a result of the Individuals with Disability Education Act (IDEA) passed in 1975, which mandates schools to provide services to children whose disability interferes with their education. Schools are legally obligated to evaluate all children suspected of having a disability. Under this federal law, services are also mandated for preschool age children. For those determined to be eligible for services, schools must provide appropriate and free special education and related services to meet each child's unique needs. Changes to the IDEA in 1991 broadened eligibility criteria to include children diagnosed with ADHD. The majority of eligible children diagnosed with ADHD are classified as "other health impaired," (18). Some children with ADHD who have coexisting problems may meet eligibility criteria under "learning disability, developmental delay," or "emotional disturbance" categories. Very recently in 2005, the most recent reauthorization of IDEA changed the name to the Individuals with Disabilities Education Improvement Act (IDEIA) that continued to alter criteria for eligibility. Finally, other federal legislation such as No Child Left Behind potentially intersects with IDEIA in how local districts and schools make decisions regarding authorizing and providing services (19).

Under the IDEAs requirements, states must ensure that schools identify and evaluate children suspected of having ADHD in public and private schools. States are obligated to provide "free appropriate public

education" to eligible children with ADHD. Additionally, states must develop and implement an Individualized Education Plan (IEP), which includes educational goals and recommended behavioral interventions. Under this federal law, states are mandated to include parents in the process and to make every effort to keep children in a regular classroom environment.

States and school districts have a great deal of discrepancy in how they provide "free appropriate education" services to eligible children. All children who need services do not receive them. The U.S. Department of Education reported in 2004 that approximately 11.5% of school-aged children receive special education services. This is below the 20% estimates of the number of youth who receive psychiatric diagnoses and have sufficient impairment to require services. Many school systems are not prepared to provide direct services, some states have contracted services to county agencies. Several potential problems arise in the context of multiple agency involvement and current federal and state budget crises (19). As a result of contractual services, there often is a lack of clarity regarding who should provide the services and how these services should be monitored and evaluated.

The state of California is one example of increasing tensions between community agencies required to provide services and a decreasing state budget for mental health and special education services, often leaving mental health agencies with budgetary deficits. A recent superior court (July 2004) decision ruled in favor of several counties so they would not be mandated to provide services without adequate state funding. The public policy debate in California, as in many states, is ongoing regarding whether services mandated under IDEA should be funded and delivered by mental health, education, state, federal, or local sources.

In theory, the addition of ADHD services under the IDEA, would have the potential to: (1) address this prevalent disorder within a system that is convenient for children and families, (2) increase the number of qualified and trained educators to address the needs of children diagnosed with ADHD, and (3) provide integrated services, which would allow for attention to academic, behavioral, and emotional functioning. In practice, local communities often do not have adequately trained staff, or enough monetary or physical resources to address mental health needs for students. Thus, services available within one school district or state may be difficult to obtain in another.

The Youth and Education Law Clinic at Stanford Law School conducted an evaluation of California's mental health delivery system to special education students (Challenge and Opportunity, May, 2004). In California, these services are provided through government code, Chapter 26.5, which created an interagency system to address the needs of special education students throughout the state. The report concluded that "Although parents

and teachers are looked to as the primary stakeholders responsible for identification and referral for Chapter 26.5 services, they may be ill-equipped to do so" (p. 39). The authors indicated several potential barriers to accessing services including shortage of appropriate school-based locations, lack of transportation to off-site services, and inconvenient appointment scheduling. Problems with accountability and responsibility for following special education plans (IEP plans) for students were also highlighted. There appears to be an inconsistent monitoring of actual service delivery for students, even those who may have outlined educational plans for ADHD services and no formal structured evaluation of the quality or effectiveness of the services.

The Stanford report highlights the detrimental impacts of federal, state, and county budget crises on the delivery of services to those most in need: "In the face of inadequate funding, eligibility criteria for Chapter 26.5 services are "narrowed" and the number of open slots and the types of services available are reduced. As a result, those students with less serious and/or less obvious mental health problems may go without any services at all, while others may receive services that are not appropriately tailored to individual needs" (p. 40).

Many of the potential barriers identified for mental health services in general also apply to children and adolescents in need of services for ADHD referred through the schools. For example, problems accessing appropriate and effective treatment, lack of transportation, limited clinic hours and no school-based services, differences between community mental health and educators regarding the importance of or approach to mental health problems, and difficulties with insurance coverage all impact delivering services to youth with ADHD.

Budget cuts have been a significant problem in providing the full range of services to special education students. In the context of extreme budget crises, parents may have even more difficulty navigating the system and obtaining the best services available. The authors conclude that "the system bears the full cost of providing the services, but students often do not receive or benefit from the services being provided" (p. 61, Challenge and Opportunity).

Children with disabilities who are determined not to be eligible for special education services under IDEA may still be protected and served under two other federal laws: Section 504 of the Rehabilitation Act of 1973 (Section 504) and the Americans with Disabilities Act of 1990 (ADA). The Office for Civil Rights in the U.S. Department of Education enforces the provisions of Section 504 and Title II of the ADA with respect to school districts, while the Department of Education administers IDEA.

Section 504 of the Rehabilitation Act of 1973 is a civil rights law designed to eliminate discrimination on the basis of disability in any program or activity receiving federal financial assistance (REFS). Eligibility for Section 504 is based on the existence of an identified physical or mental

impairment that substantially limits a major life activity. Thus, ADHD symptoms must significantly impact a child's learning or behavior (National Resource Center on ADHD) appropriate accommodation for a student with a disability under Section 504 could entail education in regular classrooms, education in regular classrooms with supplementary services, modifications and/or accommodations, special education, and related services or any combination. Local school districts typically implement the provisions of Section 504; however, ultimate responsibility for enforcing these provisions resides with the Office of Civil Rights (OCR) of the U.S. Department of Education.

ORGANIZATION: STRUCTURING THE DELIVERY OF SERVICES FOR ADHD

ADHD services are delivered within broader systems that are structured and organized based in part, though not entirely, on how they are financed. There are many examples of systemic reform in health services. For example, managed care is predominantly a reform that occurs at the system level, where fiscal changes (such as capitation) and structural changes (such as utilization review) are put in place to provide more efficient service delivery. Over the past decade, systemic reform in the delivery of children's mental health services has been promulgated largely through the system of care approach (5). The system of care model emphasizes many systems-level alterations including: developing linkages between child-serving agencies (e.g., mental health, juvenile justice, child welfare, and education), using community-based care in lieu of restrictive placements, developing a continuum of services, restructuring service financing (i.e., blended funding pools), and creating interagency policy and treatment teams for coordinated care.

Two primary realities drive the need for considering systems factors in providing services to youth with ADHD: (1) As already described, services for ADHD are currently funded through multiple public agencies, especially the schools, primary health care, and specialty mental health services, requiring creative interagency strategies for assembling viable funding strategies; and (2) ADHD is often comorbid with other psychiatric disorders and results in a diverse range of problems in daily functioning, requiring collaborative approaches across agencies.

Comorbidity and the negative consequences of ADHD lead these youth to interact with other service sectors outside of mental health. Children with ADHD may have difficulty with working memory, organization, planning, problem-solving, motivation, social skills, emotion regulation, insight, rule-governed behavior, volition, will power, self-discipline, and even sense of time (2, 20–22). ADHD, therefore, puts children at risk for a variety of problems, including school failure, social rejection,

antisocial behavior, substance abuse, psychiatric disorders including anxiety and depression, and involvement with the juvenile justice system (21). Approximately 50% of children diagnosed with ADHD also meet diagnostic criteria for conduct disorder or oppositional-defiant disorder (ODD) (2,23).

Clearly, youth with ADHD typically have problems in school, may be involved in the juvenile justice system, and may also be subject to abuse and neglect and consequently be involved with the social welfare system. ADHD does pose particular challenges for service delivery systems. Outside the school system, the majority of children diagnosed with ADHD are being treated by primary care physicians (3,24). Understanding service system delivery issues for youth with ADHD requires an understanding of how medications are delivered.

Stein and Orlando (3) report that increasingly a psychiatrist is responsible for medication management and other mental health professionals provide behavioral treatment. The researchers suggest that this change is a direct result of managed care policies to reduce the higher costs of psychiatrists by limiting their role. Recently researchers examined data from two national surveys to compare trends in the use of psychotropic medication for children over a 10-year period (1987 to 1996) (25). Olfson and colleagues (25) reported that stimulant medication use was four times higher in 1996 compared to 1987, with the exception that children without insurance were much less likely to use stimulant medication. Also, children from higher income families were more than twice as likely to receive ADHD services compared to children from low-income families in 1987, but no differences were found in 1997, suggesting an increase in public insurance expenditures for treatment of ADHD (25). The data from this study suggests that uninsured children may not have the same access to psychotropic treatments for ADHD.

Olfson et al. (18) reported a significant increase in outpatient treatment for ADHD between 1987 and 1997. The increased rate in treatment over the specified decade was greater for boys than girls and for older children (12 to 18 years) compared to younger children (3 to 11 years) (18). Also, Caucasian children were twice as likely to receive treatment as Hispanic or African-American children. Despite research findings suggesting positive treatment effects for behavioral approaches for ADHD, Olfson and colleagues (18) report a significant decrease in the number of treatment visits, with only a minority of children receiving psychotherapy as a treatment for ADHD. The researchers estimate that children who received psychotherapy received three fewer visits in 1997 than in 1987, which is likely a result of restrictions from managed care organizations.

Overall, physicians, rather than psychologists or other health care professionals, served as the provider for the majority of children treated for

ADHD. For the 1997 survey data, roughly one-third of children diagnosed with ADHD received special education services (18). The authors outlined several factors that may have influenced the increased use of ADHD services from 1987 to 1997. The inclusion of ADHD (as other health impaired) under the IDEA increased the number of students eligible for special education services and likely increased attention on ADHD in schools and school-based mental health programs. The public awareness of ADHD has led to the development of parent groups, community resources, and advocacy organizations (18).

BUILDING AND BLENDING SYSTEMS AND CLINICAL INTERVENTIONS: SPECIAL CONSIDERATIONS FOR ADHD

From the perspective of financing and organizing service systems, ADHD is similar to other disorders found in childhood such as conduct and ODD, depression, and anxiety. Because children live in complex social systems that include schools, parents, and potentially other service agencies, the coordination of varying service sectors remains both complex and essential to providing access to services and to providing mechanisms for treatment. ADHD is, however, unique in two primary ways that pose challenges for the financing and organization of services.

First, ADHD has more direct and immediate consequences on school performance that are often evident earlier in life when compared to other childhood psychiatric disorders. Consequently, many youth with ADHD receive special education services (18). Second, youth with ADHD also receive medication and though there remains considerable controversy regarding whether medication is appropriately prescribed, there is clear evidence that medication can provide reductions in symptoms and improvements in functioning, especially when combined with psychosocial interventions (15). Youth may receive medication at relatively young ages, including elementary school. Though medication may be helpful for other psychiatric disorders (especially depression and anxiety), they are relatively less frequently used, particularly for younger children and the evidence for effectiveness is not as strong (25).

The direct impacts of ADHD on school performance have lead states to experiment with innovative strategies to provide effective ADHD services to children under the IDEA. For example, the Kentucky Department of Education has included instructional strategies, accommodations, and modifications in their training programs and publications, implemented a behavior Web site with detailed information on ADHD, and developed an annual conference on ADHD. This information is designed to ensure that students with disabilities are able to participate in the general curriculum. The state of Tennessee sponsored an expert-led workshop for teachers to address ADHD topics including identification, evaluation, medication, parent training, social

skills, classroom strategies, assessment, and intervention. Similarly, the West Virginia Department of Education has sponsored teacher trainings on the specifics of the IDEA and on state regulations for special education. These are just a few examples of state-based programs to inform educators and families on the laws and regulations, individual rights, and resources available to students with ADHD.

The use of stimulants for youth with ADHD raises numerous concerns regarding access to appropriate health care and particularly psychiatric care. In 2006, over 8 million children (about 11% of the total number of children in the United States) did not have any form of health insurance. Access to specialty mental health care is limited, with over three quarters of those youth with mental disorders not receiving any services from specialty providers (26). The shortage of child psychiatrist, particularly in rural areas, is well-documented. Family practitioners are less likely to provide adequate quality of care. Consequently, providing access to high-quality medical care and medication management for youth with ADHD is a major challenge.

EMPIRICALLY SUPPORTED TREATMENTS?

This chapter began by noting that ESTs are one of the two dominant trends in mental health services research for children and adolescents. Since that point, the majority of the chapter focused on organizational and financing concerns. Optimally, ESTs and innovations in the organization and financing of services are both essential components to providing equitable, efficient, and effective services (4). Historically, many ESTs were not tested in the community, and many reforms in systems structure did not consider clinical innovations developed in academic centers. This situation is rapidly changing as service reform efforts based in the community are embracing ESTs and these treatments are, in turn, being tested in the community. The relationships between community-based services, systems reform, and empirically based treatments are complex and the understanding of their interrelationships is undergoing considerable analysis (27).

The full scope of such discussions is beyond this chapter. However, many psychosocial interventions for youth with ADHD are community based in that they exist in part or in whole within schools. Schools are the primary system impacting on youth with ADHD, however these youth are also potentially subject to how services are financed and organized within the primary health care, juvenile probation, and even social welfare sectors. Ultimately, the delivery of effective services to youth with ADHD will rest on how services are organized and financed. Conversely, in an optimal system the organization and financing of services can be driven by those treatments that have empirical support. To this point, there is no evidence that the organization and financing of services to youth with ADHD promotes effective services. There is, however, discouraging evidence that

access, equity, and efficiency are also not promoted by current organizational and systemic factors. The considerable progress in understanding how to provide more effective services to youth with ADHD has not been mirrored by similar progress in the financing and organization of services, and that ultimately will significantly hamper how many youth receive any services, let alone high quality or empirically supported care.

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Principles of Medication Titration

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INTRODUCTION

The previous chapter outlined the wide variety of medications used in the treatment of attention deficit hyperactivity disorder (ADHD) and discussed their classification as first or second line agents. This chapter will focus on the clinical use of these medications, particularly the titration of each agent to its optimal dosage for the patient. Here the science of medication treatment, as established by clinical trials of these agents, interacts with the art of clinical care where conclusions from averaged data in studies do not always apply to the individual patient. The physician must be flexible in the dosing strategy used, carefully balancing control of the symptoms of ADHD with minimization of side effects.

STIMULANTS

Stimulants are by far the most commonly used medications in the treatment of ADHD. The American Academy of Child and Adolescent Psychiatry has recently published guidelines for their clinical use (1). The National Institutes of Mental Health Multimodality Study of ADHD (MTA) study also provides valuable guidance for the titration of stimulant medication (2,3). In this study, children were randomized to one of four long-term treatment groups: community controls, medication management, psychosocial intervention or combined treatment (medication management + psychosocial intervention). Those children in the two medication management groups received a double-blind placebo-controlled crossover trial of

methylphenidate using the full range of methylphenidate doses (generally 0.3–1.0 mg/kg/dose). Teacher and parent ratings were obtained each week and blinded evaluators determined which dose of methylphenidate yielded the optimal response compared to the placebo week. This dose was selected for the child's long-term medication management. That dose was then adjusted at monthly medication visits. In contrast, those community controls treated with medication had more variable follow-up and no set titration of stimulant. At follow-up one year later, those in the medication management group had a significantly better outcome than those in the community control group (4). Children in the medication management group who received a significantly higher mean daily dose of methylphenidate, were more likely to receive a third, afternoon dose of methylphenidate, and received higher individual doses than those in the community control group (4,5).

These data suggest that doses commonly used in clinical practice (generally about 0.3 mg/kg/dose) may be too low to achieve full remission of ADHD symptoms. Typically, physicians will place a patient on a low-starting dose and schedule a follow-up within the first month of treatment. At this visit, the parent is usually queried about the child's progress. If the parent and physician are satisfied with the response, no further dose adjustment is made. The possibility that a higher dose of stimulant might lead to even greater improvement is not explored. The MTA study suggests that higher doses of stimulant should be administered if there is not near-complete remission of ADHD symptoms with the starting dose. Table 1 adopts this philosophy. The child's weight establishes the starting dose; the response of the child to each dose is assessed over a 1–2 week period. This need not necessarily be at an office visit. The parent and teacher can be provided with standardized rating scales (6) to fill out assessing the child's behavior, and these can be faxed to the office along with a scale rating side effects (Table 2). The physician can review these scales and order a dose increase for the next week if the child's symptom ratings do not fall within the normative range (7). This process continues for each week until the maximum dose is reached. If resolution of ADHD symptoms is not satisfactory or side effects are prohibitive, the given stimulant is discontinued and an alternative stimulant is tried. In general at least two different classes of stimulants should be tried before moving to any of the non-stimulant alternatives.

The advent of long-acting stimulants has made the titration of stimulant medication much easier (Table 2). Studies show that the long-acting stimulants are equally efficacious as their immediate release forms (8–11) thus there is no need to titrate the patient to a full dose of immediate release before moving the patient to a long-acting form. Side effects must be monitored closely when higher doses are used for younger children, as shown by the italicized cells in Table 1. Note that Focalin, the pure dextro

Table 1 Titration of Immediate Release Stimulant Medications

d, l-Methylphenidate (Ritalin®)

	35–50 lbs	51–70 lbs	70–90 lbs	>90 lbs
Week 1–2	2.5 am/noon	5 mg am/noon	10 mg am/ noon	10 mg am/noon
Week 2–4	5 mg am/noon	10 mg am/ noon	15 mg am/ noon	20 mg am/12 noon
Week 3–6	10 mg am/ noon	15 mg am/ noon	20 mg am/ noon	20 mg am/12 noon
Week 7	*15 mg bid*	*20 mg bid*		

Add third dose after school if necessary up to a maximum of 60–80 mg day.
For d-methylphenidate (Focalin®), doses are 1/2 those of the above.

Dextro (75%)/Levo (25%) Amphetamine (Adderall®)
Dextro (100%) Amphetamine (Dexedrine®, Dextrostat®)

	35–50 lbs	51–70 lbs	70–90 lbs	>90 lbs
Week 1–2	2.5 am & noon	2.5 mg am & noon	5 mg q am & noon	7.5 q am & noon
Week 2–4	5 mg am & noon	5 mg q am & noon	7.5 mg q am & noon	10 mg q am & noon
Week 3–6	7.5 mg q am & noon	7.5 mg q am & noon	10 mg q am & noon	15 mg q am & noon
Week 7	*10 mg q am & noon*	*7.5 mg q am & noon*	*20 mg q am/ 10 mg q noon*	20 mg q am & noon to 30 mg bid

form of methylphenidate, is given in doses one-half that of mixed racemic methylphenidate. The dosing of mixed salts amphetamine (Adderall, Adderall-XR) is the same as the pure dextroamphetamine (Dexedrine, Dextrostat, and Dexedrine Spansule). Most recently, a methylphenidate transdermal patch (Daytrana) and an amphetamine pro-drug (lisdexamfetamine dimesylate, Vyvanse) (12) have been approved by the Food and Drug Administration for use in children aged 6–12 years. These agents also show an average duration of action of 10–12 hr; their dosing is shown in Table 2. Weight-based dosing is not known for these agents, thus a standard titration is used for all children. Caution is warranted when using these agents in preschoolers as no study data has been gathered in that age group.

As the dose is titrated, the physician should assess the side effects (adverse events) listed in Table 3. A direct inquiry about the most common side effects is better than an open-ended question as it is likely to jog the parents' memory. It is, however, important to assess the frequency of these "side effect" symptoms at baseline, since many ADHD children evidence

(Text continues on page 215.)

Table 2 Titration of Long Acting Stimulant Medications

Adderall® XR, Dexedrene Spansules

	35–50 lbs	51–70 lbs	70–90 lbs	>90 lbs
Week 1–2	5 mg q am	5 mg q am	10 mg q am	10 q am
Week 2–4	10 mg q am	10 mg q am	15 mg q am	15 mg q am
Week 3–6	15 mg q am	15 mg q am	20 mg q am/10 mg q noon	20 mg to 30 mg q am
Week 7	15 mg q am	20 mg qm	20–40 mg q am	30–60 mg q am

Vyvanse (lisdexafetamine dimesylate)

	35–50 lbs	>51 lbs
Week 1–2	Unknown	30 mg q am
Week 2–4	Unknown	50 mg q am
Week 3–6	Unknown	70 mg q noon

Vyvanse (lisdexafetamine dimesylate)

	35–50 lbs	>51–70 lbs
Week 1–2	Unknown	30 mg q am
Week 2–4	Unknown	50 mg q am
Week 3–6	Unknown	70 mg q am

Concerta (Give as am dose only, average 12 hr duration)

	35–50 lbs	51–70 lbs	70–90 lbs	>90 lbs
Week 1–2	18 mg	18 mg	36 mg	36 mg
Week 2–4	27–36 mg	27–36 mg	54 mg	54 mg
Week 3–6	54 mg	54–72 mg	72 mg	72–108 mg

Daytrana (methylphenidate transdermal system)

	>51 lbs
Week 1–2	10 mg q am
Week 2–4	20 mg q am
Week 3–6	30 mg q am

Metadate-CD/Ritalin LA (Give as am dose only, average 8 hr) duration

	35–50 lbs	51–70 lbs	70–90 lbs	>90 lbs
Week 1–2	Use IR first	20 mg	20 mg	20 mg
Week 2–4	20 mg	40 mg	40 mg	40 mg
Week 3–6				60 mg

Supplement with pm immediate release methylphenidate if after school dose needed.
Focalin XR use am doses approprimately 1/2 of the above

Table 3 Side Effect Questionnaire

Is your child having any of the problems listed below?	How bad is problem?			How has medication affected the problem?		
	None	Some	Very much	Made it worse	No change	Made it better
Poor appetite						
Trouble sleeping						
Sleepiness in day						
Stomach aches						
Constipation						
Diarrhea/loose bowels						
Headaches						
Rash						
Muscle twitches						
Nervousness						
Grouchy, more angry						
Withdrawn, stares, "zombie"						
OTHER:						

poor appetite and sleeping difficulties at baseline. It also important to ask if the parent feels the symptoms has been affected by the medication. Older children, adolescents, and adults can report on side effects themselves. Height (for children and adolescents), weight, blood pressure, and pulse should be monitored at each visit. Blood pressure and pulse are particularly important to monitor in adult patients who may have asymptomatic hypertension. No laboratory monitoring of hematological measures, serum chemistry or electrocardiogram is required during stimulant treatment.

Once the most optimal dose has been established during the initial trial, the dose should remain fairly stable over the long term, except when the child grows substantially. There is little evidence of tolerance to stimulant treatment within the dose ranges described in Table 1, several studies show continued effectiveness of medication after one year of continuous treatment (13,14). The maximum dose of stimulant to be given to a patient is much debated. Initial research with long-acting stimulants was carried out in school aged children, but recent controlled trials of stimulants have focused on adolescents (15,16) and adults (17,18). These studies in older individuals show response rates to stimulants similar to that of children. Adults have been successfully managed on up to 60 mg a day of amphetamine (19) and 70–100 mg a day of methylphenidate (20,21). Thus it is permissible to exceed the maximum dose limits prescribed by the *Physician's Desk Reference*. Indeed, if amphetamine is twice as potent as methylphenidate, a dose of

120 mg a day would need to be given to achieve equivalence of methylphenidate with 60 mg of amphetamine (22). Doses in this range should be used only with extreme caution; the physician should be particularly suspicious of the adult patient who claims to need higher and higher doses of stimulant at each visit, or who insists on needing 60–100 mg doses several times a day. Such a patient may be involved in diversion, or may be developing tolerance to the stimulant.

How frequently do patients on stimulant medication require follow-up? MTA patients were seen monthly, but it is not clear that face-to-face physician contact was a key variable in improving outcome. Rather, physicians had access to detailed rating scale data that allowed them to fine-tune the child's dosages. The number of follow-ups per year may range from 2 to 12 depending on a variety of factors: robustness of stimulant response, existence of other comorbid psychiatric or medical conditions, chronic treatment with other medications or presence of psychosocial stressors. The more complicating factors are present, follow-up should occur more frequently. Height (for children and adolescents) weight, blood pressure and pulse should be monitored at each visit. Blood pressure monitoring is important in adults who may have asymptomatic hypertension. There is no need to monitor serum chemistries, hematological indices or electrocardiogram unless a medical condition other than ADHD is present (23).

Atomoxetine

Atomoxetine (Strattera®) is a non-tricyclic norepinephrine re-uptake inhibitor which has been approved for the treatment of ADHD. It shows clear superiority over placebo in several double-blind parallel group studies (24–27). In the latter study, atomoxetine dosed once-a-day was superior to placebo in reducing both parent and teacher ratings of ADHD symptoms in children and adolescents aged 6–16 years. The effect size of atomoxetine was calculated to be 0.71 (27), compared to an effect size of 1.0 that is commonly seen in stimulant studies (28). Atomoxetine was comparable to methylphenidate in a open-label trial (29), but no teacher ratings were obtained in that study and the mean mg/kg/dose of methylphenidate was not specified. Thus it is not clear that atomoxetine is equally efficacious as stimulant medications. Nonetheless, the availability of a new non-stimulant for the treatment of ADHD is important, as it will be a valuable option for those who do not tolerate stimulant medications or who have comorbid substance abuse problems.

The starting dose of atomoxetine is 0.5 mg/kg/day given as a single AM dose for 3 days, and then increased over a 1-week period to a maximum of 1.2 mg/kg/day. Side effects are generally mild and most commonly consist of gastrointestinal complaints, decreased appetite and sedation. The dose can be divided twice a day (12 hr apart) for those who cannot tolerate a

single daily dose or experience wearing off of the medication in the evening. For older adolescents and adults, the starting dose is 40 mg a day, increasing to 60 or 80 mg a day after the first week of treatment. Atomoxetine (Strattera®) comes in 10, 18, 25, and 40 mg capsules. It should be used with caution in persons taking medications which are metabolized by the 2D6 CYP 450 system. Since atomoxetine is an inhibitor of this system, the action of the other medications could be potentiated. Due to the emergence of suicidal ideation (but no completed suicides) in a small number of patients taking atomoxetine in the clinical trials, a boxed warning regarding suicidal thoughts as an adverse event is included in the package label (30).

Bupropion

Bupropion is agent which blocks the reuptake of dopamine; its metabolite blocks the reuptake of norepinephrine; it may also enhance the function of the noradrenergic system though mechanisms other than re-uptake blockade (31). Conners and colleagues (32) showed bupropion to be superior to placebo in the treatment of ADHD in children, though the effect size was lower than that seen in stimulant studies. Wilens et al. (33,34) showed bupropion to be efficacious in adults with ADHD. It is an effective second line agent for the treatment of ADHD. In children, its starting dose is 3 mg/kg/day in divided doses. After 2 weeks, its dose can be increased to 6 mg/kg/day or 300 mg/day, whichever is smaller. In adults or older adolescents the slow release or extended release form of bupropion is more convenient. The slow release form of 150 mg is given in the morning only for 3–5 days, after that it is given twice a day. The XL form is given once a day, and is available in 150 and 300 mg capsules.

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) were once the principle second–line agent after methylphenidate in the treatment of ADHD. With the advent of multiple stimulants, bupropion and atomoxetine, their use for the treatment of ADHD has declined considerably over the last decade. The TCA desipramine was associated with several cases of sudden death in children in the late 1980s (35,36), and while a causative relationship was never established, the use of desipramine for treating ADHD was effectively ended. Furthermore, the experience with desipramine lead to standards regarding electrocardiogram monitoring in any children treated with any other of the tricyclics (imipramine, nortriptyline). This had made their use cumbersome, but TCAs may still have uses in children who have not responded to stimulants and patients with comorbid tic disorders. In such patients, tricyclics will reduce tics as well as ADHD symptoms (37).

Imipramine is typically started at doses of 1 mg/kg/day in divided doses, with titration to doses of 2.0–2.5 mg/kg/day over a 1–2 week period. If the ADHD symptoms respond to this dose, no further titration is required. If there is non-response or an inadequate response, then the imipramine dose should be increased at a rate 1 mg/kg/day per week up to a maximum of 5.0 mg/kg/day. At doses above 2.0 mg/kg/day, serum levels should be obtained to document that the level has not exceeded 200 ng/mL. If the level is below the therapeutic level for depression treatment, but the ADHD symptoms have adequately responded, there is no need to raise the dose further. Once stable, blood levels and EKG should be repeated annually or whenever a dose adjustment is made. Nortriptyline is used in doses one-half that of imipramine.

During treatment with a TCA, resting heart rate should be less than 130 bpm, the PR interval less than 200 msec, the QRS interval should not be widened over 30% of the baseline value, and the QTc interval should be less than 460 msec (37). Most TCAs are metabolized by cytochrome P450 2D system. Thus medications which inhibit this system such as cimetidine, many SSRIs, phenothiazines, aspirin, oral contraceptives, and phenytoin may raise TCA levels and EKG abnormalities that correlate with higher TCA levels.

Alpha-Agonists

The alpha-agonists clonidine and guanfacine were widely used despite relatively little published data on their efficacy and safety. There has been an ongoing debate as to their safety with regard to cardiovascular side effects (38,39). Alpha agonists have also been used for a variety of indications apart from the treatment of ADHD per se. Clonidine, the more sedative of the two alpha agonists, has often been given a single dose at bedtime to treat stimulant-induced insomnia or evening rebound when the last stimulant dose of the day has worn off (40). There are no controlled trials of this practice. Clonidine has also been combined with stimulant to treat comorbid aggression, although the first small controlled trial of this practice was negative (41). A subsequent, larger study did show clonidine was superior to placebo when added to methylphenidate for the treatment of aggression (42). While studies of the efficacy of clonidine in ADHD are limited in number and have numerous methodological problems, a metaanalysis of these studies did show a significant effect size relative to placebo (43). Guanfacine has been shown to be efficacious in the treatment of ADHD in children with comorbid tics, though with an effect size for reducing ADHD symptoms less than that of stimulants (44).

The dose titration of both clonidine and guanfacine is shown in Table 4. Guanfacine is only one-tenth as potent as clonidine. Blood pressure and pulse must be monitored carefully. Alpha-agonists should not be terminated abruptly, as rebound hypertension may occur (31). This raises

Table 4 Titration of Alpha-Agonists

Preadolescent doses	Clonidine	Guanfacine
Day 1–4	0.05 q hs	0.5 q hs
Day 5–9	0.05 q am & hs	0.5 q am and q hs
Day 10–14	0.05 tid	0.5 mg tid
Day 14 and up	0.05 qid	1 mg bid
Adolescent (>100 lbs)		
Day 1–4	0.05 q hs	0.5 q hs
Day 5–9	0.1 q hs	1 mg hs
Day 10–14	0.1 bid	1 mg bid
Day 14 and up	0.1 tid/qid	1 mg tid

Note: Need baseline BP and pulse (standing, lying), repeat when dose stable or cardiovascular symptoms presence. Reduce dose if patient complains of dizziness, cheat pain, palpitations, sedation.

questions about the safety of such medications used as one time dose in the evening for sleep, as they are wearing off in every morning as the child awakes. Nonetheless, nearly all adverse events with clonidine were reported in children taking multiple doses per day (38).

CONCLUSION

A wide variety of psychopharmacological agents are available for the treatment of ADHD. The physician should be guided by a number of key principles: (1) Quantify the ADHD symptoms at baseline, (2) use the appropriate starting dose of the agent and follow-up with parent and teacher ratings to document response, (3) continue to titrate the agent upward until full remission of ADHD symptoms occurs (unless discomforting side effects prevent this), (4) switch to alternative agent if a given medication does not achieve remission, and (5) monitor long progress once the acute symptoms are in remission. By careful use of the many therapeutic agents discussed here, the physician will be able to substantially improve the quality of life for patients with ADHD.

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Section V: Special Populations

22

Clinical Assessment of Preschoolers: Special Precautions

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INTRODUCTION

The clinical assessment of preschoolers poses several challenges. These challenges relate primarily to the evaluation of symptoms relative to behavior considered to be within the normal range, understanding symptoms relative to the child's developmental status, and the assessment of functional impairment for children who are not in school and have limited social encounters outside of the family. These issues are exacerbated by the limited developmentally informed clinical research in preschoolers with attention deficit hyperactivity disorder (ADHD). Additionally, clinicians must consider differential diagnosis with other disorders of early childhood, including oppositional defiant disorder (ODD), speech and language disorders, and developmental disorders.

ADHD IN PRESCHOOLERS

Although the diagnostic criteria for ADHD require that the symptoms onset prior to 7 years of age (20), and community-based studies report rates of ADHD in preschoolers ranging from 2% to 6% (1,2), the overwhelming majority of research in ADHD has been conducted with school-aged children. The few systematic studies of clinically-referred preschool children suggest that ADHD preschoolers, relative to non-ADHD preschoolers, have difficulties with peer and family interactions, language impairments, and

academic difficulties (3–6). Preschoolers with ADHD, like older children with ADHD, have also been shown to have problems in working memory (7), and high rates of comorbid disorders (8). Existing data suggest that ADHD in preschoolers parallels ADHD in school-aged children in terms of symptom expression, functional correlates, and comorbid disorders. However, there are important differences in cognitive, behavioral, motor, and social development in preschoolers relative to older children that need to be considered in the evaluation process (22,23).

Developmentally Informed Assessments

A comprehensive and developmentally sensitive evaluation of ADHD in preschoolers is critical so that children with levels of inattention, impulsivity and activity that are within the normal range for the preschool period are not inaccurately diagnosed with ADHD. A proper evaluation can also ensure that an appropriate diagnosis is made in cases where behavioral symptoms significantly interfere with development and social functioning. The delay in diagnosis and treatment of preschoolers with ADHD that is functionally impairing might result in additional developmental problems, the onset of comorbid disorders, and other consequences of untreated mental health problems. This is of particular concern because ADHD that onsets in the preschool period may, in fact, represent a potent version of the disorder (5,9).

Although there have been only a limited number of clinical studies with preschoolers with ADHD, studies of developmental psychopathology and normal development during the preschool period provide a basis for consideration of special issues related to assessing preschoolers. Developmental studies suggest that relative to older children, the behavior of preschoolers is highly sensitive to context, and the normal variation for attention, activity level and impulsivity is wide. Furthermore, symptoms must be considered in relation to the child's cognitive developmental status, speech and language development, and motor development. Preschoolers have rapidly emerging skills in these three areas; each area of development is also highly variable within the preschool period. Functional impairment must also be considered in light of the child's developmental status as well as in the context of important relationships and demands of the preschool period. During the preschool period, there are growing expectations regarding compliance and independence. Additionally, early educational settings add demands for attention, impulse control, and regulation of behavior (6). Thus, clinicians must be aware of developmentally appropriate expectations for a preschooler. Finally, due in part to the convergence of certain aspects of development in the preschool period, certain comorbid disorders, (e.g., ODD, speech and language disorders, and pervasive developmental disorders) are more likely to onset in the preschool period.

Therefore, special consideration should be given to comorbid disorders in the evaluation of a preschooler with ADHD.

Context Matters

Preschooler's behavior, as well as neurobiological functioning, has been shown to vary according to context (10). Accordingly, the clinical assessment of preschoolers requires consideration of behavior across contexts, taking into account factors such as time of day, peer composition (same or mixed sex peer group), relationship factors (preschoolers tend to behave differently with mothers vs. fathers), and social, cognitive, and behavioral demands of the setting. For example, child behavior is likely to vary significantly between relatively structured settings with high demands for attention and impulse control (e.g., preschool circle time, church services) and those that are unstructured yet socially challenging (e.g., neighborhood playground).

Gathering information from multiple informants (such as mother, father, teacher, daycare provider, and older sibling) who observe and relate to the child in different contexts is important for achieving a comprehensive picture of the child's behavior. Each informant is likely to observe the child in different settings and under different environmental conditions. Context-sensitive information from multiple informants can then be integrated to inform diagnostic conclusions and tailor treatment planning (24). For example, different treatment plans would be developed for an ADHD preschooler whose symptoms are exacerbated at daycare when he is tired or hungry versus a preschooler who is able to follow verbal directions at school when provided in a low stimulation environment but has trouble when there are too many visual or auditory distractions. Evaluations that provide this level of detail about symptom expression related to contextual variables are likely to be highly useful for treatment planning.

Observations in Naturalistic Settings

In addition to obtaining information from multiple informants, clinicians should consider observing the child in a naturalistic setting. This is especially important if discrepant information is provided by different informants, or if questions about functional impairment exist. A range of core ADHD behaviors can be observed in naturalistic settings such as the home or school environment, including spontaneous verbalizations, fidgeting, excessive motor behavior, and off-task behaviors. School observation measures of ADHD symptoms originally designed for school-aged children have been used successfully with preschoolers (11). The clinician should select the setting for observation that is most likely to allow for observation of the specific presenting problem behavior(s) of interest. Observations in familiar settings not only permit clinicians to evaluate core symptoms, but they also

can inform treatment planning by helping the clinician to understand how core behaviors impair academic or social functioning, and whether there are features of the environmental context that elicit, maintain, or exacerbate symptoms.

Distinguishing Symptoms from Normal Variation

Another challenge in assessing preschoolers concerns differentiating ADHD symptoms from behaviors that may be considered developmentally appropriate. Developmental variability is one of the hallmarks of the preschool period. To determine whether a specific child behavior (e.g., inattention, distractibility, or hyperactivity), meets criteria as a symptom of ADHD, the clinician must compare the behavior to developmental expectations or normative behavior for the preschooler. This is complicated by the fact that there is a wide range of "normal" or "acceptable" levels of inattention, activity, and impulsivity during the preschool period (12,13).

There are a few parent and teacher DSM-IV (20) referenced ratings scales of ADHD symptoms, such as the Conners Rating Scales (14) and the Early Childhood Inventory-4 (ECI-4; 15) with norms specific to the preschool period that can be helpful in this aspect of evaluation (16,17). However, the options are much more limited for evaluating preschoolers with ADHD relative to older children. This is unfortunate, and may result in the underdiagnosis of preschoolers by clinicians who are reluctant to view the behavior of preschoolers as atypical without a solid empirical basis for making this conclusion. The assessment of inattention in preschoolers can be particularly difficult and even fewer psychometrically sound rating scales capture this core feature of ADHD in preschoolers (18).

Developmental Status

An understanding of the child's cognitive developmental level, language skills and social and motor development are necessary for evaluating individual symptoms of ADHD as well as functional impairment. For example, consideration of the child's level of receptive language skills is important for establishing whether a child is "not listening" or "not following directions." Similarly, consideration of the child's play skills is critical for evaluating whether the child is "having difficulty playing quietly," and understanding of the child's level of social awareness is necessary for determining if the child is "having difficulty waiting his or her turn."

There are several cognitive tests currently available for preschoolers, some of which can be completed in fewer than 60 min, which can provide a basis for evaluating cognitive developmental status [e.g., Differential Abilities Scale; Ref. (19)]. Many cognitive tests are accompanied by observational ratings to be completed by a psychometrician during testing. These observations of behavior during structured cognitive testing (e.g.,

out-of-seat, requiring multiple directives, difficulty following directions) can also be informative as part of the comprehensive assessment of preschoolers.

Evaluating Functional Impairment

A diagnosis should only be made if the ADHD behaviors are causing "clinically significant distress or impairment in social, occupational or other important areas of functioning" (20). The evaluation of clinical impairment in preschoolers can be particularly challenging. The impact on academic or school functioning is difficult to evaluate in children who have not yet entered school; similarly the impact on peer relations and social functioning can be hard to assess in children who have not had opportunities to engage with same-age peers on a regular basis (25). In cases where children are not yet in school or have not had much peer exposure, clinicians should consider distress or impairment as related to parent–child relationships, sibling relationships, developing sense of self and self-esteem. When possible, functional impairment should be assessed in whatever social environments are relevant (e.g., play with same age peers, playdates, informal peer group play).

Differential Diagnosis

Finally, the clinical assessment of preschoolers requires consideration of issues of differential diagnosis with disorders of the early childhood period. Disorders of early childhood to be considered in the evaluation of ADHD include ODD, autism-spectrum disorders, and speech and language disorders. The differentiation of ODD and ADHD symptoms in the preschool period can be particularly challenging, especially for children who are not in school-like settings. Sole reliance on parent report to make such distinctions can be highly problematic (21). Observations of the child in multiple contexts may be essential for making this distinction. Differential diagnoses involving speech and language problems or autism-spectrum disorders may require a multidisciplinary team approach. If a team approach is not feasible, consultation with a speech-language therapist or a developmental specialist in disorders of early childhood may be helpful.

CONCLUSION

The assessment of preschoolers requires attention to developmental issues that influence all aspects of behavior and functioning during the preschool period. Given the considerable variability and degree of contextual influence on behavior during the preschool period, a multimethod, multiinformant approach to evaluation is required. This involves collecting data from parents, teachers, and other caregivers who observe the child in multiple naturalistic settings. Furthermore, the assessment of ADHD during the

preschool period raises particular challenges, not unique to the disorder, regarding how behavior is evaluated in light of developmental status and normal individual variation. Differential diagnoses of ODD, speech and language problems, and autism-spectrum disorders are of particular relevance to the evaluation of ADHD during the preschool period. Clinicians must consider these issues as part of an informative and comprehensive clinical assessment of ADHD in preschoolers.

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Psychosocial Treatment for Adolescents with ADHD

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OVERVIEW

Epidemiological data suggest that attention deficit hyperactivity disorder (ADHD) affects between 2% and 4% of adolescents in the general population. Similar to children with ADHD, problems for adolescents with the disorder typically include academic difficulties, discipline problems at school and at home, and conflict with peers; however, adolescents tend to experience more serious consequences than children. For example, problems such as school dropout, substance abuse, and legal problems become more common among youth with ADHD as they mature. In addition, between 25% and 75% of adolescents with ADHD meet diagnostic criteria for other disruptive behavior disorders (1), resulting in significant additional impairments. Treatment for these youth therefore requires a comprehensive, multimodal approach that addresses impairment across multiple domains and contexts (2).

The most widely used treatment for adolescents with ADHD is stimulant medication, but many questions and concerns still surround the use of stimulants among adolescents. Professional literature is replete with studies of stimulant treatment for children with ADHD (3); however, as of 2000 we found only 20 controlled studies of the use of stimulants with adolescents (4–6). Overall, the research on stimulant treatment with children suggests that stimulants are efficacious, but result in improvement rather

than a normalization of functioning. The current literature on adolescents suggests a similar conclusion, with one study reporting that between 9% and 29% of the adolescent participants demonstrated no benefit from taking small, medium, or large dosages of methylphenidate on measures of academic performance and classroom behavior (4). In addition, stimulant medication appears insufficient for treating the common problems of parent-teen conflict (7) and social functioning (8). Other limitations of medication treatment include the lack of sustained adherence to medication regimens and resistance by some families and youth to taking medication. Medication is an effective treatment option for many adolescents with ADHD; however, it has limitations and additional treatments are needed in order to address the problems frequently associated with adolescents with ADHD.

Although some studies suggest that benefits due to medication treatment may indeed generalize from childhood to adolescence (9), the continuity of efficacy for psychosocial treatment from childhood to adolescence is largely untested. Since the vast majority of literature on the treatment of ADHD has focused on elementary school-aged children, the temptation exists to simply extrapolate psychosocial treatments from studies of children with ADHD and apply them to the treatment of adolescents. However, the independence, differing social influences, greater ability to defy adult directives, and dramatically different school environment associated with adolescence influence the feasibility and effectiveness of treatments that may have proved effective with children. As a result, investigations into psychosocial treatments specifically designed for the adolescent population are important and some studies have begun to address this deficiency in the literature. The following review describes psychosocial interventions for adolescents with ADHD and is organized in terms of domains and providers. Since physicians are frequently the initial and primary caregiver for adolescents with ADHD and their role in psychosocial treatment is increasing, interventions physicians can implement are described first. Most other psychosocial treatments developed for adolescents have included school interventions and/or family treatment and the literature pertaining to each is reviewed in subsequent sections.

PHYSICIANS

Physicians are increasingly called to play important roles in the delivery of universal and selective psychosocial mental health services (1), and represent a primary source of contact with the health care system for most adolescents and their families. Diagnostic evaluations and medication treatment are typically provided by physicians, as well as psychoeducation regarding other mental health treatment options (1). Basic psychoeducational interventions are well suited to a physician's office where families can learn about the

disorder and the available treatments. Given the wide range of impairments associated with adolescents with ADHD, many treatments may be appropriate and necessary, so physicians are often the primary source of referrals to other mental health professionals. Collaborating with a qualified psychologist or mental health counselor with the expertise of working with adolescents and using behavioral techniques can enhance care by making available coordinated multimodal treatment; however, there are a large number of communities that do not have providers with behavioral health expertise. As an alternative, school counselors and teachers at secondary schools may provide many of these services in active collaboration with the primary physician.

As other providers become involved, the coordination of care is a central issue and can be facilitated by the sharing of information about the services and measures of progress. Although collaborative treatment planning between physicians, mental health counselors, parents, and educators is recommended, it is difficult to achieve due to the demands placed on each of these individuals. Web-based systems that allow for efficient information sharing between parents, schools, physicians, and others have been developed and are currently being field tested (10) although early attempts have proven problematic (11). Clearly, much more work is needed to improve collaboration to achieve truly interprofessional mental health care coordination.

An area that has received little attention in the psychosocial literature is the potential supporting role that psychosocial interventions may play in increasing adherence to medication regimens. While this is a common approach with other chronic disorders, such as asthma and diabetes as well as bipolar disorder and schizophrenia, it has not been studied for adolescents with ADHD. Such interventions appear warranted since children with ADHD frequently discontinue their use of stimulant medication when they reach adolescence (12,13). The lack of medication compliance is not always obvious to the prescribing physician since it is usually manifested as the absence of visits. Unless the physician is monitoring in such a manner as to note omissions and actively follow up when they occur, the discontinuation of medications may go unnoticed. In our experience, we have found that when children with ADHD reach adolescence they often believe that they do not have a problem and therefore do not need medication. Unlike young children, adolescents are often effective at actively defying their parents' requests, so struggles around medication can develop within families. Physicians, nurses, or other staff may provide appropriate education and counseling to adolescents and their parents that can help increase adherence to medication regimens. In order for this to be successful, the omission of a follow-up visit would have to be noticed and prompt additional interventions have to be made.

FAMILY

Family-based interventions are frequently recommended for adolescents with ADHD (14) and Barkley and colleagues have conducted two studies that have examined their efficacy (15,16). In the first, three types of family-based treatments were compared: (1) parent training in behavior management skills, (2) structural family therapy, and (3) problem-solving and communication training. The three treatments performed about equally well and produced statistically significant improvements in parent-child communication, school adjustment, and child and mother symptoms as assessed by a variety of rating scales completed by parents and adolescents. However, few subjects exhibited clinically significant improvement and the authors concluded that long-term, multimodal treatments were needed. Subsequently, Barkley and colleagues (16) reported that increasing the dosage (doubling the number of sessions), and combining behavioral management training with problem-solving communication therapy led to lower rates of dropout from family therapy than problem-solving communication therapy alone; however, combination treatment did not improve outcomes above that of problem-solving communication therapy alone. Overall, neither treatment produced reliable change in the majority of families who received therapy leading the authors to conclude that the family may not be the preferred target in interventions for adolescents with ADHD.

Although Barkley and colleagues (15,16) concluded that family therapy provides little benefit to families of adolescents with ADHD, others have reported benefits from family treatment. For example family therapy (FFT) is effective for many of the problems experienced by adolescents with ADHD, including substance abuse, poor peer relations, and strained family relationships (17). FFT is a family systems oriented, behaviorally based prevention and intervention program that requires anywhere from 8 to 30 sessions depending on the severity of the problems, and consists of two to five phases. A common description of this treatment indicates that there are three phases: (1) engagement and motivation, (2) behavior change, and (3) generalization. Early sessions focus on engaging the family and maximizing their motivation to change. Assessment procedures targeting interactional and functional aspects of behavior are completed in order to gain an understanding of the family system and the individual relationships. Later sessions focus on changing behaviors and generalizing these changes. Waldron and colleagues (18) found that participants who received 12-hr of FFT, either alone or combined with individual Cognitive-Behavioral Therapy (CBT), showed significant decreases in marijuana use. Bolstering these findings are numerous studies that demonstrate that FFT significantly reduces recidivism and the cost of treatment (19). As such, FFT has been deemed by many to be an effective treatment and prevention model, but it has yet to be studied with a sample of families with an adolescent with

ADHD. Since many of the areas of impairment successfully treated through FFT frequently occur among adolescents with ADHD, FFT may be a viable treatment modality for adolescents with ADHD.

Another example of a comprehensive prevention and treatment program that targets problems similar to those experienced by adolescents with ADHD is the Adolescent Transitions Program (ATP). The ATP is a multilevel ecological intervention and prevention program that includes direct interaction with youth, consultation and training, and the media (20). There are three levels of the ATP strategy: (1) universal, (2) selected, and (3) indicated family interventions. The first level reaches the most people, involves the least amount of professional support, and typically takes the form of a family resource center (FRC) in a school system. The FRC staff typically involved in multiple activities which include implementing curriculum in classrooms, conducting parent nights, presenting an introduction of the FRC at parent orientation, utilizing public access television and newsletters to teach family management techniques, conducting summer check-ins with families to plan for the next academic year, and conducting workshops for school staff. The second level, the family check-up broadly targets at-risk families and is designed to build motivation for change. The family check-up consists of an initial interview, an assessment, and a feedback session, each based on motivational interviewing techniques. The assessment involves gathering many types of data from the adolescent, parents, and teachers that indicate how the adolescent is performing in multiple domains and some versions of the family check-up include structured observations of family interactions. The feedback session utilizes the stages-of-change model and motivational interviewing and typically ends with the therapist and parent(s) collaborating to develop a menu of change options.

The third level of the ATP reaches the least amount of families and requires the highest level of professional support as it involves providing direct treatment and intervention services to at-risk families. At this level, practitioners specifically address three broad parent skill areas: (1) using incentives to encourage behavioral change, (2) setting limits for and monitoring adolescents, and (3) improving relationship skills such as listening, problem solving, and negotiation. Intervention options include parent training, establishing a school/home communication and monitoring system, periodic telephone calls from the therapist, family management therapy, and parent networking (e.g., parents meet with their adolescent's friends' parents and the group problem-solves how to keep their adolescents safe and out of trouble).

To our knowledge, there are currently no published studies evaluating the FFT or ATP with a sample of adolescents with ADHD; however, both treatments target youth with problems similar to many of those experienced by teens with ADHD and have yielded beneficial results. It is very likely that youth with ADHD have comprised some portion of the samples in studies

given the inclusion criteria that have been used; however, research on families of adolescents with ADHD using these family therapy techniques is needed. Given the lack of positive findings reported by Barkley and colleagues with respect to family therapy (15,16), along with the positive findings reported for FFT and ATP (18–20), these family interventions merit some attention as potential components of an effective psychosocial treatment approach.

SCHOOL

Adolescents with ADHD continue to have serious problems at school and the consequences of these problems frequently lead to dropouts, long-term suspensions, and academic failure (21). While medication can be effective in improving academic performance and social functioning at school (4,22), school problems are still very common among adolescents taking stimulant medication (23) and they do not appear to have a long-term beneficial effect on academic functioning (24). Furthermore, since 1991 schools have been required to provide psychosocial and educational interventions for adolescents with ADHD who meet eligibility criteria for special education services (25), but there has been very little empirical literature to guide the implementation of these interventions. As a result, there continues to be a need to develop and evaluate psychosocial and educational interventions for problems at school for these youth.

Fortunately, treatment development work in this area is advancing and there is a set of psychosocial treatment studies with small sample sizes that have reported encouraging findings. One promising intervention for adolescents with ADHD was demonstrated in a case study that evaluated the effects of self-monitoring for a student who received social and tangible reinforcement for on-task behavior (26). The result of this treatment was a large improvement in on-task behavior. In another study, self-management procedures were found to improve the classroom preparation skills of three middle school-aged youth with ADHD (27). Students were taught to be on time for class, have all of their materials, complete work, and self-monitor their proficiency achieving these goals on a daily basis. Outcome data suggested that this intervention maintained behavior gains over time and was acceptable to teachers and students. Thus, self-monitoring training for adolescents with ADHD may bolster the effects of classroom-based behavioral interventions, especially in the context of heightened structure imposed by contingencies for accurate monitoring and appropriate behavior.

Another promising intervention involves the use of a functional assessment followed by classroom-based interventions. In a case study that utilized this approach in a middle school setting (28), functional hypotheses were developed for chronic off-task behavior observed for two boys. Based

on the results of the functional assessment, recommendations were offered to classroom teachers who selected intervention strategies based on practicality and perceived effectiveness. Following implementation, the investigators found large improvements in the on-task behavior of both boys in the targeted classrooms. Thus, teacher consultation for behavioral interventions delivered in the classroom may be an effective component in a multimodal program.

Many interventions for adolescents with ADHD have targeted education outcomes. In their comprehensive review of the relevant literature, Raggi and Chronis (29) described a series of academic interventions that have targeted impairment frequently associated with youth with ADHD. For example, in one study adolescents were taught to take structured notes while they listened to a lecture-format American history class (30). Following this note-taking training, adolescents with ADHD showed improvement on measures of comprehension and increased levels of on-task behavior compared to when they simply listened to the lectures. The effect size for the note-taking intervention was in the moderate range. Other interventions have been developed and assessed only on adolescents with related disorders (e.g., learning disabilities) and, as a result, may need modifications to effectively address the needs of adolescents with ADHD. Although these interventions alone may not deal with the full range of problems exhibited by adolescents with ADHD, they each may be a useful component in a multimodal treatment.

Some research has examined the possibility of combining intervention strategies in a comprehensive fashion to address multiple areas of home and school impairments associated with ADHD. For example, the Challenging Horizons Program (CHP) was designed to be a comprehensive school-based treatment program for middle school students with ADHD targeting behavioral, academic, and social functioning. Initially developed and piloted in 1999 (31), there has been continuous treatment development and evaluation work completed across three sites and two distinct models of the CHP have emerged.

The first model of the CHP is as an after-school program that operates two to four times per week for just over 2 hr/day. The second model that was developed was a consulting model that involved classroom teachers providing CHP interventions during the school day. Both models of CHP included interventions targeting academic problems. Organization and task completion are two of the most problematic areas of impairment at school. To target these problems, program staff help students set up a system to organize and maintain their binders, bookbags, and lockers. The system included frequent monitoring, supervised adherence, and behavioral contingencies to help students advance toward independence. All students in the CHP are required to use an assignment notebook provided by the school. Students are required to record homework assignments for each class, or

write "none" if homework is not assigned. Teacher signatures are usually required in the early phases of this intervention to ensure accurate recording. The requirement for signatures may be tapered as students progress toward independent mastery of this skill. The CHP counselors or mentors check the assignment notebook frequently and school and home contingencies are used to improve performance. These organization interventions are provided to all participants in both models of the CHP.

Many other interventions are provided to middle school-aged youth who participate in the after-school model of the CHP. Some of these interventions target academic problems and are provided during education group and include note taking and study skills. During education group students are taught how to make and use flash cards, acronyms, and other tools for preparing for tests. Students learn methods of note taking from lecture and text (30), how to prepare written summaries of text, and how to create and use outlines to help them write coherent papers. After demonstrating mastery within the CHP, students are required to bring examples of having used the study skills and notes at home and in their classes. Complete mastery of a skill is not achieved until competency was demonstrated both within the CHP and in their regular classrooms.

To address difficulties with homework, three individual sessions are offered to help parents develop and implement an individualized Homework Management Plan (HMP). The HMP manual includes procedures for teaching parents how to use behavior management techniques to create a homework routine for their adolescent. Parents set a mandatory homework time, typically 30 min to 1 hr, that the student must complete 5 days/week. The student is required to to work the entire time regardless of the amount of homework assigned. If the student does not have homework or does not bring home the necessary materials to complete homework, he/she is required to use the time to study for upcoming tests, read, prepare written summaries of reading material, or parents assign the student work such as writing summaries of newspaper articles. The most common rewards are access to privileges, such as phone, television, and video games. This system removes parents from battles over things they cannot control such as the child knowing what is assigned, when it is due, and bringing materials home. It allows parents to focus their effort on things that they can control such as time spent studying at home.

The after-school model of the CHP also includes interventions to target disruptive, defiant, and annoying behaviors frequently exhibited by adolescents with ADHD. When a student exhibits a targeted behavior in the after-school program, a counselor announces (calls) the behavior aloud to the child and records it on a behavior-tracking card. These behaviors include both positive behaviors, such as contributing and complimenting, and negative behaviors such as teasing, complaining, blurting, and repeated noncompliance. The calls draw students' attention to these behaviors, raises

their awareness of problematic behaviors, and serves as praise or reprimand. Many behaviors are successfully modified without explicit contingencies beyond the consistent behavior calls. When the rate or intensity of a behavior needs to be modified and it is not sufficiently responding to the behavior calls, individualized contingencies are applied. Following successful behavior change at the CHP, interventions shift focus to modifying these behaviors in other settings. One frequently used technique to achieve this generalization involves the use of a daily or weekly report card (32). Report cards are lists of two to four operationally defined behaviors that briefly describe a problem the adolescent is experiencing in a school setting. These descriptions are defined in positive terms and space is provided next to each item for an adult to rate the behavior as achieved/not achieved or on an incremental scale (e.g., not at all, just a little, pretty much, and very much). Report cards for classroom teachers are completed at the end of class or the end of the week to reflect behavior exhibited over the defined time interval, and parents or CHP counselors provide contingencies based on these ratings. Point systems are used to reinforce appropriate behavior. These report cards are also used at home so parents may complete the ratings and students receive contingencies within the CHP. In addition to providing a mechanism to reliably provide rewards and consequences, the data produced by these cards may be used to measure progress.

Because the social problems of children and adolescents with ADHD are so pervasive, persistent, and detrimental for long-term prognosis, investigators include interventions to improve the social functioning of middle school-aged children as part of the treatment provided in the after-school CHP. The majority of the programs that are currently available utilize a Social Skills Training (SST) approach that teaches participants new social behaviors. Unfortunately, most SST programs have failed to demonstrate efficacy in improving the social problems of children with ADHD (33–35). There is little reason to believe that they would be beneficial to a slightly older sample of children (ages 11–14) who are the focus of the CHP. As a result, the interventions targeting social impairment in the CHP have been developed and piloted over the last 8 years.

One component of the social interventions that remains consistent throughout this treatment development process is the instruction and practice with social problem solving. Previous studies have reported consistent benefits to these procedures over time with samples that were likely to include many participants with ADHD (36,37). Although potentially helpful, these procedures are unlikely to be adequate for most children with ADHD. Considering the findings from the social cognition literature and recommendations regarding generalization of treatment gains (38) the investigators incorporated children reviewing videos of themselves in social situations, live coaching during social activities, and instruction and practice on reading social cues into their treatment development work. Outcome

data on the various iterations of this development process are not yet available. Given the debilitating effects of social impairment (39), treatment development and research on causes of social deficits in youth with ADHD is an area requiring extensive resources and effort.

Whatever is learned through this research and treatment development, it seems that coaching generalization will likely be an activity that persists in successful interventions targeting social impairment. Counselors working in the CHP are trained to use subtle and direct prompts to facilitate appropriate social behaviors in as many settings as possible. One activity during the CHP that specifically targets this is a 30-min recreation period. Adolescents spend time playing sports such as soccer, basketball, and American football and counselors modeled, prompted, and promoted appropriate social interactions. These activities challenged the adolescents' social skills because it is difficult to implement appropriate social behavior in the "heat of a game" when one may perceive that a child has fouled him/her and no one is making a corrective call. It also provides a context to practice positive skills such as complimenting. In addition, students are provided instruction and practice in how to play these popular sports. The goal is to help them gain sufficient knowledge, confidence, and skill mastery so they are able to participate in neighborhood pick-up games or recreation league activities. It has been our experience that these adolescents' history of social impairment and difficulty with organized group activities contributed to a lack of sufficient skill to engage in sports activities, thereby reducing the number of available social opportunities.

A series of pilot studies were conducted to investigate the feasibility and outcomes of the after-school model of the CHP (23,31,40–42). These studies were conducted in a variety of middle schools across three different cities. When the CHP was provided for at least one semester, the outcome data were in the moderate to large effect size range. In one pilot study where implementation was less than one semester (10 weeks) the outcomes were less favorable, although parent satisfaction was still high (42). Operating the CHP in these settings was feasible assuming that there was university-school collaboration. This collaboration has been necessary due to the expense of operating a fairly labor intensive after-school program between 2 and 4 days/week.

In an attempt to develop a less expensive model of the CHP, the developers modified many of the treatment procedures so they could be provided by educators and other school staff during the school day (43). Not all of the CHP interventions were able to be provided in this manner. In a study of the school consultation model of the CHP, teachers, administrators, and school counselors implemented interventions similar to those used in the after-school model; however, school staff provided the interventions during the school day in collaboration with a CHP consultant. Similar to the role of the counselor in the after-school model, a school staff member functioned as a mentor for a child with ADHD. Students met regularly with their mentors to implement and evaluate the educational and

behavioral interventions. The consulting model was designed to provide services similar to the after-school model without the need for as many staff. In the initial study, the interventions were provided over a 3-year period and small but meaningful gains across the 3 years were reported. In addition, grades improved by approximately one letter grade for the treatment group during the second semester and grades for students in the control group remained the same or declined (44). Treatment fidelity by the educators was variable as some provided the interventions with great integrity and consistency, others ignored their agreement to provide the services to the targeted child, and some claimed that ADHD did not really exist and attempting to help these children was a waste of time. Although costing much less to provide than the after-school model of the CHP, there are implementation costs involved in the consultation model related to quality that may compromise outcomes.

Preliminary results of a randomized trial of the after-school version of the program indicate that effect sizes for symptoms and impairment are notably larger for this version of the CHP than the consultation model. Nevertheless, there may be children with ADHD for whom the consultation model is adequate. Future research on the CHP should focus on moderators of treatment response and relative benefits of differences in costs and treatment intensity of the two models.

SUMMARY AND CONCLUSIONS

Continued research and development is needed for the CHP as well as for other psychosocial interventions for this population. The current lack of empirically supported psychosocial treatment leads to many problems in the health care and education system. For example, for many providers it is easier to get payment from most health insurance companies to provide play therapy to treat the impulsivity of a child or adolescent with ADHD than it is to get payment for a school-based behavioral intervention. Unfortunately, this creates incentives for providing treatment that is unlikely to work while discouraging the use of practices with an increasing amount of empirical support. The absence of empirically supported psychosocial treatments also negatively impacts the public education system. Since 1991 schools have been obligated to provide accommodations for students with ADHD who meet criteria for special education (25). Given the lack of effective techniques, many educators have adopted techniques that actually have the effect of reducing expectations instead of helping students achieve increased independence and improved functioning. Temporary relief of expectations may be necessary while providing instruction, training, or some other form of intervention prior to reestablishing the normal expectation once the individual has progressed; however, many times these accommodations take the form of permanent reductions in expectations or a "lowering of the bar."

This approach is rewarded because it reduces problems and may improve grades without a need to do the work to produce a commensurate improvement in functioning. For example, one common practice by those trying to help adolescents with ADHD in school is to relieve them of the responsibility for keeping track of classroom assignments. The well-intentioned teachers gather the assignment information for the students and keep track of assignment completion by communicating directly with the students' teachers. This can help a student keep track of assignments because someone does it for him or her, but this strategy alone does nothing to improve the functioning of the student. When there are not empirically supported psychosocial and educational interventions available and the schools are required to make accommodations for these youth, the temptation to placate situations by lowering expectations has appeal.

Policies and procedures related to the provision of psychosocial interventions for adolescents with ADHD are vague and inefficient in our current health care and education systems resulting in compromised care and few alternatives for families. Further evidence of these problems can be gleaned from state education records on due process hearings. Due process hearings are grievance procedures related to special education that are managed by a state's department of education. A review of recent records in Virginia revealed that almost half of all due process hearings in a recent year were related to children with behavioral and emotional problems (including ADHD) when these youth (emotionally disturbed and other health impaired) represent approximately 13% (45) of the special education population. This overrepresentation of cases with behavioral and emotional problems is another sign that our system of caring for these children is not working.

Finally, almost all of the studies reviewed in this chapter were conducted with young adolescents (i.e., middle school ages). There is a real need for treatment development and evaluation of older adolescents (ages 14–18) with ADHD as the impairment continues and these youth encounter even greater potential problems as they begin to drive, become sexually active (46), and experience a greater exposure to drugs and alcohol. Schools and the health care system are the sources of care for most adolescents with ADHD (47) and the systems in place are fraught with problems. Continuing to develop and evaluate effective psychosocial interventions for these youth is an important part of remediating these systems and providing treatment that can make a positive difference.

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24

ADHD in Girls

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Although attention deficit hyperactivity disorder (ADHD) has garnered considerable research, controversy, and even notoriety among researchers as well as the popular media in recent years, only a small amount of our knowledge is based on studies of girls. Boys with ADHD outnumber girls with ADHD at a ratio of approximately 3:1 in community samples, and often at a far higher ratio in clinical samples (1,2). Nonetheless, the vast predominance of male-dominated samples in the ADHD literature extends beyond these ratios. Several key samples comprising a large percentage of the literature on ADHD are, in fact, exclusively male, and most mixed-sex samples have too few girls for separate analysis of female manifestations and mechanisms. There has been a surge of research on girls with ADHD in the past decade (3–7), but the field's predominant models still reflect what is known largely about males. Because ADHD is potentially underrecognized in girls and clearly underinvestigated in female populations, despite its significant impairments and influences on key life domains, investigation of ADHD in girls and women is a priority.

In this chapter, we first provide some historical perspective on the roots of this male-dominated literature in the field. We then summarize what we know about both the prevalence rates and manifestations of ADHD among girls versus boys and the processes and mechanisms through which

ADHD affects girls. Finally, we address the clinical relevance of these points, concluding with some theoretical implications and future directions for research.

HISTORICAL PERSPECTIVE

Girls with ADHD have been neglected both scientifically and clinically for several reasons. First, like most other developmental disorders that become salient prior to adolescence, ADHD more often appears in boys than in girls, making males with ADHD simply more visible (8). Second, boys with ADHD tend to have more concurrent aggression, oppositional behavior, and conduct problems than do girls with ADHD (3,5,9). Such externalizing symptoms were previously seen as part of the ADHD spectrum, so boys were more often selected for research investigations. Additionally, these externalizing symptoms are likely to attract the attention of parents and teachers, making boys prone to be referred for treatment, and then to become study participants in clinic-referred samples. However, recent assessment instruments that disentangle ADHD from externalizing behaviors (10), as well as formal recognition of the Inattentive type of ADHD (11), suggest that the field is beginning to recognize forms of the disorder that are more salient for females. Finally, we note that that there has been a general historical tendency for all biomedical sciences to prioritize research with males. However, this too has changed recently. Since the early 1990s the National Institutes of Health have explicitly required that grant applicants address adequate representation of females and ethnic minorities (and now children) in all proposals. Because of these changes, the door seems to be open for increasing recognition of ADHD in girls and women.

EPIDEMIOLOGY

Although definitive data on the prevalence of ADHD are limited, the best available evidence suggests that preadolescent boys outnumber girls by a ratio of approximately 3:1 in community samples but by 9:1 in clinic-referred samples (2), again because boys with ADHD are more likely to display concurrent aggressive behavior that elicits concern from parents and teachers. By adolescence, however, sex ratios in community samples may lower somewhat, with boys outnumbering girls 2:1. Furthermore, there is some suggestion that sex ratios may become equal by adulthood (12,13). However, because these latter data are cross-sectional, we cannot draw valid conclusions about developmental progressions. For example, females with ADHD could be more likely to persist in their symptoms; they could simply be more veridical in terms of self-report; or females with ADHD could be more likely to develop their symptoms later than do males. The field needs a

larger number of prospective longitudinal studies to answer these sorts of process-oriented questions.

Regarding subtypes of ADHD, girls appear relatively more likely to display the inattentive type of ADHD than do boys, in both clinical as well as community samples (14,15). Indeed, the Inattentive type of ADHD may be particularly salient for girls, and so long as parents, teachers, and clinicians focus on the more noticeable and disruptive hyperactive/impulsive symptom cluster (11), girls will continue to be overlooked.

COMORBIDITY AND IMPAIRMENT

Results from meta-analytic reviews on the topic of sex differences and ADHD suggest several trends regarding comorbidity and impairment. Referral source appears to moderate a number of key findings. Among clinic-referred samples, boys and girls with ADHD are largely indistinguishable on most measures of comorbidity and impairment, with some suggestion that clinical samples of girls have lower IQ scores (5) and greater amounts of inattention (9) than clinic-referred boys. By contrast, in community (nonclinic referred) samples, girls with ADHD often seem less impaired than their male counterparts, although most sex differences are small in effect (5).

Most notably, girls with ADHD appear to have lower rates of comorbid disruptive behavior disorders (e.g., ODD, CD), than do boys with ADHD (5,9,14), but still demonstrate higher rates of disruptive comorbidity than do girls without ADHD (3,6). Additionally, girls may be more likely to display relational aggression as opposed to overt forms of aggression more typical of boys (Crick and Grotpeter, 1995); this form of aggression has been found to be more prevalent among girls with ADHD relative to girls without ADHD as assessed by adult-informant rating scales, peer nominations, and observation in a computerized game (16,17).

Findings are mixed regarding comorbidities with internalizing disorders (e.g., depression, anxiety). Whereas some studies suggest girls with ADHD have higher rates of internalizing comorbidities than do boys with ADHD (9), others in fact suggest the opposite (5), especially for community-based samples. Girls with ADHD, however, do appear to demonstrate higher rates of internalizing disorders than do girls without ADHD (6). Of note, few studies have examined sex differences in comorbidities past childhood. Rucklidge and Tannock (18) found that, particularly for internalizing symptomatology, adolescent girls with ADHD were more impaired than males with ADHD. Relatedly, other all-female samples have found girls with ADHD to have more internalizing comorbidities in adolescence than do girls without ADHD (4,7). An implication is that, by adolescence, ADHD may become an increasing burden for girls compared to boys, although prospective longitudinal studies comparing both sexes are needed to test this hypothesis.

Despite suggestive evidence that girls with ADHD have lower IQ scores than boys with ADHD (5), it may be the case that girls with ADHD have fewer diagnosable learning disabilities, as defined by discrepancy-based reading or math disabilities (14). Still, it is clear that girls with ADHD, relative to girls without ADHD, have significantly more school-related problems (e.g., special education placement, grade retention, speech/language difficulties) as well as lower academic and cognitive performance, including IQ and achievement test scores (3,6,7,19).

Some preliminary evidence also suggests that girls with ADHD are at risk for developing several problems specifically relevant to adolescence. First, girls with ADHD may be at higher risk for comorbid substance use disorders than are boys with ADHD (14,20), and girls without ADHD (4,7). Preliminary evidence also suggests adolescent girls with ADHD may display more bulimia nervosa symptoms and diagnoses than boys with ADHD (21) or than girls without ADHD (53).

Regarding neuropsychological functioning, girls with ADHD appear to demonstrate relatively comparable deficits to boys with ADHD in a wide variety of domains. First, when tested without medication, girls with ADHD show significant executive function deficits (e.g., response organization, planning, and set shifting), in contrast to girls without ADHD, and such deficits are similar in magnitude to those found in boys with ADHD (22–25). Executive function deficits (as well as other neuropsychological problems) have been found to persist in girls with ADHD as evidenced via longitudinal studies; such problems are particularly strong in girls who continue to meet criteria for ADHD from childhood to adolescence (4,26). On the continuous performance test, however, an objective measure of inattention and impulsivity, another study found that girls with ADHD were in fact less impulsive than were boys (27).

Regarding actual neural deficits, a magnetic resonance imaging study showed that, similar to boys with ADHD in relation to male controls, girls with ADHD had significantly smaller total cerebral volumes than did comparison girls. However, most other brain regions that had differed between boys with and without ADHD did not differ for girls. Exceptions to this trend were noted for the caudate and posterior-inferior cerebellar vermis, which were reduced in volume for girls with ADHD relative to the control group. Finally, adolescent girls with ADHD appear to have less efficient prefrontal processing on working memory tasks than do girls without ADHD, as indicated through functional MRI (29).

Next, girls with ADHD show clear impairment in their social relationships with peers, family members, and nonparental adults such as teachers and camp counselors. Although not part of the diagnostic criteria for ADHD, impairments in the social domain have been consistently demonstrated for children with ADHD (30). Girls with ADHD are highly peer rejected relative to girls without ADHD both in childhood (6) and

adolescence (7). Some scant existing evidence suggests that girls with ADHD may in fact be more likely to be peer rejected than boys with ADHD (31), although other studies have found no sex differences in the high level of rejection associated with ADHD (30). Yet the symptoms of ADHD (e.g., intruding into a conversation, having trouble waiting one's turn in line, being inattentive to social cues) are perhaps more unusual in a normative sense when displayed by girls, and more disruptive within female peer groups than in male peer groups. Additionally, children with ADHD tend to have cognitive and language deficits, which may put girls at a particular disadvantage given the strong focus on verbal interchange in female peer groups (32). We also note that a critical distinction exists between children's general status in the peer group (i.e., acceptance or rejection) and their participation in dyadic friendships. Girls with ADHD also have trouble making and keeping stable friendships, and their friendships tend to be marked by high conflict (33).

In addition to their troubles with peers, girls with ADHD suffer impairment in their relationships with adults. First, girls with ADHD were found to be less popular with nonparental adults such as camp teachers and camp counselors than were comparison girls (34). This population also reports more contentious relationships with classroom teachers (18). Second, like their male counterparts (35), girls with ADHD have substantially impaired relationships with parents. Relative to those of comparison girls, the parent–child relationships of girls with ADHD appear to be marked by high levels of authoritarian parenting, verbal conflict during laboratory tasks, as well as high levels of "expressed emotion"—i.e., hostility/criticism and overinvolvement (6,36). Additionally, girls with ADHD (particularly the combined type) have been found to exhibit higher rates of abuse histories than do comparison girls, with such histories associated with externalizing behavior and peer rejection (37).

In sum, although there is a dearth of research about girls with ADHD, a body of emerging literature suggests that girls with ADHD suffer clinically significant impairments in functioning in a wide variety of domains. Indeed, the findings from Biederman et al. (3, p. 966) "…stress the severity of the disorder in females." The limited amount of prospective longitudinal data currently available strongly suggests that such impairments persist at least though adolescence in girls with this condition (7).

DEVELOPMENTAL PROCESSES

Realizing, however, that girls with ADHD are symptomatic and impaired in multiple domains does not inform us of the processes by which such problems emerge or by which some girls may show resilience. A developmental psychopathology perspective can address these questions, often via prospective longitudinal studies through which relevant mechanisms can

be evaluated (38,39). As just noted, the field is only beginning to collect evidence about the longitudinal course of symptoms, comorbidity, and impairment of girls with ADHD, as well as process-oriented studies to examine the mediators and moderators of these effects. In this section, we attempt to address what we know about sex differences in the developmental process.

First, it appears that family and genetic loading exerts relatively similar influences on ADHD in girls as in boys. In both sexes, ADHD is moderately to strongly heritable (40). Whereas girls with ADHD are substantially more likely than non-ADHD girls to have relatives with ADHD, the rates of familial disorder seem comparable to those of boys with ADHD (41,42).

Additionally, it appears that whereas nongenetic risk factors such as low birth weight and maternal use of tobacco and other drugs during pregnancy are risk factors for ADHD, the effect of such factors does not seem to differ based on child sex. In other words, these risk factors seem equally likely to predispose girls as well as boys to ADHD (43,44).

What is the developmental course of ADHD? Again, our knowledge about this in girls is restricted by the few prospective follow-up studies of this topic. Studies of boys suggest a gradual reduction, over time, of the core symptoms of hyperactivity and impulsivity; however, inattentive symptoms seem more likely to persist (45). This pattern appears to be similar in girls with ADHD followed into adolescence (7). Nonetheless, up to 80% of children with ADHD still suffer from impairing symptoms of ADHD in adolescence. Rates of persistence into adulthood are more controversial, with several methodological factors (e.g., unsuitability of extant criteria for adults; need for multi-informant adult evaluations) highly influential in determination of exact rates of diagnostic persistence (46,47). Because girls with ADHD tend to display more inattentive symptoms than do boys with ADHD, it may be that ADHD is particularly likely to persist in girls as they reach adolescence and adulthood. Indeed, this fact could explain why the male: female sex ratio tends to become more equal in adolescent and adult samples.

Additionally, adult males with childhood histories of ADHD are at high risk for externalizing disorders (including antisocial personality disorder), academic failure, and employment problems (48). Even though girls with ADHD are somewhat less likely than their male ADHD counterparts to display these aggressive comorbidities in childhood, preliminary evidence suggests that girls do remain at high risk for both externalizing as well as internalizing problems in adolescence (4,7). This finding suggests that girls with ADHD may display multifinality with regards to adolescent and young adult outcomes, similar to what is found in follow-up studies of girls with aggression. That is, aggressive behavior in boys is more stable across time than aggressive behavior in girls, but girls with conduct problems are likely

to develop disparate negative adult outcomes, including serious relationship problems and a propensity for internalizing symptomatology (49–51). The same pattern could hold for girls with ADHD, who may show higher risk than boys with ADHD for depression, anxiety, eating pathology, substance abuse, and serious relationship problems later in life. This provocative hypothesis awaits clearer tests via long-term prospective research.

Longitudinal work on mechanisms predicting competence and impairment among girls with ADHD has been conducted in our laboratories. First, we have found that both childhood ADHD and peer rejection independently (and additively) predict (1) girls' lower adolescent academic achievement, after controlling for childhood achievement, and (2) adolescent eating pathology symptoms (52,53). Similarly, ADHD status and peer rejection predict adolescent externalizing and internalizing behaviors (but not after controlling for baseline levels of those constructs). Importantly, childhood self-perceived scholastic competence (with control of actual academic achievement) is associated with resilient outcomes in several domains, for both girls with ADHD and without ADHD (52). Both ADHD and harsh/critical parenting practices in childhood independently predict girls' adolescent eating pathology, and the predictive relationship between parenting practices and eating pathology is stronger for girls with ADHD than for girls without ADHD (53), suggesting a mechanism that may operate differently for girls with ADHD.

Second, Lee and Hinshaw (53) found that girls' adolescent conduct problems, internalizing problems, and substance abuse were best predicted by childhood hyperactivity and noncompliance. A similar pattern had emerged for boys with ADHD, in that, childhood noncompliance and covert antisocial behavior outweighed early ADHD in predicting later delinquency (54). However, girls' adolescent academic achievement and school suspensions/expulsions were predicted only by childhood inattention problems. Overall, the field is just beginning to understand the predictors of, and mechanisms underlying, the longitudinal outcomes of girls with ADHD.

CLINICAL RELEVANCE

Investigations of girls with ADHD raise several crucial issues regarding assessment and intervention with this population. First, regarding assessment, we believe that clinicians, parents, and teachers need to increase their awareness that ADHD exists in girls and that, when it occurs, significant impairment is likely. Indeed, in one survey, 97% of people reported that they knew a male with ADHD, but 50% said they did not know ADHD even existed in women (P. Quinn, personal communication, February 11, 2003). Girls may be especially likely to escape detection if they have the Inattentive type of ADHD, which is marked less by disruptive behavior and more by disorganized, unfocused performance that may not come to

professional attention (11). Standard parent and teacher reports of symptoms, which focus on observable behaviors that are externalizing in nature (including hyperactivity/impulsivity), may not be as sensitive for assessing girls who display inattentive and/or internalizing symptomatology. When girls with ADHD are referred, they are more likely to be older than boys, and the primary concern is more often a comorbid disorder rather than ADHD symptomatology per se. In addition, the diagnostic criteria for ADHD insist that symptoms must appear by the time the child is seven years of age; this particular criterion, however, may be overly restrictive for children with primarily inattentive symptomatology (55), a disproportionate number of whom are girls (14,15). Nonetheless, as indicated throughout this chapter, ADHD is substantially impairing in girls; underdiagnosis may well lead to a lack of appropriate services and interventions.

Related to the issue of assessment, debate exists about whether sex-specific clinical cutoffs should be used when diagnosing ADHD. Like many mental disorders, ADHD represents a cluster of behaviors (inattention, hyperactivity/impulsivity) that fall in a continuum across the population. With respect to genetic etiology, there is no single gene linked to the disorder, and the heritable contribution to ADHD appears across the entire continuum of relevant symptomatology (56). In short, there is no one gene, nor cutoff score, which clearly denotes ADHD versus its absence. As a result, one line of argument maintains that because girls in the population have lower rates of the core symptoms of ADHD, diagnostic thresholds should be sex specific (57). Having a lower threshold for girls would ensure that girls with high rates of sex-specific symptomatology would not be missed just because they happened to have less symptomatology than the most extreme boys. Counterarguments maintain that sex-specific cutoff scores may not yield truly impairing levels of symptomatology (58,59).

Clearly, this is an empirical question, and one that is a priority for future research. At present, we note that several large clinical investigations in the field have used a two-pronged screening strategy: (1) initial rating scales and checklists feature sex-specific norms (to ensure that potentially diagnosable girls are not missed as "false negatives" in the preliminary assessment phase), and (2) sex-neutral diagnostic interviews for the final phase of determining "caseness," to ensure that truly impaired participants are included (6,60).

With respect to treatment and intervention implications, the limited data in the field suggest that there are few, if any, differences in intervention response for boys versus girls. In three treatment studies, sex failed to moderate the effectiveness of medication as well as behavioral treatment, across a range of outcomes (61–63). However, these studies have primarily focused on prepubertal girls and girls with the Combined type of ADHD. First, if sex differences in medication effectiveness exist, they may be most likely to emerge during adolescence when differences in hormones and metabolism increase. Clinical anecdotes support this contention (64), although the limited existing

data on medication effectiveness among postpubertal adolescents has not found sex differences (65). Second, it may be the case that different treatments are associated with maximum effectiveness for the Inattentive type of ADHD, a subtype that, once again, may be more salient for girls. Individuals with the inattentive type of ADHD may show a preferential response to relatively low doses of stimulant medication (66,67), suggesting that girls with ADHD may need lower doses of medication or more careful medication management to ensure that they are not overmedicated. Also, to the extent that girls with ADHD may be at least somewhat more likely to show associated internalizing symptomatology than their male counterparts, they may respond better to behavioral treatments. Indeed, children with ADHD who displayed comorbid anxiety disorders showed a relatively greater response to an intensive behavioral treatment program than did children without such comorbidity, in the Multimodal Treatment Study of Children with ADHD (62). However, we emphasize that systematic, empirically based investigations of the effectiveness of different treatments are needed before the field can draw any conclusions about sex differences in treatment response.

THEORETICAL IMPLICATIONS AND FUTURE DIRECTIONS

The study of girls with ADHD is a growing endeavor, but it is still relatively new. Overall, we can confidently assert that ADHD does exist as a real and substantially impairing condition in girls. However, we are in need of greater numbers of longitudinal, prospective studies that explore the course of ADHD throughout the life span, including adulthood. We note that ADHD seems to be particularly salient for adult women (at least according to self-report), so that the developmental precursors and concurrent manifestations of this phenomenon are an especially fruitful area for future study (68,69). Additionally, prospective longitudinal studies can elucidate mechanisms through which girls with ADHD develop impairment, as well as the mechanisms through which some girls with ADHD show resilience. Such knowledge has great potential to inform conceptual models of ADHD. For instance, if it continues to be confirmed that girls with ADHD are relatively more likely to display the inattentive type of the disorder than are boys, this finding would call into question the model of ADHD as a disorder characterized by faulty inhibitory processes that lead to predominantly impulsive behavior patterns (70,71). Additionally, the model of childhood ADHD as associated with early externalizing behavior patterns, inevitably leading to conduct disorder or serious aggressive problems in adulthood, may not apply for girls or at least may not apply as saliently as it does for boys. Finally, it is our hope that this deeper understanding of sex differences in ADHD will lead to both conceptual advances and more specific and fruitful assessment and treatment recommendations for boys and girls with this condition. The study of sex differences is essential for theoretical and

practical reasons; relevant basic research and treatment research have the potential to improve both domains.

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ADHD in Adults

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INTRODUCTION

Adults with attention deficit hyperactivity disorder (ADHD) are increasingly presenting for diagnosis and treatment in psychiatric and primary settings. ADHD affects 4–5% of adults and is characterized by childhood-onset and persistent symptoms of inattention, hyperactivity, and impulsivity. Many adults with ADHD suffer from co-occurring depressive, anxiety, antisocial, and addictive disorders. Research has documented familial and genetic underpinnings, neuropsychological deficits, frontal-striatal, and catecholaminergic dysfunction. Treatment strategies include stimulant and non-stimulant medications as well as structured psychotherapies.

ADHD is a prevalent disorder worldwide estimated to affect 3–9% of school age children worldwide (1). Converging data on prevalence in adults suggests that 4–5% of college-aged students and adults have ADHD (2,3). Although historically ADHD was not thought to continue beyond adolescence, long-term controlled follow-up studies have shown the persistence of the disorder or prominent symptoms of the disorder plus impairment in approximately half of adults diagnosed as having ADHD in childhood (4). Although the diagnosis of adult ADHD has been questioned (5), evidence supports the syndromatic continuity of the disorder from childhood into adulthood as well as descriptive, face, predictive, and concurrent validity of diagnosing ADHD in adults (6,7).

Longitudinal studies in ADHD youth growing up show that, though the symptom clusters of hyperactivity and impulsivity decay over time, inattention tends to persist (8–10). Studies of clinically referred adults with

ADHD show that about half endorse clinically significant levels of hyperactivity/impulsivity and 90% endorse prominent attentional symptoms (11). Like some youth with ADHD, adults with ADHD tend to have additional cognitive deficits (known as executive function deficits) including problems in encoding and manipulating information; and difficulties with organization and time management (12).

Compared to adults without ADHD, adults with ADHD typically have childhood histories reflecting school dysfunction including deficits in educational performance, discipline problems, and higher rates of repeated grades, tutoring, placement in special classes, and reading disabilities (13,14). School problems faced by ADHD children often continue or worsen in college resulting in academic underachievement, low-grade point averages, lower completion rates, and more time to complete degrees (15). Adults with ADHD tend to have lower socioeconomic status, lower rates of professional employment, more frequent job changes, more work difficulties, and high rates of separation and divorce (16). Similarly, adults with ADHD have more speeding violations, drivers license suspensions, accidents, and poorer performance in driving simulators (3,17). Individuals with ADHD may have sleep disturbances both exacerbating ADHD symptoms (underarousal, poor attention) and being aggravated by the presence of ADHD (18). Adults with addictions (e.g., drugs or alcohol, smoking, gambling), repeated traffic violations (speeding, failure to renew license), and recurrent life failures (occupational, managing finances, academic)—especially in context to a family history of ADHD-should be screened for ADHD (see below).

DIAGNOSIS

ADHD can be diagnosed reliably in adults by carefully querying for developmentally appropriate symptoms from the DSM-IV attending to the childhood-onset, persistence, and current presence of these symptoms. Research shows that diagnosing ADHD based on the retrospective self-reports of adults is a valid method of diagnosing the disorder. For example, Murphy and Schachar reported high correlation (R's > 0.75) between childhood ADHD reports from adults with ADHD and their parents, and between current self- and partner-reported ADHD symptoms (19), however the use of rating scales alone may lead to underreporting in ADHD adults and overreporting in non-ADHD adults (20), necessitating a clinical interview for the diagnosis. Adult self-report scales such as the ADHD rating scale and the Conner's rating scales are valid and reliable instruments that have embedded the DSM criteria for ADHD; whereas the Brown-ADD and Wender-Reimherr scales are also used commonly to diagnose ADHD (and comorbidity) in adults (21). Clinical interview remains necessary in the final diagnosis of ADHD.

Common Histories of Adults with ADHD

- Difficulties in elementary and/or secondary school
  - Behavioral issues: Fidgety, hyperactive, disruptive, inability to stay seated
  - Reports of "Not living up to potential," spacey, forgetful, or overactive
  - Academics: Underperforming, discrepancy in abilities versus achievement
- College Performance
  - Poor study skills, procrastination on larger projects
  - Incomplete or longer duration to complete degree, difficulty engaging in further education
- Occupational Difficulties
  - Underachievement (mixed reviews), more absences, frequent job changes
  - Low efficiency: requiring more time to complete tasks than peers
- Home Problems
  - Disorganized, shifts activities prematurely, does not complete tasks
  - Procrastination
  - Poor time management
  - Strained relationships with spouse and children
  - General interpersonal disruption

Co-occurring psychiatric and learning problems exist in a majority of adults with ADHD. Adults with ADHD manifest higher rates of anxiety, depression, cigarette smoking, and substance use disorders than adults without ADHD (16). Conversely, approximately 15–20% of adults with substance abuse disorders, anxiety, depressive disorders, and bipolar disorders have ADHD (22–26). One comorbidity of great concern in adults with ADHD are the substance use disorders (27). Untreated adults with ADHD are at increased risk for an earlier onset, higher risk (50%), and longer duration of substance use disorders (28–30); conversely, substance abusers with ADHD have more severe substance problems and more difficulty going into remission (26,31,32). Since attentional dysfunction may be evident in a host of other disorders (e.g., depression, anxiety, dementias), careful attention to the existence of longitudinal symptoms and impairment of ADHD coupled with the possibility that the manifest cognitive deficits may be related to another co-occurring disorder are necessary for an accurate diagnosis. Adults presenting with diagnostic dilemmas or clinically significant co-occurring disorders such as depression, bipolar disorder, panic disorder, and substance abuse should be referred to a practitioner with experience in treating ADHD.

Assessment and Diagnosis

- DSM-IV is gold standard
- Several scales are available to aid assessment including the ADHD Rating Scale (RS), Brown Attention Deficit Disorder Scales, Conner's Adult Attention Deficit Scale, and the Wender Utah Rating Scale
- Reports validate reliability of data collected from adults with ADHD
- Neuropsychological testing to identify cognitive abilities, information processing, learning disabilities—not diagnostic of ADHD
- Potential use of neuroimaging and genetic testing to identify certain subtypes of ADHD—not diagnostic of ADHD
- Disentangling comorbidities and associated impairments are clinically derived

NEUROBIOLOGY OF ADHD IN ADULTS

Genes in ADHD in Adults

There is robust data suggesting biological underpinning of ADHD in adults (7,33,34). Family, twin, adoption, and molecular genetic studies show that genes influence the etiology of ADHD. The heritability of the disorder, about 70%, is among the highest within psychiatry (35). Family studies show that ADHD is more prevalent among the relatives of ADHD children, and the children of ADHD adults are at high risk for having ADHD themselves (36). For example, from 25% to 50% of children of parents with ADHD have ADHD (36,37). This high familial loading of adult ADHD led to the notion that biological factors may be stronger in adults than in pediatric ADHD (33).

Studies of children and adults have found evidence for the involvement of several genes in the etiology of ADHD: the D2 dopamine receptor gene, the dopamine-beta-hydroxylase gene, the dopamine transporter (DAT) gene, the SNAP 25, and the D4 dopamine receptor gene and others (38–40). The data for the D4 receptor are especially compelling because the gene variant associated with ADHD is known to mediate a blunted response to the neurotransmitters norepinephrine and dopamine (41), important neurotransmitters associated with the pathophysiology of ADHD.

Adults With ADHD Have Brain Anomalies

A substantial body of literature implicates abnormalities of brain structure and function in the pathophysiology of both childhood and adult ADHD (42–45). We have known for decades that ADHD youth show impaired performance on tasks assessing vigilance, motoric inhibition, organization, planning, complex problem solving, and verbal learning and memory. A recent meta-analysis has demonstrated that a smaller but substantial literature shows similar problems also impair adults with ADHD (43).

Consistently neuropsychological deficits have been documented in studies of adults with ADHD (44). These adults tend to have impaired performance on tasks assessing vigilance, motoric speed, response inhibition, verbal learning, and working memory (42,43). Age, learning disabilities, psychiatric comorbidity, and gender do not account for these impairments (43). While neuropsychological testing is not used clinically to diagnose ADHD in adults, such testing aids in identifying learning disabilities, subaverage intelligence, and specific information processing deficits.

As recently reviewed (34), current thinking suggests that a network of interrelated brain areas are involved in the attentional—executive impairments of ADHD children. The cingulate cortex plays a role in motivational aspects of attention and in response selection and inhibition. A system mainly involving the right prefrontal and parietal cortex is activated during sustained and directed attention across sensory modalities (34,46). The inferior parietal lobule and superior temporal sulcus are polymodal sensory convergence areas that provide a representation of extrapersonal space which plays an important role in focusing and selecting a target stimulus. The brain stem reticular activating system and reticular thalamic nuclei regulate attentional tone and filter interference, respectively. Working memory deficits implicate a distributed network including the anterior hippocampus, ventral anterior, and dorsolateral thalamus, anterior cingulate, parietal cortex, and dorsolateral prefrontal cortex (34,46).

Neuroimaging Studies of Adult ADHD

Reviews of the neuroimaging literature show that nearly all the structural imaging studies, using either computerized tomography or magnetic resonance imaging, found group evidence of structural brain abnormalities among ADHD individuals (46). The most common findings are smaller volumes in frontal cortex, cerebellum, and subcortical structures (45).

Functional imaging studies are consistent with the structural studies in implicating fronto-subcortical systems in the pathophysiology of ADHD (47). For example, in a positron emission tomography (PET) study of adult ADHD, Zametkin et al. (48) found reduced global and regional glucose metabolism in the premotor cortex and the superior prefrontal cortex. Three subcortical structures implicated by the imaging studies, caudate, putamen, and globus pallidus, are part of the neural circuitry underlying motor control, executive functions, inhibition of behavior, and the modulation of reward pathways. These frontal-striatal-pallidal-thalamic circuits provide feedback to the cortex for the regulation of behavior. Adults with ADHD also demonstrate less activation of the anterior cingulate than adults without ADHD (49). Of interest, functional imaging studies in children with ADHD show that stimulant medications do not affect brain growth adversely (50,51).

ADHD is thought to be mediated by catecholaminergic dysregulation-of dopamine and norepinephrine. While discrepancies remain, studies have shown increased DAT density in the striatum (52,53)—particularly important given that the DAT in the striatum is the site of action of stimulant medications used to treat ADHD (54).

Neurobiology and Genetics of ADHD

- ADHD is a highly familial disorder with heritability estimated to be 0.8
- Primary disturbance of catecholamine neurotransmission
- Anterior cingulate, frontal cortex, basal ganglia, corpus callosum, and cerebellum manifest decreased size in ADHD
- Variations in genes that code for DAT protein and dopamine D4 receptor (DRD4), SNAP 25, associated with distinct ADHD subtypes
- No current role for neuroimaging or genetic testing currently in diagnosis of ADHD

TREATMENT

Despite increased recognition that children with ADHD commonly grow up to be adults with the same disorder, the treatment of this disorder in adults remains under intense study. In addition, complicating the diagnostics and treatment strategy, many adults with ADHD have depressive and anxiety symptoms, as well as histories of drug and alcohol dependence or abuse. Thus, with the increasing recognition of the complex presentation of adults with ADHD, there is a need to develop effective therapeutic strategies. Formal guidelines on the treatment of adults with ADHD are lacking. Support groups (e.g., www.chadd.org) assist the newly diagnosed adult by providing ADHD education, available resources, and peer support. Coaching and organization training appear useful but remain unstudied (14). In general, it is important to set clear realistic treatment goals with the patient. Identify specific symptoms and problematic areas of functioning as targets of treatment. Response-based rating scales such as the Conner's and ADHD RS can be used to monitor outcome. Use additional therapies to support and compliment the effects of medication. As with children, college students, and adults returning to school may require additional educational services to succeed. Prioritize treatment if clinically significant psychiatric comorbidities are present with ADHD—typically sequencing treatment for the most severe disorder initially .

Although the efficacy of various psychotherapeutic interventions remains to be established, limited data suggests that standard interpersonal psychotherapies may not be particularly useful (55). In contrast, recent data suggests that specific cognitive-behavioral therapies adapted for medicated adults with ADHD may be useful (56). One open and one controlled trial have demonstrated efficacy of cognitive-behavioral therapies for medicated

adults with ADHD showing improvement in not only ADHD but comorbidity and functioning outcomes (57,58).

Although medication therapy is well studied in treating ADHD in children, the use of pharmacotherapeutic agents for adults with ADHD remains less established. The medications used to treat ADHD largely affect catecholaminergic neurotransmission including dopamine and norepinephrine. A recent review of the literature (59) identified 15 studies ($N = 482$ subjects) of stimulants, and 28 studies of nonstimulant medications ($N = 1179$ subjects) including noradrenergic reuptake inhibitors, antidepressants, and cholinergic agents that may be useful for the treatment of ADHD in adults (Table 1).

Stimulants

The only FDA approved agents to date in adults with ADHD include the mixed amphetamine compounds, and the noradrenergic specific reuptake inhibitor, atomoxetine. Mechanistically, the stimulant medications—amphetamine, methylphenidate, and pemoline—block the presynaptic reuptake of dopamine (54) and norepinephrine while amphetamine additionally releases directly dopamine and norepinephrine (60); all resulting in accumulation of norepinephrine and dopamine in the synaptic cleft (61). Controlled clinical trials with stimulants (62–64), atomoxetine (65), and the catecholaminergic antidepressants (66,67) demonstrated significant short-term improvement in ADHD symptoms compared to placebo in adults (60). The stimulants methylphenidate and amphetamine are the most commonly used and highly effective in a dose-dependent manner for ADHD in adults (62–64,68). The stimulants have an immediate onset of action and may last from 4 to 12 hr based on the formulation of the agent (immediate, extended release). Longer term trials with methylphenidate in adults support the ongoing effectiveness and tolerability of stimulants (60,69). The most common side effects with stimulants include edginess, insomnia, headache, and mild increases in heart rate/blood pressure necessitating monitoring (62–64,70).

The side effects of the stimulants in ADHD adults have been reported to be mild with the following side effects most frequently reported: dry mouth, insomnia, edginess, diminished appetite, weight loss, dysphoria, and headaches (62–63,70). Mild increases in heart rate (+ 2–4 beats) and blood pressure (2–4 mmHg) occur necessitating monitoring blood pressure prior to and periodically with treatment (70). While the stimulants have an abuse liability (71); few reports of stimulant abuse in controlled or retrospective studies of adults with ADHD have emerged. Nevertheless, because of the potential for diversion (72) and misuse, careful monitoring and the use of extended release stimulants should be considered (73). For adults who manifest edginess or minor blood pressure problems with stimulants, the

Table 1 Medications Used in Adults With Attention Deficit Hyperactivity Disorder

Medication (generic)	Medication (brand)	Daily dose[a] (mg)	Daily dosage schedule	Common adverse effects
Stimulants				
Methylphenidate		20–100		Insomnia
	Ritalin		Twice to four times	Decreased appetite/weight loss
	Focalin			Headaches
	Metadate CD		Once	Edginess
	Concerta			Mild increases in pulse/blood pressure
	Ritalin LA			
Amphetamine		10–60		
Dextroamphetamine	Dexedrine		Twice or three times	
Mixed amphetamine salts	Adderall			
	Adderall XR[b]		Once	
Magnesium Pemoline	Cylert	75–150	Once or twice	Same as other stimulants Abnormal liver function tests
Noradrenergic Agent				
Atomoxetine	Strattera[b]	40–120	Once or twice	Sleep disturbance GI distress, nausea Headache Mild increase in pulse/blood pressure

Antidepressants				
Tricyclics (TCA) desipramine; imipramine	Norpramin, Tofranil, Pamelor	100–300	Once or twice	Dry mouth, constipation
nortriptyline		50–200		Vital sign and ECG changes Insomania
Bupropion	Wellbutrin Wellbutrin SR/Xl	150–450	Three times once or twice	Risk of seizures (in doses >6 mg/kg) Contraindicated in bulimics
Venlafaxine	Effexor	75–225	Twice	Nausea Sedation GI distress

[a] Denotes typical daily doses.
[b] FDA approved for ADHD in adults.

addition of low-dose beta-blockers (i.e., propranolol at 10 mg up to three times daily) or busipirone (5–10 mg up to three times daily) may be helpful (74). The interactions of the stimulants with other prescription and non-prescription medications are generally mild and not a source of concern (75).

Stimulants

- First-line pharmacotherapy for ADHD in adults
- Two main types of stimulants, methylphenidate and amphetamine compounds have different effects and are metabolized differently
- Methylphenidate does not show up on urine drug screens
- Stimulants are not effective for comorbidities within ADHD
- Stimulants generally have few medication interactions (except with MAOIs)

Atomoxetine

Another FDA approved agent for ADHD in adults, atomoxetine, has been demonstrated in two large multisite trials to be effective in adults with ADHD (65). Atomoxetine specifically inhibits presynaptic norepinephrine reuptake resulting similarly in increased synaptic norepinephrine (65) with some increase in dopamine in the prefrontal cortex (76). In addition to the treatment of both inattention and hyperactivity/impulsivity in adults with ADHD, atomoxetine may be particularly useful when anxiety, mood, or tics co-occur with ADHD. Although untested, because of its lack of abuse liability (77), atomoxetine may be particularly of use in adults with current substance use issues. Atomoxetine should be initiated slowly (0.5 mg/kg/day for 2 weeks) and increased to therapeutic dosing over 1 month. Dosing of up to 100 mg/day is indicated, though increases up to 1.8 mg/kg/day may be necessary in refractory cases. Common side effects include dry mouth, gastrointestinal upset, sleep changes, and sexual dysfunction (males) (65). Additionally, because of mild increases in cardiac vital signs, adults should be checked prior to initiating treatment and periodically thereafter.

Antidepressants

Other available medications shown effective in adults with ADHD though not FDA approved for this indication include bupropion, desipramine, and pemoline—the latter two requiring serum level (desipramine) or frequent liver function test monitoring (pemoline) (60). Bupropion has been demonstrated in multiple open and controlled trials (78,79) to be useful for ADHD. Dosing of 400 to 450 mg (sustained release) appears optimal for best efficacy. Side effects include insomnia, edginess, and a theoretical risk for seizures with immediate release preparations. While a large literature suggests positive effects of tricyclic antidepressants in children and

adolescents with ADHD (80), only one controlled trial exists in adults. Dosing of up to 200 mg daily of desipramine resulted in dry mouth, constipation, and sedation as the main side effects. Bupropion and desipramine may be particularly useful in adults with ADHD with comorbid anxiety, depression, tics, and substance use disorders (81).

Recent data suggest that procholinergic medications (e.g., nicotinic) may have a particular role in improving areas of inattention and executive functioning but data are limited. Modafinil, while shown useful in children with ADHD, has limited data suggesting efficacy in adults (82). Serotonergic antidepressants (e.g., fluoxetine) while useful for comorbid mood and anxiety, do not appear useful for ADHD in adults. A limited data suggest that pharmacotherapeutics of ADHD improve driving performance (83) and are associated with the prevention of substance abuse (84). Monitoring of treatment includes monthly visits initially until stable and then periodic reassessments subsequently (14). Although treatment is chronic, yearly reappraisals of the need to continue therapy are recommended.

Nonstimulants

- Atomoxetine is among first-line pharmacotherapy for ADHD in adults
- Atomoxetine may be particularly useful in treating comorbidity in ADHD
- Few drug interactions exist with atomoxetine; increasing use concomitantly with stimulants
- Tricyclic antidepressant and bupropion are second-line therapies
- Antidepressant dosing of the agents appears necessary for ADHD efficacy
- Empiric use of combinations may be appropriate in refractory and comorbid patients

Refractory Cases

Despite the availability of various agents for adults with ADHD, there appears to be a number of individuals who either do not respond, or are intolerant to adverse effects of medications used to treat their ADHD. In managing difficult cases, several therapeutic strategies are available. If psychiatric adverse effects develop concurrent with a poor medication response, alternate treatments should be pursued. Severe psychiatric symptoms that emerge during the acute phase can be problematic, irrespective of the efficacy of the medications for ADHD. These symptoms may require reconsideration of the diagnosis of ADHD and careful reassessment of the presence of comorbid disorders. For example, it is common to observe depressive symptoms in an ADHD adult which are independent of the ADHD or treatment. If reduction of dose or change in

preparation (i.e., regular vs. slow-release stimulants) do not resolve the problem, consideration should be given to alternative treatments. Neuroleptic medications should be considered as part of the overall treatment plan in the face of comorbid bipolar disorder or extreme agitation. Concurrent nonpharmacologic interventions such as behavioral or cognitive therapy may assist with symptom reduction.

SUMMARY

ADHD in adults is a valid and reliably diagnosed disorder with clinical features highly reminiscent of the pediatric form of the disorder. Diagnosis is based on clinical assessment using the DSM-IV criteria with helpful ancillary information derived from diagnostic rating scales and neuropsychological testing. Many adults with ADHD suffer from co-occurring disorders and manifest academic, occupational, driving, and interpersonal impairments. Studies of biological features support a genetic etiology for the disorder, associated neuropsychological deficits, brain abnormalities, and catecholaminergic dysregulation. Treatment strategies are emerging that include structured psychotherapies, stimulant, and nonstimulant medications.

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Section VI: Controversies

26

More Rewards or More Punishment?

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The first inclination adults often have when trying to handle unruly child behavior is to become stricter and to follow the old adage, "spare the rod and spoil the child." Indeed, attention deficit hyperactivity disorder (ADHD) youth are exposed to more punishment and fewer rewards than children without ADHD or other mental health problems. Studies show that teachers and parents tend to rely on punishment to manage the disruptive, impulsive, and noncompliant behavior of ADHD youth and to get through the frequent behavioral and attentional problems surrounding execution of routine activities of daily living (1). The increasing recognition for a genetic or other biological basis of ADHD, suggests that children with ADHD elicit these interaction styles from adults (and other children) rather than the reverse. This may well be a result of a lack of response among children with ADHD to typical contingencies used with children. Unfortunately, the higher rates of punishment and lower rates of rewards typically being used are not serving to "normalize" their behaviors and may even exacerbate their problems. Answers to the questions of how and why ADHD children respond to contingencies are critical for understanding the best contingency mix for improving their behaviors.

THEORETICAL UNDERPINNINGS

Differences in motivational systems have been proposed to underlie the lack of response of ADHD youth to typical contingencies (2; Sonuga-Barke, and Derryberry in this volume). Haenlein and Caul (3) propose that

ADHD is linked to having an elevated reward threshold. In this model, the reward systems for ADHD and normal children are proposed to differ such that children with ADHD require greater amounts of reinforcement to sustain maximal performance than do normal children. Similarly, Douglas and Parry (4,5) suggest that ADHD involves differential sensitivity to rewards. In support of these theories, experimental laboratory data shows that children with ADHD show greater improvement in performance than normal children when continuous, relative to partial reinforcement is provided and perform less well than normal children under a partial reinforcement schedule, but show a similar performance when continuous reinforcement is provided (4,5).

Also consistent with these models, children with ADHD appear to be particularly sensitive to factors affecting reward magnitude and value. Haenlein and Caul (3) note that the amount of effort required to do a task may be one such factor. For easy tasks (presumably more rewarding), the performance of those with and without ADHD was shown to be similar; but on harder tasks (presumably less rewarding) the performance of ADHD youth was shown to be much less than normal children.

Timing of reinforcement is another factor affecting reward magnitude. Numerous studies document that ADHD children have a heightened response to immediate reinforcement and show greater frustration and decrements in performance under conditions of delayed reinforcement (3). Delayed reinforcement is thought to reduce the value of the reward for those with ADHD due to impaired signaling of delayed rewards (6). The "delay aversion hypothesis" (6) refers to a negative emotional reaction to the imposition of delay which results in attempts to avoid or escape the delay. Consistent with the delay aversion hypothesis, children with ADHD show a preference for small, immediate rewards over large, delayed rewards (6,7). Sagvolden et al. (8) suggest that individuals with ADHD have a shorter and steeper delay of reinforcement gradient than those without ADHD whereby the reinforcing effect is greatest when the reward is provided immediately after the response. Interestingly, a recent study found that children were more willing to wait for the larger reward if extra stimulation (looking at a cartoon) was provided during the waiting period (7). Neural evidence for diminished reward anticipation among adolescents with ADHD was recently reported (9).

Another motivational theory posits involvement of the behavioral inhibition system (BIS) in the apparent diminished response to punishment exhibited by ADHD youth. Quay (10) applies Gray's model of emotion and anxiety and theorizes that an underactive BIS underlies the poor response inhibition, motivation, and regulation difficulties of ADHD youth. Quay (10) posits that ADHD children are less avoidant or cautious to cues of punishment or nonreward because of a weak inhibition system. Physiological data such as that reported by Iaboni et al. (11) showing

increased skin conductance during extinction trials and increased heart rate habituation to rewards, supports a weak BIS explanation for ADHD. However, other studies are not consistent in finding support for a weak-BIS model (12).

Dysfunctional reward responding as described above has been linked to other aspects of Gray's model (12). The behavioral activation system (BAS) leads to approach behavior when signals of reward are detected or active avoidance to escape punishment (e.g., child avoids teasing peers). As noted above, children with ADHD may be underresponsive to rewards, suggesting a weak BAS. Other findings suggest that children with ADHD may be overresponsive to reward (and hence have an overactive BAS), especially to immediate rewards. This overresponsiveness is proposed to be related to the frequent finding that ADHD children show high levels of impulsive response or difficulty inhibiting responses when cues for rewards are present. Dysregulated BIS and BAS systems may also play a role due to failure of response modulation (13). There is also some evidence for ADHD subtype differences in motivation. Huang-Pollock et al. (14) found that children with ADHD-I tended to give up more easily than those with ADHD-C when rewards became less available on a reward-based variation of the stop-signal paradigm.

Although the focus on this chapter is on motivational factors, poor response inhibition, and attentional problems are not fully accounted for by these factors (15–17), suggesting that other factors perhaps related to arousal or regulatory difficulties play a role as well (see also this volume Sonuga-Barke, pp. 111 and Derryberry, pp. 85). Nevertheless, these motivational theories help guide our understanding of potential mechanisms underlying the atypical response to contingences observed among children with ADHD.

THE EFFECTS OF MODIFYING CONTINGENCIES

The motivational theories cited above imply that the behavior and performance of children with ADHD should improve by carefully modifying external contingencies for behaviors in the classroom and at home. Although some have argued that external rewards may operate to decrease motivation and therefore be ill-advised, existing data challenges this belief (18). In their meta-analysis of research on intrinsic task interest and creativity, Eisenberger and Cameron (18) reported that tangible rewards for completing tasks or meeting a standard of quality did not impact time spent on the task when the reward was eliminated. In addition, verbal reward increased time on task after the reward's removal and task-liking improved after rewards dependent on performance quality. Reward contingent on creative performance was also shown to increase generalized creativity. The

only detrimental effects of reward occurred when reward was provided regardless of performance.

Studies with youth having ADHD support the positive impact of external rewards. Consistent with theories cited above, both experimental and applied studies clearly demonstrate that children with ADHD perform more poorly than controls in the absence of external contingencies. Carlson et al. (19) found that response cost improved accuracy on an arithmetic task relative to reward, but that both rewards and response cost had beneficial effects on motivation (desire to complete the task again) compared to no contingencies; the use of rewards was associated with the highest ratings of wanting to do the task again. The study also revealed that response cost seemed to promote greater intrinsic motivation on a behavioral measure. Neither rewards nor response cost was associated with negative effects on self-reported or observed motivation. In a second study, Carlson and Tamm (20) also found positive effects of both rewards and response cost on performance during high- and low-interest tasks; response cost actually normalized performance. Having a high-interest task also improved performance relative to a low-interest task. Importantly, neither rewards nor response cost reduced motivation, except that during a low-interest task, response cost seemed to reduce task liking.

Applied studies in classroom environments suggest that the value of rewards and punishment depend on how and when they are used. When contingencies consist of primarily praise, the effects are not much different from those without any contingencies (21,22) and are well below those achieved with reprimands alone (22). However, when more potent, individualized incentive systems are used (e.g., stars exchangeable for work breaks, special activities, running errands, stickers, extra recess, special toys, special award tag, posting work, and good note home) and the frequency of positive consequences are increased, on-task behavior and academic accuracy is improved and approximates that achieved when negative consequences are used (23). However, this all-positive approach to classroom management seems to be most effective after children have learned the rules (via negative consequences) and following the gradual removal of the negative consequences (24). Consideration of using such an approach is also dependent on the availability of teacher time and effort, both much higher with the all-positive compared to the combination approach. In addition, the appropriateness of rewards is dependent on the type of behavior they are designed to change. For at least some children, rewards in the form of encouraging comments (keep it up, etc.) contingent upon off-task behavior seem to exacerbate such behavior (25).

In the case of punishment, effectiveness is highly dependent on the specific type of punishment used. Punishment that is "prudent" (e.g., calm, consistent, concrete) is far more effective than imprudent punishment (e.g., loud, emotional, inconsistent) when it comes to on-task behavior and work

productivity in the classroom and compliant behavior with parents (22). In fact, imprudent negative consequences appear to be even more deleterious than not using negative consequences at all (22). A number of specific parameters of punishment influence effectiveness. Abramowitz and O'Leary (26) found that immediate reprimands resulted in much lower rates of interactive off-task behavior in the classroom than delayed (by 2 min) reprimands—although differences in noninteractive off-task behavior (e.g., daydreaming) were not detected. Lengthy reprimands have also been shown to be far less effective than brief ones in lowering off-task behaviors in the classroom (27), and consistent reprimands are more effective than inconsistent feedback (sometimes using reprimands sometimes using permissive responses) for reducing inappropriate solicitations (28). Response cost appears to be more effective in decreasing off-task behaviors than reprimands, particularly when delivered consistently (29).

Similar to the experimental studies, reward and cost token programs have been shown to be equally effective in substantially increasing on-task behavior relative to low rates of praise and reprimands only. There was superior maintenance of on-task behavior following fading of response cost relative to reward, especially for the children rated high on hyperactivity and aggression (30), possibly because the fading procedure was more discriminable in the reward than response cost condition. Children with disruptive behavior problems may be particularly sensitive to the fading of rewards due to the motivational theories cited previously.

Other evidence supporting the importance of enhanced positive consequences and prudent negative consequences comes from intervention studies with ADHD. Outcomes from parent training studies with families having a child with ADHD show that parent increases in contingent positive consequences and "good" commands were related to improvements in child compliance (31). In the Multisite Treatment Study of ADHD (MTA Study), children received either combined medication or behavior therapy (BT), only medication, only BT or "treatment as usual" as offered in the community. One of the components of BT was intensive training for parents in the use of more powerful rewards and prudent punishments. The value of this training is clearly seen in the finding that the success of combination treatment for school outcomes (social skills, disruptive behavior) was related to reductions in negative and ineffective parenting practices at home (32,33).

OTHER FACTORS INFLUENCING EFFECTS OF CONTINGENCIES

Medication

Decisions about contingency choices may depend on whether medication is being used. Animal studies show that stimulant medication affects

reward centers in the brain and operate to decrease reward thresholds (3,17). A number of studies suggest that this may be true for children with ADHD as well. For example, early studies show enhanced performance with stimulant treatment (ST) on effortful tasks, presumably because the reward value of the task increases with ST (3). More recent studies have found that ST may increase the reward value of reinforcers such as money (34), may dampen inappropriate responding to the arousing and distracting effects of reward and may also increase sensitivity to punishment (35). Along these lines, Abramowitz et al. (36) found that ST reduced the need for the most intense negative consequences (i.e., immediate reprimands) and Fabiano et al. (37) report that low doses of ST increased efficacy of low-intensity behavior modification in the classroom. Reports from the MTA Study show that children in the medication only condition, who by definition did not receive programmed changes in contingencies at school or at home, showed significant improvement relative to the community care control group (38). These findings are consistent with the notion that ST may improve the response to everyday low-intensity contingencies for at least some children.

Comorbid Disorders

The presence of one or more comorbid disorders may also moderate response to contingencies. For example, children with disruptive behavior disorders without anxiety have been reported to have a reward-dominant style, meaning that effects of reward are stronger than the effects of punishment. This style would lead to deficits in avoidance learning when competing rewards and punishments are present. On the other hand, the presence of anxiety has been shown to increase response to cues for punishment and frustrative nonreward, hypothesized to be due to an overly active BIS (39). One implication is that anxious ADHD children may be particularly sensitive to very mild forms of punishment, and more intense punishment may be contraindicated for these children. The MTA findings also show that the effects of behavioral treatment (having a heavy emphasis on contingency management, particularly use of positive consequences) were particularly strong for those with comorbid anxiety (40). Those with a disruptive behavior disorder but without anxiety may be less affected by mild punishment, but very responsive to powerful rewards.

Comorbid oppositional defiant disorder (ODD) and/or CD may also have implications for specific contingency combinations. For example, in the case of impulsive aggressive behavior, prudent punishment is often necessary to stop the behavior immediately, but powerful rewards for self-control at other times would be expected to be important as well. Very little research has been done on how to tailor contingencies for maximal effects

across comorbid disorders and behaviors, and the need for such research seems clear.

CLOSING COMMENTS

Relative to normal children, those with ADHD report a preference for less challenging tasks and a greater reliance on external (rather than internal) criteria for success (41). Similarly, parents and teachers report that children with ADHD-C and ADHD-I show motivational deficits including a lack of intrinsic interest in learning, preference for easy work, and a lack of a mastery approach to learning. Booth et al. (41) also report that children with ADHD-I are motivated more by pleasing the teacher and making good grades than by their own internal curiosity or interest. These findings and those cited above strongly support the need for modifying external contingencies to boost the motivation and performance of ADHD youth.

Although the natural tendency is for parents and teachers to decrease their use of rewards and increase their use of punishment to handle the negative behaviors of ADHD youth, the most successful approaches in natural settings appear to involve dense schedules of each, but with a very healthy ratio of powerful rewards to prudent negative consequences, for example, a ratio of at least 5:1 positive to negative comments/consequences (42). Perhaps even more important than the ratio, however, are how and when rewards and negative consequences (punishment) are used. Rewards need to be immediate, frequent (if not continuous when teaching new behavior), of high value and contingent on specific desired behaviors. In addition, reinforcement for competing behaviors should be kept to a minimum. Negative consequences need to be delivered prudently; i.e., immediately, briefly, unemotionally, and backed up with a loss of privilege (response cost) or time-out when necessary. When administered properly, these consequences can produce dramatic improvement in performance without untoward effects on motivation or intrinsic interest in the task.

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Against the Grain: A Proposal for a Psychosocial First Approach to Treating ADHD—the Buffalo Treatment Algorithm

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Attention deficit hyperactivity disorder (ADHD) is a prevalent and chronic mental health disorder associated with adverse outcomes through the life span. These include severe disruptions in relationships with parents, teachers, peers and siblings during childhood, academic problems throughout the school years, delinquency in adolescents, and substance use difficulties in adulthood (1). With a prevalence rate of 2% to 9% (2,3), it is one of the most common problems encountered in mental health, primary care, and educational settings. Further, the prevalence of ADHD is consistent with this rate throughout the rest of the world (4).

Because of its adverse outcomes and prevalence, ADHD is a costly problem for society. It is estimated that the annual per child cost of illness (COI) of ADHD in the United States in 2005 is more than US $14,000—more than US $40 billion annually—and that this number is likely underestimated by 50% due to lack of available figures (5). Of this total, estimates for pharmacological treatment with a long-acting stimulant (currently used in over 80% of cases) are US $1440 per year (not including physician's costs); other health care costs associated with ADHD (e.g., emergency room visits due to accidents) average US $1000 annually per child. Much larger amounts are spent annually by schools, juvenile justice systems, and, though limited data are available, families. These costs approximate those of major depression and stroke in the United States (5). Thus, ADHD is a major public health problem in the United States and worldwide.

There are currently three evidence-based treatments for ADHD: (1) behavior modification, (2) stimulant medication, and (3) their combination (2). Stimulant medication, behavioral treatment, and multimodal treatment all have well-established proof of efficacy in short-term studies—hundreds of studies of stimulants (6), 175 studies of behavioral treatments, and 25 studies of combined interventions (7,8). The acute effects of the two modalities are quite substantial and generally comparable, with moderate to large effect sizes across a range of measures, including symptoms of ADHD (e.g., as rated by parents and teachers), classroom behavior and seatwork productivity, compliance with adult requests, and interactions with peers (9). The impact of medication is generally larger on symptom scales, while behavioral treatments have larger effects on functional measures (8,9). Current guidelines call for medication to be administered across settings and days of the week. Behavioral treatments with solid evidence include those provided to parents (parent training), in schools (behavioral classroom management), and to ADHD children themselves for problems with peers (8).

Despite the large evidence base and comparable effects for the two treatments, most medical professionals believe that medication is more effective than behavioral treatments. Indeed, leading ADHD researchers have argued that the effectiveness of medication means that most ADHD children do not need behavioral treatments (10–13). Prominent psychiatric and advocacy groups who have published guidelines in the past 5 years have advocated that stimulant medications be the first-line and often the only treatment provided to ADHD children (3,14–17). In contrast, we are aware of only a single guideline that has suggested that behavioral interventions be employed first-line (9) and only one that states that either treatment could be so employed (2). As a result of this emphasis on medication, the great majority of identified ADHD children receive pharmacotherapy, which is widely available and commonly funded by insurance carriers. Current estimates are that stimulants are taken by 5% to 7% of the elementary-aged U.S. population—70% to 90% of identified ADHD children (3), and prescription rates are even increasing exponentially for preschoolers (18). A recent report (19) showed that utilization of ADHD medications increased by 49% from 2000 to 2003. The extensive pharmaceutical industry marketing to consumers and physicians no doubt contributes to this increase. Further, FDA approval of six new formulations of medications for ADHD in the past 5 years will increase these trends for the near future. This dramatic increase in use has led to growing concern among the media and the lay public about whether medication should be so widely used. Much of the controversy surrounding this issue results from a lack of information regarding whether all of these children need to be medicated.

Given that there are three evidence-based treatments for ADHD, a central question that faces every practitioner and family of ADHD children

following identification and diagnosis is the following: Which of the treatments should a given child receive and in what sequence? Clearly physician practice is to begin treatment with medication and rely on medication alone. Parents' and teachers' preferences are to begin treatment with behavior therapy and only add medication if necessary. The most prominent parent advocacy group for ADHD children has argued that all children should receive multimodal treatments, with both modalities started simultaneously (www.CHADD.org). Given the availability of behavior modification and the fact that many parents prefer it to medication, a pertinent question is whether children who begin treatment with behavior therapy need medication—that is, whether medication use (or dosage) would decrease if behavioral treatments were begun first. Similarly, for parents who do not mind using medication alone with their child, medication alone might be the less costly treatment, and certainly involves less effort than does medication on the part of parents and teachers. If parents prefer to combine the two modalities, the use, dosage, and cost of behavioral treatments might be minimized if children were started on medication first and only subsequently received behavior therapy. Which of these strategies yields greater benefit for ADHD children in the short term? Which is likely to lead to the best long-term outcomes?

Despite all of the guidelines recommending medication as first-line treatment, the extant research literature has evaluated whether the treatments work in the short term when implemented independently or simultaneously. There have just begun to be studies of the appropriate sequence of treatments for a given patient that would provide guidance to address some of the questions raised above. The decision regarding with which treatment to begin in a given case must currently be based on factors other than the extant literature. We believe that a risk:benefit assessment of the two main evidence-based treatments that is provided clearly to parents is the primary consideration that should be used to develop treatment strategies for a given patient. What is known about the relative risks (and benefits) of the two evidence-based treatments?

RISKS AND BENEFITS OF THE INTERVENTIONS

Pharmacotherapy

Despite their widespread use and acute benefits, stimulant medications have limitations when used as the sole form of intervention for ADHD. For example, not all ADHD children show positive responses to stimulant drugs—70% to 80% are responders—and less than half show sufficient improvement for their behavior to fall within the normal range on teacher rating scales (20,21). Further and most important, there is a uniform lack of evidence that the drugs improve ADHD children's long-term prognosis, either in development of antisocial behaviors or in academic achievement

(22,23). Forty years of research have failed to show that medication provided as the sole intervention alters the abysmal long-term outcomes that characterize most ADHD children.

Furthermore, the stimulants are associated with risks of serious side effects, in addition to the well-known acute side effects (e.g., appetite suppression, motor tics, insomnia), (1) reductions in growth (12), (2) cardiac effects as recently cited in the FDA safety advisory panel's recommendation that stimulants receive a black box warning, as well as the FDAs decision to add warning language to all stimulants and to direct the development of parental warnings (54), and (3) possible increased risk of later substance use/abuse (24–26).

While some of these concerns may be minimized by employing very low doses, the trend among psychatrists is in the opposite direction. In general, studies have shown that increasing stimulant dose beyond a low-to-moderate level increases side effects at a faster rate than improvement (27,28). However, current influential practice guidelines argue for titrating dose to a level just below that at which side effects are obtained and no further room for improvement is available (2,3,10,11). However, this dosing strategy results in escalating doses—25% increase annually—to maintain effectiveness (29) and is associated with reductions in growth of 1 cm per year over 2–4 years (12). This trend is clearly toward using higher doses, prolonging active dosing well into the evening hours [e.g., with the long-acting stimulants that comprise the majority of the stimulant market, medicating 7 days per week, and toward continuing medication treatment for many years (3,14)]. A typical ADHD child who takes one of the newer long-acting formulations of methylphenidate (MPH; e.g., Concerta) and is medicated daily for a decade will consume nearly 150,000 mg of MPH over his childhood/adolescent years. Such a medication regimen has been widely recommended in recent years by ADHD experts (6,16). That dose is 15 to 30 times higher than the typical lifetime doses that were consumed in the medication regimen that was common in the 1980s and early 1990s, when the norm was short-acting stimulants for school hours only for a year or two (30). The safety and efficacy of such a high-dose, long-term stimulant regimen has never been investigated (24).

In short, although it has clear and often large acute beneficial effects on ADHD symptoms, stimulant medication is not without risks, which are largely unknown in the long run. What do we know about the risks and benefits of behavioral treatments?

Behavioral Interventions

As noted above, a large body of research has shown that behavioral treatments are acutely effective for children with ADHD (8,31). Furthermore, behavioral treatments specifically address the problems in functioning that

predict and mediate long-term outcomes and therefore lead to long-term improvement if remediated (e.g., parenting skills, peer relationships, and academic functioning) that medication alone does not address (22,32,33). Furthermore, behavioral treatments have major impacts on these domains—typically larger than medication (8). Although there are not yet long-term studies as these findings suggest that behavior therapy should result in improvements in long-term outcomes for ADHD children. Finally, behavioral interventions do not have adverse side effects. Behavioral parent training and classroom management programs have no known side effects. Although some have suggested that group-based peer interventions have iatrogenic effects, systematic evaluations of this putative effect have not supported this speculation (34,35). Thus, behavioral interventions have no known side effects. Furthermore, parents strongly prefer nonmedication treatment to medication treatment for their children (36). In the multimodal treatment for ADHD (MTA), strong parent satisfaction with treatment was doubled from one-third to two-thirds of families when a behavioral component was present (38). Not surprisingly, family attitudes toward treatment are predictive of long-term treatment adherence (38), which is essential when dealing with chronic diseases such as ADHD.

Unfortunately, most children with ADHD in the United States receive psychosocial treatments that are not evidence-based in community mental health settings (39,40). These frequently used and often commonly reimbursed treatments include individual psychotherapy, play therapy, generic counseling, neurotherapy or biofeedback, sensory integration therapy, and occupational therapy. However, none of these interventions have any scientific support (8,9,16,39,40). In other words, they do not work. The result is that insurers and governmental entities that underwrite community-based treatments both locally and nationally are faced with paying for costly treatments (e.g., individual counseling for the child) that are not proven to be effective but use valuable resources (e.g., therapist time) and therefore ultimately contribute to the economic burden of mental healthcare in United States.

Thus, in contrast to a medication-first or usual clinic care model for treating ADHD, some professionals have begun to argue that a "do-no-harm" or "safety-first" approach, which characterizes most of pediatric care, should be applied to ADHD (9). Such an approach would prioritize evidence-based psychosocial (i.e., behavioral) treatments as a first-line treatment with medication as a second-line, adjunctive treatment. What might be the benefits of such an approach?

BENEFITS OF A BEHAVIORAL-FIRST TREATMENT APPROACH

The major potential benefits of a behavioral-first approach involve reducing the need for medication and thus the number of medicated children and

reducing the dose of medication that will be necessary if a behavioral intervention is insufficient and adjunctive medication is needed. We will briefly illustrate these outcomes with results from several recent studies.

In the MTA study, children in the combined treatment group (behavior therapy plus medication) were receiving endpoint doses that were 20% less than those in the medication only groups (10,11). The reason for the difference is that medication had to be increased over the intervention year in the medication group in order to maintain efficacy (29). Although this was an impressive reduction in medication dosage, design factors in the MTA study limited the reduction in dose that could be obtained in this group. For example, reductions in dose were prohibited unless driven by side effects, that is, a child could not have his or her dose reduced if the therapist thought that it was unnecessarily high. Previous studies had suggested that dose could be reduced by as much as 50% in a combined versus medication alone group (41) but this was not systematically attempted in the MTA.

To examine this question, we recently conducted a study to find out whether concurrent behavioral treatment could produce even larger reductions than the MTA and earlier research, in the dose of medication that is needed if behavioral treatments are implemented. In that study, comparative and combined impacts of different doses of behavioral intervention (none, low, and high) and MPH (pl, 0.15, 0.3, and 0.6 mg/kg per dose t.i.d.) were evaluated in a summer program setting (42,43). The low behavioral "dose" involved rules, consistent staff praise and feedback, daily "when…then" contingencies, and a daily report card (DRC) with weekly rewards; the enhanced or high behavioral "dose" involved the same low dose variables plus a point system and daily rewards. All of the above were removed in the control, no-treatment condition. Results showed that the higher dose of behavioral intervention was more effective than the lower dose in both classroom and recreational settings on multiple measures of functioning (Fig. 1 for results on classroom rule violations). The same was true for medication. Unexpectedly and in contrast to medication, the behavioral intervention function appeared to be quadratic rather than linear—lower behavioral doses were closer to higher behavioral doses than to no treatment, implying that the higher dose may not have been necessary for many children. The low behavioral dose was comparable to the moderate dose of MPH, while the enhanced behavior modification condition was comparable to the high doses of medication. As Figure 1 illustrates and as in previous studies (41), effects of MPH beyond the lowest dose were minimal in the presence of behavior modification.

What is novel about this study is that the dose of MPH on which effects were maximized, 0.15 mg/kg per dose, was half that employed in earlier studies (44). This result suggests that if appropriate behavioral interventions are employed, then the dose of MPH necessary as an adjunct might be reduced by as much as 75%—in this study from an average dose of 20 to 5 mg/dose. At this low dosage level in this study, there were no side

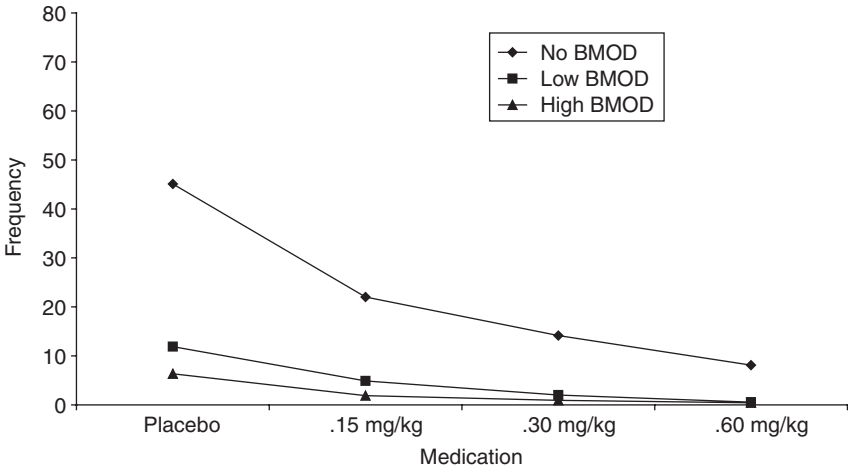

Figure 1 Rule violations in the classroom as a function of treatment condition.

effects, including no tics, no increase in heart rate and blood pressure, no appetite suppression, and no insomnia (45).

These findings are interesting but are limited, as is the MTA by the fact that the two modalities were provided concurrently rather than sequentially. As low as the dose that maximum benefit was, it is possible and even likely that some children functioned so well with the behavioral treatment alone that they did not need adjunctive medication. After all, the difference between the placebo and low dose conditions in Fig. 1 is rather small. We thus decided to ask the question of whether medication was needed at all in these children had behavioral interventions been initiated first?

The children were enrolled in a follow-up study in which they returned to their regular schools at the beginning of the school year without medication (46). All parents had received nine sessions of weekly large group parent training during the summer study. At the beginning of the school year, they were randomly assigned to receive behavioral intervention as follow-up (the opportunity to attend monthly large group parent booster sessions) or to receive nothing as follow-up. A DRC was implemented by a consultant in the classrooms of the children who were assigned to the behavioral follow-up condition. Regular evaluations were conducted to examine functioning in school, at home, and the need for adjunctive medication. If medication was needed according to the regular evaluations, it was provided either at home or at school or both, as indicated.

For analysis, subjects were divided into those who had begun their treatment with behavioral intervention (e.g., had not been medicated prior to

the study), and those who had been previously medicated. By the end of the school year, more than 90% of the children who had not been previously medicated and whose parents received parent training and behavioral follow-up remained medication-free in the home setting, and two-thirds of those were also medication-free at school. These rates were reduced dramatically if children had been previously medicated or if parents were not receiving follow-up behavioral interventions. Only 35% and 15% of parents of children who had been previously medicated (i.e., had received medication prior to the behavioral treatment) and who did not receive follow-up were successful in keeping their children off medication at home and school, respectively.

This follow-up study thus suggests that the majority of ADHD children can be maintained with good functioning at school and especially at home if their treatment is begun with a clinical level of behavioral intervention (standard behavioral parent training and a school DRC). There are limitations to this conclusion that include the fact that the children were all exposed to medication and to a summer treatment program in the context of the summer study, but the findings are provocative.

The findings of one additional study, the MTA study, are relevant to this discussion. Seventy-five percent of the children assigned to the behavioral treatment only group (equivalent to the high dose behavior modification group described above) in the MTA study "survived" the treatment year without medication, with that figure rising to 85% for children who had not been previously medicated (10,11). Further, more than 80% of those children remained medication-free 1 or 2 years later (12,13). Thus, although the MTA was not planned as a sequencing study, its results can be interpreted as supporting our contention that the vast majority of ADHD children can be well treated and maintained without medication if a comprehensive behavioral intervention is provided as first-line treatment.

Considered together, the MTA study and our studies shed light on the dosage of behavioral intervention that might be necessary to avoid medication. The amount of parent training provided in our studies—a standard set of 9 large group (16 families) weekly sessions with monthly large booster group sessions available—was far less than that provided in the MTA study [35 planned sessions divided into weekly small group (6 families) and monthly individual sessions]. However, the results in terms of preventing need for medication at home were similar, 85% versus 90%. In addition to the results shown in Fig. 1, this comparison suggests that for many families of ADHD children, a standard course of group parent training may be sufficient to produce functioning that parents consider adequate to avoid using medication. In other words, many if not most of the parents in the MTA study may not have needed the intensive parenting intervention that they received.

Regarding school intervention, our follow-up behavioral treatment involved only two brief contacts with the child's teacher to establish a home-based DRC, compared to 20 weekly teacher contacts, 5 parent–teacher

meetings, and a 9-week half-time aide in the MTA study. Eighty-five percent of the previously unmedicated MTA children with this intensive intervention were maintained without medication versus 60% of our previously unmedicated children with a much less intensive intervention (vs. 35% of our previously unmedicated children with no follow-up intervention). This comparison suggests four conclusions: (1) that parent training alone may apparently be sufficient to enable some parents to maintain their children without medication at school; (2) that a consultant-facilitated, teacher-implemented DRC can nearly double that number; (3) that a far more intensive behavioral intervention might be needed and effective for an additional 25% of the children; and (4) that the remaining 15% may need adjunctive medication at school.

Altogether, these studies suggest that most ADHD children can be treated effectively with a relatively simple behavioral intervention and will not need adjunctive medication or intensive behavioral interventions. Conceivably, such an approach to treatment might reduce the number of ADHD children in the US receiving psychoactive medication from more than 4% to no more than 1%. This outcome would be well received by families of ADHD children. An important question is what impact will this have on the societal cost of ADHD? While it is widely believed that medication is less expensive than psychosocial treatment, an evidence-based but low-intensity behavioral treatment (e.g., 12 group parent training sessions plus a consultant to visit the child's teacher to establish a DRC) may be implemented for a cost (approximately US $1500) that is less than that the annual cost of today's long-acting stimulant preparations [about US $1800 per year, assuming quarterly physician contact (5)]. Furthermore, because of the lack of long-term gains, medication must be continued indefinitely once it has begun, whereas effective behavioral treatments have been shown to produce longer term maintenance of treatment gains (12,13). A liberal estimate of the cost of the intensive behavioral or combined treatment provided in the MTA was US $6000 to US $8000 (13)—about equally divided among the parent training, school intervention, and summer treatment program. This was considerably more than the cost of medication in the MTA study, but as our discussion above shows, the majority of ADHD children do not need either adjunctive medication or behavioral treatment of this intensity. Thus, provision of a low dose of behavioral intervention as the starting treatment for ADHD children may be more cost-effective than medication alone and can avoid the expensive, intensive treatments provided in the MTA study if they are not needed for a given child.

IMPLICATIONS FOR TREATMENT

What can be concluded about how clinicians should be implementing treatment with ADHD children? We believe that the literature and a

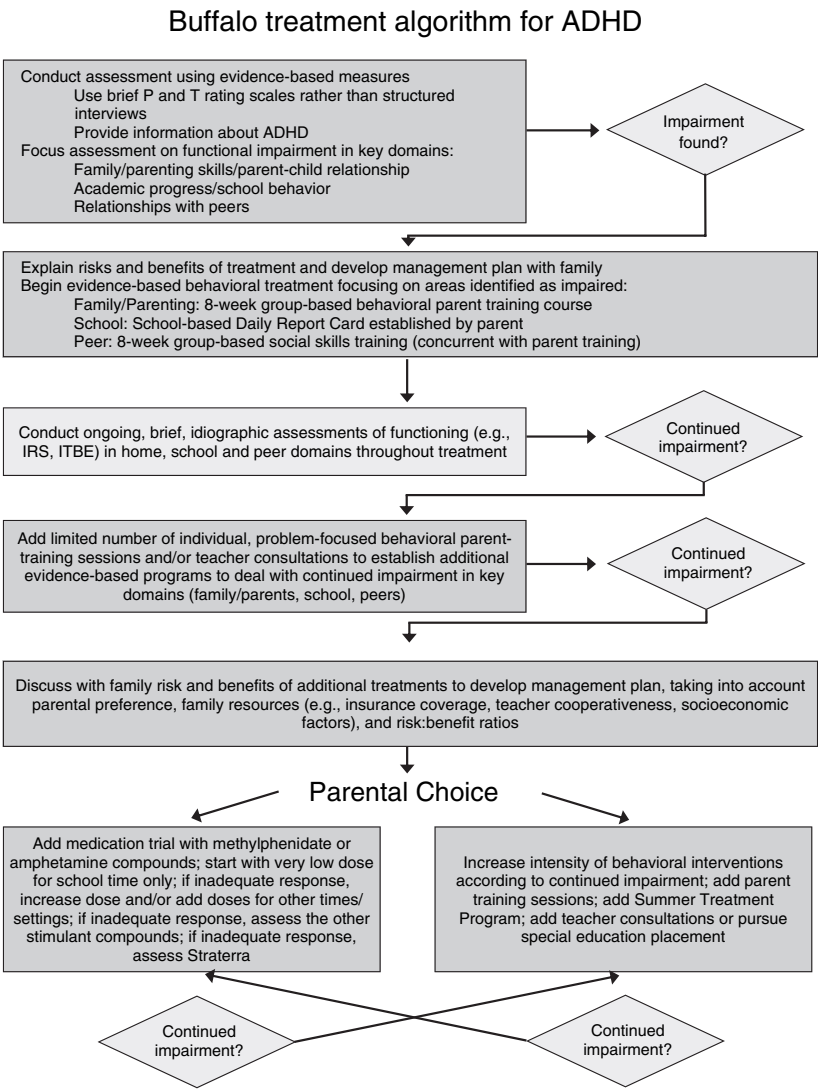

Figure 2 Buffalo treatment algorithm for ADHD.

risk: benefit assessment suggest the treatment algorithm that we present in Fig. 2, the Buffalo treatment algorithm. First, evidence-based treatment should begin with an evidence-based assessment that is focused on functional outcomes rather than DSM symptoms. Because there is little evidence that psychiatric comorbidities make a difference in treatment planning or outcome, the diagnostic process should be conducted as efficiently as

possible. Thus, rating scales rather than systematic structured clinical interviews should be employed so that relatively more professional time can be devoted to treatment development than to diagnosis. Functional analyses should be conducted to select target behaviors and identify the antecedent and consequent variables that influence them and will be utilized in treatment, and these should be ongoing using simple, inexpensive instruments (47; instruments downloadable at http://ccf.buffalo.edu) as new targets are identified and addressed (48). When such assessments reveal dysfunction in peer, classroom, and family domains, as will typically but not always be the case, a management plan should be discussed with the family explaining what treatments could be initiated. Based on the literature on parent preferences, our assumption is that the vast majority of parents will elect to begin intervention with the clinical behavioral approach shown in the algorithm. If selected by parents, children with ADHD should have school-, home-, and peer-based behavioral treatments initiated, as indicated, with the management plan developed with the family.

Given the importance of cost of services in a public health model, we propose (1) that initial behavioral treatment be relatively simple and inexpensive, (2) that need for additional behavioral components treatment be based on ongoing assessments (see above) in domains of impairment, and (3) that the treatment be adaptively determined based on need. Thus, a standard course of any one of the evidence-based group behavioral parent training (BPTs) (49–52; Webster-Stratton, www.incredibleyears.com) should be implemented initially. A limited number of individual sessions (53) could be used after the parenting group, if indicated by ongoing brief assessments. A DRC should be concurrently implemented with parent training. Because the effectiveness of DRCs has been ubiquitously documented in the studies with ADHD and because they are relatively simple interventions, a DRC would clearly be a first-line classroom program. A standardized packet for developing and implementing a school-based DRC that has been used in multiple studies can be downloaded at http://ccf.buffalo.edu. DRC implementation can be a topic in parent training groups, and parents can take the lead in initiating this with their child's teacher. As with individual parenting sessions, more intensive classroom programs can be implemented subsequently with a limited number of contacts as necessary. In a clinic setting, this would typically involve having a consultant work with the classroom teacher directly or through a school psychologist or counselor, assisting in the development and implementation of behavioral programs in the child's classroom. When initial assessment identifies problems in peer relations, an evidence-based peer intervention should be included. There is limited evidence for social skills training but some evidence that provided concurrently with parent training weekly groups can be helpful (54).

If such a behavioral intervention has been insufficient, then one of two alternatives for increasing treatment intensity should be presented to the family—adjunctive or increased dose of stimulant medication (depending on whether it has already been utilized) or enhanced and more complex behavioral interventions (e.g., enhanced individualized parent training, a summer treatment program for peer or academic problems) and/or more restrictive educational placement. Based on parent preferences, resources, and a discussion of risk:benefit tradeoffs, families should be counseled to select one of these alternatives. If the chosen alternative is insufficient, the other would become the only remaining option based on the current literature regarding intervention for children with ADHD (i.e., second-line medications show little evidence of efficacy and other psychosocial approaches to treatment also lack an evidence base).

ADHD is a chronic disorder (2). As in the case of other chronic disease states it is inappropriate to think that a brief, time-limited treatment regimen, whether behavioral, pharmacological, or combined, will be a sufficient and effective intervention for a child with ADHD. For most children with ADHD and their families, sustained treatment that is palatable for the family and that promotes engagement and adherence to the selected regimen for protracted periods of time will be required. It is our firm belief that the treatment approach outlined in the Buffalo treatment algorithm that begins with behavioral interventions best meets these goals. By minimizing medication use and dose, this approach reduces risk of adverse effects–both known short-term side effects and unknown long-term adverse events. By emphasizing treatment components that impact on the key domains that mediate long-term outcomes—parenting, school functioning, and peer relations—this approach has the best chance of maximizing the long-term adaptive outcomes of children with ADHD and their families. By minimizing adverse effects, maximizing adaptive outcomes, and cost-effectiveness, the approach we have outlined should also reduce the societal costs of ADHD.

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Stimulants in ADHD: Effects on Weight and Height

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INTRODUCTION

Issues about growth patterns in individuals with attention deficit hyperactivity disorder (ADHD) have long been of interest to families and professionals. By far the greatest attention has been paid to the possible effects of stimulants on height and weight, since these medications typically are used to treat ADHD in children during a significant interval of the growth development. Current evidence indicates that, on average, persistent use of stimulants does result in decreased rates of growth for both height and weight, especially during the first several years when used in prepubertal children. The magnitude of the effect seems to be related to total medication exposure. Less clear is whether stopping the medication either with "drug holidays" or completely while a child is still growing permits for "growth rebound." This latter issue relates, in part, to unresolved questions about whether ADHD itself may be associated with changes in growth patterns.

As thoroughly documented in other chapters of this volume, ADHD has been a well-recognized disorder for many years. It is perhaps not a coincidence that stimulants have been widely accepted as an effective treatment for ADHD for many of those years, dating back to at least the early 1960s (1). Although other medication and nonmedication interventions also have clear benefits for ADHD, stimulants remain the gold standard for medicating individuals with this disorder (2). Since 1990, use of stimulants for this purpose has expanded markedly in multiple ways: more individuals are receiving higher doses for more days of the week, more weeks

of the year, and more years (3). This expanded use of stimulants has had many contributing factors, two important ones being relatively high efficacy rates and acceptable side effect profile.

Although potential effects of growth, specifically height and weight, may initially seem only peripherally interesting as a medication side effect, clinicians quickly learn otherwise. Most parents are intensely interested in the eating habits of the children; so, a notable decrease in appetite, let alone loss of weight or even a failure to gain weight typically is a cause for concern. Similarly, at least in the United States, being tall is a valued trait especially for males and increasingly for females. Therefore, information about medication effects on either weight or height is of understandable interest.

Concerns about possible effects especially on height are not new. For example, Safer et al. (4) proposed that stimulants slowed physical growth rates. However, by the late 1970s and into the late 1990s, the general consensus was that effects on growth were of minor concern (5,6). In fact, some research suggested that, even if stimulants did have a short-term effect of growth suppression, this effect was negated by growth rebound once stimulants were discontinued (7).

This sanguine view of the impact of stimulants on growth has been shaken in the past few years by a number of studies that indicate that the growth-suppressive effects of stimulants are more persistent than earlier studies suggested. As discussed below, the magnitude of those effects and their importance in clinical management remain to be determined.

It may seem surprising that, with stimulants having been widely used for decades, there would be any remaining uncertainties about their effects on weight and height. However, it is important to keep in mind the changes that have occurred in stimulant use (cf. 3). Up through the mid-1990s, the most common way of administering stimulants was as an immediate-release, short-acting form once or twice a day just on school days; usually, stimulant use stopped sometime around the onset of puberty. Now, children routinely take stimulant preparations that work for 8 to 12 hr a day or longer, often 7 days a week, all year long. In addition, they may start taking stimulants at a younger age and are apt to continue taking them throughout adolescence, that is, during their entire growth phase.

STIMULANT EFFECTS OF WEIGHT

The acute effect of stimulants on appetite is not controversial: most individuals who take stimulant experience a notable suppression of appetite that typically lasts for several hours with short-acting preparations. Usually, the effect is most notable with medication-naïve individuals, but the effect often persists and may be severe enough to be perceived by patients or their parents as an unacceptable side effect. More commonly, however, the acute

appetite-suppressing properties of stimulants change the pattern of eating during the day, with most caloric intake occurring in the morning and late afternoon or evening. Less well-studied are possible effects on the types of calories consumed, with parents sometimes reporting that children crave certain types of foods, for example, carbohydrates, when they are hungry.

One potential effect of appetite suppression is decreased overall caloric intake, with resulting slowing of weight gain or even actual weight loss. In one of the few controlled studies of using stimulants to treat ADHD over a prolonged period, the Multimodal Treatment of ADHD (MTA) found that, over 14 months of treatment, subjects with ADHD who received stimulants daily, gained on average 1.2 kg/year less than those who did not receive stimulants (8). By 36 months, the difference in weight between these two groups was 2.7 kg (9). Similarly, a recent study of the use of stimulants in preschoolers with ADHD found a slowing in weight gain at 1 year (10).

However, not all studies have shown such sustained differences in weight as a result of stimulant use. For example, Kraemer et al. (11) followed a sample of children with ADHD, treated with stimulants as children, into adulthood and found no statistically significant effects on weight compared to unmedicated family members or community controls. Spencer et al. (12) have proposed that an apparent initial effect on weight might actually reflect an ADHD-related delay in maturation. However, their methodology used a cross-sectional evaluation. The longitudinal results from the MTA (9) failed to support such a hypothesis.

Pragmatically, clinicians should warn parents and children that use of stimulants may have an effect on appetite, especially early on. Parents need to know that children often will have little to no interest in lunch and that the best times for encouraging them to eat a healthy meal will be at breakfast and then later in the day. Occasionally, especially with higher doses of long-acting formulations of stimulants, appetite does not return till late evening. Under such circumstances, it may be appropriate to arrange for the child to have a healthy meal shortly before bedtime; it is essential that parents be warned not to allow any guilt they may feel, about having caused their child's poor appetite, to result in their letting the child indulge at such times in poorly balanced snacks of low nutritional value.

If appetite suppression is severe and persistent and results in weight loss or even just a failure to gain weight at the expected pace, it may be necessary to consider using another medication. Sometimes switching to a different preparation or to a different stimulant is sufficient. Other times, it may best to utilize a nonstimulant medication.

STIMULANT EFFECTS OF HEIGHT

As noted earlier, the effect of stimulants on height has been more controversial than that on weight. Early studies suggested that stimulants

decelerated height growth rates (4). However, later reports suggested that early effects on height were either transient or reversed once stimulants were stopped (7,13). Further, studies done in the late 1980s that followed samples of patients into adulthood (11,14) found no differences in ultimate height as a function of exposure to stimulants during childhood. As mentioned earlier, Spencer et al. (12) proposed that the apparent observed effect of stimulants might simply reflect a maturational lag that co-occurs with ADHD.

More recent studies of growth, however, again raised concerns about possible immediate effects of stimulants on growth, although the results are inconsistent. In independent studies of children in the United States (15) or Australia (16) researchers found evidence of growth reduction in children taking stimulants; these chart-reviews found no evidence of growth rebound over the 3 years studied. However, two other chart-review studies found no such reduction in growth (17,18).

The MTA, mentioned earlier, is one of the few studies that combine random treatment assignment with long-term follow-up. At the time the study was designed (19), effects on height and weight were thought to have been settled and were not a major focus of the research plan. However, measures of both were included at regular intervals. The first assessment of the impact of treatment on height revealed that, compared to those who received no medications, subjects who received stimulants during the 14 months of active treatment grew an average of 1cm/year more slowly (8). This effect was sustained at 3 years, the most recent data reported (9), with a 3 cm difference between the groups. An intermediate group with exposure to stimulants that was more intermittent resulted in intermediate rates of growth.

The MTA results (8,9) also raise questions about the hypothesis of maturational delay. The researchers found that, if anything, unmedicated children with ADHD grew at a faster rate than did normal controls. In fact, they proposed that one possible explanation for reports of growth rebound in other studies was that the children with ADHD resumed their more rapid pattern of growth once off medications. Among their subjects, they found no evidence for rebound or for maturational delay.

The mechanism by which stimulants might affect growth remains unknown, but it almost certainly is independent of their effects on appetite and caloric intake (20). Whatever the cause, the MTA data seem to suggest that the effect of stimulants on height is incremental and directly related to persistent exposure to stimulants.

CLINICAL IMPLICATIONS

Clinically, the available data suggest that clinicians need to inform families of the potential effects of stimulants on weight and height. Regular

measurement of both in standardized fashion should be a routine part of care, with use of growth charts to monitor how the child is doing over time. It is quite likely that the effects are not uniform, with some children potentially having profound growth reduction and others having little to none. In the latter cases, no studies have suggested any possibility of a "sleeper effect": if a child shows no deviation from his or her growth curve potential, no unanticipated abrupt loss of height or weight will occur later.

On the other hand, if children show marked reductions in acquisition of either height or weight over time, then it behooves the clinician to bring such side effects to the attention of the family and help them consider options. Here, research is relatively silent. Clinical experience suggests that switching from one stimulant to another may result in a different side effect profile. Alternatively, several new nonstimulant medications are now available. Most of these are still so new that scant information exists about their possible long-term effects on growth, but they at least offer a potentially viable alternative. In the end, the family and clinician will, as usual, have to balance perceived benefit with potential risks in deciding on the most appropriate clinical course.

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Why Controversy Over ADHD Won't "Go Away"

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Several years ago I noted a pediatrician's frustration with the persistence of criticism over the attention deficit hyperactivity disorder (ADHD) diagnosis and the use of prescription stimulant drugs like Ritalin in the United States. He complained, what with the thousands of studies supporting the validity of the ADHD diagnosis and the effectiveness and safety of the stimulant drugs, why critics, like me, continue to raise concerns. Enough already, was his conclusion; let's move on to other important concerns of our times where real questions remain unanswered. At least with ADHD and Ritalin, according to this pediatrician, the important questions have been settled.

Indeed, controversy over stimulant drugs for children's performance and behavior problems has been present since Bradley's first report of the effects of benzedrine in hyperactive children in 1937 (1). Despite nearly 70 years of use and the plethora of research associated with these drugs and ADHD, some of the original ethical concerns about these medications continue to resonate despite the pediatrician's lamentation. The explosive growth of the ADHD diagnosis and the use of stimulants beginning in the early 1990s, initially in school-age children and then spreading to teenagers and adults, have only heightened concerns about the long-term effectiveness and safety of these medications. And if one is of a questioning nature (who in this case is also a physician who has routinely prescribed stimulant drugs for over a quarter century), this more recent, wide use of the ADHD diagnosis and stimulant drugs, raises even broader questions about our society's values and beliefs about children.

The most fundamental assumptions of any belief system are invariably also the most challengeable. The medical model is most commonly invoked as

the scientific and ideological underpinnings upon which ADHD diagnosis and use of stimulant drugs rest. That framework emphasizes biological process that are genetic and biochemical in nature. Even most ardent proponents of the medical model do not deny some importance attributed to experience when it comes to behavior. However, "nurture" is not routinely invoked with mainstream ADHD research, presentations, or professional publications.

Yet even the devastating effects of a thoroughly well-described genetic condition like phenylketonuria (PKU) deficiency can be avoided by making changes in the environment (avoiding foods that contain phenylalanine). Such a child can otherwise lead a completely normal life.

I often mused over the meaning of the heritability of ADHD. It's contribution to the variance of the syndrome is said to be as high as 0.8 or similar to the genetic contribution towards adult height. Such data have been used politically and emotionally to justify ADHD as a genetically based disorder that has nothing to do with parenting.

But I wonder whether the full penetrance or expression of an ADHD set of heritable personality characteristics (as an aside I believe qualities of persistence and intensity to be far more problematic in the raising of children than impulsivity, but practically speaking all are often lumped together as ADHD) would appear if, say between the ages of 24 and 60 months, the child and family received the kind of intensive, in-home behavior modification programs offered at a similar age to children with another biological-based problem, that of autis (2).

While complete remission of autistic signs occurs in only 10% to 20% of those children who received such interventions, nearly 80% become compliant, an outcome worth noting when contemplating a similar intensive psychosocial regimen for ADHD. Many of these autistic children are also inattentive and hyperactive but if they respond to a "no" then medication is not likely to be necessary in their management.

The parenting/interventions of applied behavioral analysis (ABA) are fairly rigorous (the equivalent of kiddie boot camp, according to some). It may not be for the faint hearted parent who is committed to a more cognitive conflict avoidance type of parenting that has gained predominance culturally in our country. Indeed, while the reasons are legion for the explosive growth in the past 15 years of the ADHD diagnosis and stimulant use in our country, one contributing factor might be the ADHD temperament profile, which has always been part of the spectrum of human behavior (at least since the Ice Ages), in combination with our current parenting styles in America. The genetics of ADHD—is not to be ignored—but may not be the complete explanation for behavior expressed in the current epidemic.

Stimulant medication works to improve the behavior and performance of children with ADHD—there are no questions about that at all. And 70 years experience suggests, despite recent negative publicity and the lack of long-term (more than 2 years) randomized studies, that stimulants are also

quite safe (at least in the under teen population—see below). But the effect that stimulant drugs have on improved focus and concentration and decreased impulsivity is true for everyone, not just ADHD children, or adults for that matter (3). This too we have known through studies for 25 years but it is also confirmed by the current widespread illegal use of prescription stimulants by teens and young adults.

However, that stimulants work and are relatively safe do not make them the equivalent to addressing the needs of children at their schools and home with nondrug interventions. But nearly all the scientific literature operates within the constraints and limitations of the medical model which ignores ethical considerations. Consider the following circumstances.

Critics of critics like me invoke well-run studies like the Multimodal Treatment Study of Children with Attention Deficit Hyperactivity Disorder (MTA) or Klein series which purport to prove that psychosocial treatments neither work as well as stimulant drugs in addressing the symptoms of ADHD, nor do they really add much to improvements achieved by stimulant drugs alone. It does not matter that both sets of studies can be (and have been) deconstructed to make a better case for psychosocial interventions for ADHD.

But to go beyond the analyses of these studies, surely the qualities of impulsivity, inattention, and hyperactivity fall within a bell-shaped dimensional model for all children. When considering ADHD in gross terms one looks at the left side of the curve (Fig. 1) at those with the most extreme and clear problem behaviors. They will be few in number compared to those children with a mild or borderline condition for ADHD.

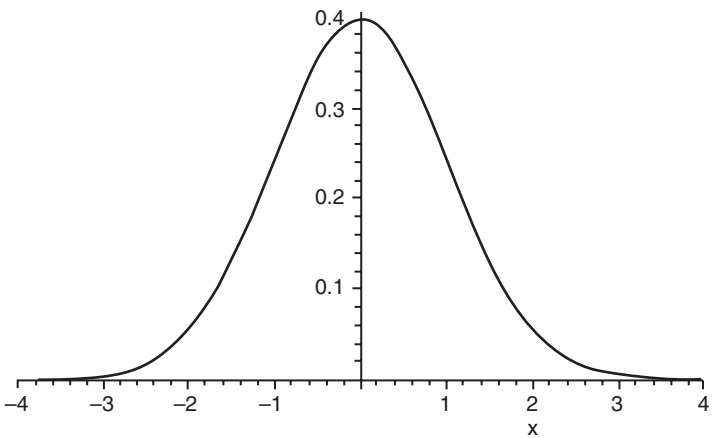

Figure 1 Bell-shaped dimensional model for ADHD.

University studies undoubtedly screen children more rigorously for ADHD diagnosis compared to community standards. Children within MTA and Klein were far more likely to have serious ADHD compared to those diagnosed in the community and treated with stimulant medication (4,5). The Great Smokey Mountain Study offers clues to how medication is actually used on the community level (6). A medication rate of 5% in this population of 4000 children seemed reasonably appropriate given many other studies of ADHD prevalence and medication rates.

Researchers found that 75% of the children who met ADHD criteria were receiving stimulants. However, over half the children being prescribed stimulant medication in this sample did not meet threshold criteria for ADHD or were being treated for a variety of other behavioral and performance issues. The authors did not even address the relative impairment of the medicated children, which ultimately should be the determining factor for treatment, but limited themselves to using the current judgment criteria of our day which was a count of DSM-based symptoms for ADHD.

Other surveys of ADHD prevalence and medication use demonstrate wide variability based on geographic region, ethnicity, and income level—which support the kind of treatment picture we get from the Great Smokey Mountain Study. What we are left with is a very wide set of children being treated with stimulants in our country compared to those carefully screened well-diagnosed children of the MTA and Klein series. It is within the community diagnosed set of children that ethical questions of equivalency of means of treatment can be especially raised.

Just because one kind of treatment works equally well compared to another does not make them morally equivalent (7). Certainly in cases with extreme ADHD, drugs are both indicated and are most likely quite necessary, no matter what environment, or what other nondrug interventions might be available to those children. But for the vast bulk of children in the community being treated with stimulant drugs the same caveat does not apply.

Pelham and others have shown quite clearly that behavioral interventions will reduce ADHD behavior and lower the dose of, or the need for, psychostimulant drugs (8). Just because Ritalin works does not make it the same as offering parents and teachers effective behavioral tools for intervening with impulsive or inattentive behavior. Since children are being treated with stimulants for a variety of behavioral and school performance issues in the real world, making certain educational and learning needs are being addressed in the classroom, with special educational interventions, is ethically required.

I offer a Swiftian "modest proposal" in order to make this lack of moral equivalency clearer. With an estimated 3 million children currently taking stimulant medication in our country, and classroom size averaging about 29 children per class, I propose we increase the number of children on medication to 5 million and in the process we could probably increase

classroom size to 40 children per class and save our communities a great deal of money in teachers' salaries. Are there any takers to my offer? Most politicians and community leaders would reject such an offer as completely unethical—that medication is not the equivalent of giving children proper or enough attention. Yet to a degree that already happens in our country today in many communities and areas.

Critics of the critic often respond with medical analogies. But "Would you deny insulin to a diabetic child?" or just simply try to change the environment. The charge is disingenuous. There is a small group of ADHD children (relative to those treated in the United States) who are like insulin-dependent diabetic children. They would need their Ritalin regardless of family, community, or culture. But they represent a minority (my guess is one-eighth to one-tenth of whom we treat medically today). Ironically the diabetes metaphor for ADHD can be used to justify psychosocial interventions. Type II diabetes is clearly a medical problem and is probably a better analogy for ADHD than Type I. Type II diabetes does respond to insulin or oral hypoglycemic agents, but the first interventions recommended are typically environment related—diet and exercise. Only after they fail (and they often do) are medical interventions employed (as should be the case with ADHD—yet official recommendations are for drugs as the first-line treatment).

America's love affair with legal and illegal stimulant drugs raises many questions about the nature of our society. One wonders whether the fact that the United States uses 80% of the world's legal stimulant production is a sign of our advanced thinking on these problems, or some perverse fixation we have on performance at any cost (9). More recently I have come to the conclusion that our obsession with performance drug use in children is an ironic response to our over concern about our children's self-esteem and self-image. However, the cultural implications of this speculation go beyond this essay and the reader is referred to essays in "The Last Normal Child" (10).

My final area of concern has to do with growing signs and evidence of prescription stimulant misuse and abuse particularly in teenagers and young adults. America has experienced three waves of doctor prescribed stimulant abuse since World War II and we are currently deeply into our fourth. The last prescription stimulant abuse epidemic occurred in the 1970s when doctors routinely prescribed amphetamine for weight loss primarily in women. Many patients became addicted to the drug. In the end society judged (through congressional hearings and individual state laws prohibiting doctors from prescribing stimulants for weight control) that the benefits of these drugs for weight loss far outweighed the risks involved.

As I mentioned, stimulants have an enviable safety record in children. In the past our society (also true in Europe and Japan) has concluded that stimulant drugs are potentially dangerous to adults—the main reason that

Ritalin, Concerta, and Adderall are all Schedule II controlled substances in the United States. Beginning in the mid-1990s the diagnosis of ADHD in teens and adults burgeoned, as did the use of prescription stimulants. Recent surveys by Medco have prescription rates doubling in this age group between 2000 and 2003 (11). Centers for Disease Control (CDC) estimates of adult prescription stimulants use is at 1.5 million in 2002 but is likely to be much higher now.

Anecdotal reports of widespread availability of prescription stimulants on high school and college campuses abound. Up to one quarter of college students at certain campuses admit to the illegal use of prescription stimulants (12). In early 2006 a study of data collected in 2002 first reported on the number of individuals over the age of 12 who had illegally used prescription stimulants (13). Twenty-one million people overall admitted to illegal use at least once. Three million used only prescription stimulants. Seventy-five thousand between the ages of 12 and 25 admit to a level of use which meets DSM criteria for addiction and abuse. This number represents about 1 in 10 young persons who admitted to casual use.

This data analysis for the first time gives physicians and the general community a handle on the scope of prescription stimulant abuse. The information was from a 2002 survey. Undoubtedly, the number of seriously affected individuals four years later is higher. My own experience prescribing to college students over the last five years has been regularly problematic. I have been less concerned about over use by these individuals. Rather, their use appears sporadic and intermittent until exam time when binging is likely. Despite vigorous efforts on my part to have a regular connection with these patients (via telephone, email, in person appointments, etc.), such use does not treat ADHD effectively and potentially permits and/or exacerbates an ADHD lifestyle of procrastination with intense catch-up activity under high anxiety. I suspect, but cannot be certain, that some of my patients share or sell their medication. The widespread illegal use of these drugs has to be coming from some legitimate source.

Even in more responsible adult patients, tolerance—that need for increasing dosages in order to maintain effectiveness or length of action—appears to develop in about one-quarter of the patients I have treated for 5 years or longer. There is nothing in the medical literature as of September 2007 on this phenomenon in ADHD adult patients. Tolerance is rarely if ever seen in children (even younger teens). But tolerance was absolutely a problem for the women of the 1970s who took stimulant medication for weight control. The Santayana conclusion—those who do not study history are condemned to repeat it—comes to mind.

The answers to my concerns about legitimate prescription stimulant use for ADHD in adults as of this writing are not forthcoming. In part there is no monetary incentive on the short term to study any drug beyond the drug approval period of several months. The history of stimulant use in this

country screams out concern but has been overwhelmed by short-term studies and the anecdotal reports of success promoted by drug companies to physicians and patients alike.

We may be entering a period shortly when a backlash against stimulant drugs develops once news of abuse hits the front pages of the newspaper and are discussed in the halls of Congress. Even without this major specter of a fourth wave of stimulant abuse hovering, ethical concerns will continue about the balance between the use of stimulants and nondrug interventions for children who misbehave or under perform in our country. I'm afraid these worries will not go away; nor should they.

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Section VII: Consensus

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The American Academy of Pediatrics ADHD Practice Guidelines: A Critique

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In 1996 the Committee on Quality Improvement of the American Academy of Pediatrics (1) selected a subcommittee composed of pediatricians, four developmental and behavioral pediatricians, one neurodevelopmental disabilities pediatrician, and one pediatric neurologist. Joining the committee and participating as liaison representatives was one representative from each of the following organizations: the American Psychiatric Association, the Child Neurology Society, the American Academy of Family Physicians, and the Society for Pediatric Psychology. The aim of this subcommittee was to develop practice guidelines for general pediatricians to provide competent (1) diagnosis of attention deficit hyperactivity disorder (ADHD) of 6- to 12-year-olds, and (2) treatment and management of 6- to 12-year-old children who are diagnosed with ADHD (2–6).

The subcommittee collaborated with the Agency for Healthcare Research and Quality to develop the evidence-based literature on the topic of the diagnosis of ADHD. For the treatment guidelines segment the committee partnered with the Agency for Healthcare Research and the evidence-based practice center at McMaster University, Ontario, Canada, to develop the evidence-based literature in the areas of treatment and management of ADHD. A "Clinical Practice Guideline" was produced for

the diagnosis of ADHD, and a subsequent "Clinical Practice Guideline" was produced for the treatment of the school-aged child with ADHD (5).

The Committee on Quality Improvement of the AAP undertook this project due to ADHD being "the most common neurobehavioral disorder" of childhood. It is estimated that between 4% and 12% of school-aged children or as many as 3.8 million children, most of them boys, have ADHD. The AAP recognizes that ADHD is among the most prevalent chronic health conditions affecting school-aged children. The National Institute of Health's Consensus Statement (7) found ADHD to be a major public health problem in the United States. Also of concern were the increasing public interest in ADHD and the debate in magazines, newspapers, television, and the internet concerning the diagnostic and treatment strategies (8).

DIAGNOSIS

The diagnostic portion of the AAP practice plan begins by affirming the behavioral requirements for ADHD in its three forms [predominantly inattentive type (PIT), predominantly hyperactive-impulsive type (PHT), and combined type (CT)] as defined in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) (9). The practice guidelines clearly delineate the core IA symptoms along with the core HI symptoms from the DSM-IV. It maintains that ADHD is the most common neurobehavioral disorder of childhood. Additionally, since a wide variety of other psychological and developmental disorders (e.g., oppositional defiant disorder, conduct disorder, depression, Tourette's, anxiety disorder, and learning disorders) frequently coexist in children with ADHD, the importance of a thorough assessment is emphasized. The National Institutes of Health in their Consensus Statement (7) affirmed the core behaviors in DSM-IV to be optimum symptoms at that time.

Diagnostic Recommendation #1

"In a child 6 to 12 years old who exhibits inattention, hyperactivity, impulsivity, academic underachievement, or behavior problems, primary care clinicians should initiate an evaluation for ADHD (Strength of evidence: good; strength of recommendation: strong)."

Pediatricians are often the first medical professionals that parents bring their child to when they are concerned about the child's ability to attend and/or behave appropriately. As aforementioned, since ADHD is comorbid with a number of other disorders, it is pertinent that the primary care physician (PCP) evaluate the ADHD patient for associated mental health conditions. Unfortunately, there is a scarcity of both developmental/behavioral pediatricians and child psychiatrists. Therefore, screening parents of patients

during routine visits may assist in early recognition that a child may need to receive a thorough ADHD evaluation. Following the new practice guidelines, the PCP should be able to evaluate straightforward cases of ADHD.

Diagnostic Recommendation # 2

"The diagnosis of ADHD requires that a child meet DSM-IV criteria (strength of evidence: good; strength of recommendation: strong)."

The diagnosis must be based on the 18 DSM-IV symptoms that occur in two separate scales. This includes nine symptoms on the IA scale and nine symptoms on the HI scale. The physician needs to recognize the criteria for the three subtypes:

- ADHD-PIT (exhibiting at least 6/9 IA behaviors)
- ADHD-PHT (exhibiting at least 6/9 HI behaviors)
- ADHD-CT (exhibiting at least 6/9 HI behaviors AND at least 6/9 IA behaviors)

Symptoms must have been present before 7 years of age, have persisted for at least 6 months, and occur in two or more settings (i.e., home and school). Furthermore, these symptoms must be accompanied by a significant functional impairment in at least one of the following areas:

- Academic failure
- Occupational failure
- Social failure

Finally, the physician or psychologist must determine that these failures are not due to another mental health or neurological disorder.

The AAP subcommittee adapted four other recommendations for the diagnostic practice guidelines.

Diagnostic Recommendation # 3

"The assessment of ADHD requires evidence directly obtained from parents or caregivers regarding the core symptoms of ADHD in various settings, the age of onset, duration of symptoms, and degree of functional impairment (strength of evidence: good; strength of recommendation: strong)."

Diagnostic Recommendation # 4

"The assessment of ADHD requires evidence directly obtained from the classroom teacher (or other school professional) regarding the core symptoms of ADHD, the duration of symptoms, the degree of functional impairment, and coexisting conditions… (strength of evidence: good; strength of recommendation: strong)."

Diagnostic Recommendation # 5

"Evaluation of the child with ADHD should include assessment for coexisting conditions (strength of evidence: strong; strength of recommendation: strong)."

Diagnostic Recommendation # 6

"Other diagnostic tests are not routinely indicated to establish the diagnosis of ADHD (strength of evidence: strong; strength of recommendation: strong)."

The PCP who has the experience and the time to evaluate comorbidity should be able to manage generalized anxiety disorder, disruptive behavioral disorders, and dysthymia. The PCP with the help of the child's school district or a private child psychologist should be able to help determine if the child has a learning disability. However, more complex comorbidity such as possible bipolar disorder should be referred to a child psychiatrist.

A meta-analysis of published data on the reliability, sensitivity, and selectivity of behavioral questionnaire scales was performed by the National Initiative for Children's Healthcare Quality (NICHQ) group. The results demonstrated that broadband scales' sensitivity for ADHD was less than would be required to support a diagnosis. For example, broadband scales analyzed were the CBCL/4–18 Parent Form and the CBCL/TRF, Total Problem Scale (Achenbach, 1991), and the DSMD-Total Scale (Devereaux Scales of Mental Disorders; 10) all of which failed to yield a specific diagnosis for ADHD. These results are published in "Diagnosis of Attention Deficit/Hyperactivity Disorder" (3).

Results from the Green et al. (3) study, however, reached significantly different conclusions in their analysis of ADHD-specific short-band questionnaires. The Conners Parent Rating Scale—1997 Revised Version: Long Form, ADHD Index Scale (CPRS-R:L-ADHD Index) for 6- to 17-year-old males and females had an effect size of 3:1 and 95% confidence limits of 2.5, 3.7. The Conners Teacher Rating Scale—1997 Revised Version: Long Form, ADHD Index Scale (CTRS-R:L-ADHD Index) for 6- to 17-year-old males and females had an effect size of 3:3 and 95% confidence limits of 2.8, 3.8. Finally, Barkley's School Situations Questionnaire-Original Version, Number of Problem Setting Scale (SSQ-O-1) (Breen 1989) for 6- to 11-year-old females had an effect size of 1.3 and 95% confidence limits of 0.5, 2.2, and the SSQ-O-1, Mean Severity Scale had an effect size of 2.0 and 95% confidence limits of 1.0, 2.9. In conclusion, short-band questionnaires appear to more validly assess ADHD due to its sensitivity to ADHD symptomology.

The subcommittee dealt with comorbidity, but failed to address mimic disorders. If the practice guidelines contained a description of each mimic disorder, the focus of the guidelines would be diminished and the length could decrease the number of PCPs who take the time to read the guidelines.

However, these multiple disorders that could be mistaken for ADHD should be added to the toolkit. The PCP needs to be reminded of sickness and other conditions that often include the ADHD core symptoms (11,12).

TREATMENT

The first point the committee established was that since ADHD is a chronic condition, treatment must be managed like all other chronic medical conditions (e.g., diabetes, asthma, sickle cell). The subcommittee, partnered by the Agency for Healthcare Research and Quality and the Evidence-Based Practice Center at McMaster University (5), developed treatment recommendations for the school-aged ADHD child between the ages of 6 and 11 years. The recommendations also integrated important findings from the MTA study (13,14). The key recommendations include:

1. Primary care clinicians should establish a treatment program that recognizes ADHD as a chronic condition (strength of evidence: good; strength of recommendation: strong).
2. The treating clinician, parents, and the child, in collaboration with school personnel, should specify appropriate target outcomes to guide management (strength of evidence: good; strength of recommendation: strong).
3. The clinician should recommend stimulant medication (strength of evidence: good) and/or behavioral therapy (strength of evidence: fair), as appropriate to improve target outcomes in children with ADHD (strength of recommendation: strong).
   For children on stimulants, if one stimulant does not work at the highest feasible dose, the clinician should recommend another.
4. When the selected management for a child with ADHD has not met target outcomes, clinicians should evaluate the original diagnosis, use of all appropriate treatments, adherence to the treatment plan, and presence of coexisting conditions (strength of evidence: weak; strength of recommendation: strong).
5. The clinician should periodically provide a systematic follow-up for the child with ADHD. Monitoring should be directed to target outcomes and adverse effects by obtaining specific information from parents, teachers, and the child (strength of evidence: fair; strength of recommendation: strong).

William E. Pelham, Ph.D., a professor at SUNY-Buffalo and a consultant to the guidelines committee, reported that one of the most crucial functions of the guidelines is its emphasis on the chronic nature of ADHD and the necessity for the treatment plan to reflect this chronicity. In addition, Dr. Pelham notes another important strength of the guidelines including its focus on difficulties of daily life, rather than just the clinical

symptomatology of ADHD. Finally, its recognition of the vast research findings that medication and behavioral therapy are the two most empirically validated treatments is another important strength of the guidelines (15,16).

Another benefit of the guidelines is that it can provide additional opportunities for the fields of pediatrics and psychology to collaborate. Specifically, now that PCPs are being encouraged to utilize behavioral treatment in conjunction with medication in the treatment of ADHD, psychologists play a crucial role. Some psychologists receive specialized training regarding assessing/evaluating ADHD, providing school consultations with teachers of ADHD students, and providing useful behavioral interventions for children with ADHD (individual therapy, parent training, social skills groups) (6,17).

On the other hand, the guidelines also have weaknesses. Some believe that the guidelines are both vague and unrealistic. Specifically, they argue that the guidelines fail to provide specific information to help clinicians determine the appropriate treatment approach for specific, individual patients. Additionally, the guidelines seem to be less helpful in treating children with comorbid mental health conditions.

The treatment guidelines will hopefully add Atomoxetine as an ADHD drug in the near future. Atomoxetine was not yet available at the time of publication. Eli Lilly carried out a 5-year placebo versus Atomoxetine investigation that clearly demonstrated that ADHD patients on Atomoxetine are significantly more attentive and less hyperactive. Safety issues were closely investigated and there were no significant negative cardiovascular side effects. A further study demonstrated Atomoxetine to be as effective as short-acting methylphenidate when both are compared to a placebo (18,19).

THE AAP ADHD TOOLKIT

The "Caring for Children with ADHD: a Resource Toolkit for Clinicians" was codeveloped by the AAP and the NICHQ and published in 2002 (20). The goal of this toolkit was to simplify and organize the process by putting all of the most effective tools for diagnosing and treating ADHD in one place. It mirrors the AAP guidelines and is designed to streamline the practice guidelines for pediatricians.

This toolkit includes:

- An introduction
- Diagnostic materials
  - Introduction explaining the diagnostic process
  - NICHQ ADHD primary care evaluation form
  - Scoring instructions for the NICHQ Assessment Scales

- NICHQ Vanderbilt Assessment Scale-PARENT Information
- Cover letter for teachers
- NICHQ Vanderbilt Assessment Scale-TEACHER information

A drawback to the toolkit is that the NICHQ Vanderbilt Assessment Scale-PARENT and TEACHER Information was not a part of the meta-analysis that Green et al. (3) conducted for the AAP Subcommittee on ADHD. Additionally, scoring fails to consider different norms for gender or age changes deeming the results for middle school-aged children less specific than scales that include gender and age norms. This is particularly problematic because at the National Institute of Health Consensus Conference, the panel of scientists agreed that current measures of ADHD are flawed because they do not take into account the ADHD child's age. For example, the norms for CPRS-R and the CTRS-R both reflect the decline of hyperactivity symptoms over the age span. This leads to the concern that boys over the age of nine years may be misclassified as ADHD-IA (PIT) (7). Therefore, the consensus concludes that clinicians and investigators must take into account age in tools that are developed for ADHD diagnosis, and the toolkit currently ignores this factor. With the exception of this tool, the NICHQ toolkit is generally based on evidence-based research and at this time can be considered a solid working device for the PCP who adheres to the practice guidelines.

Several regions of the country have begun to establish networks making the diagnosis and treatment of ADHD more feasible for the PCP (21,22). Leslie et al. (23) published results of a two and half year attempt to implement the AAP diagnostic guidelines. Money from a national grant paid for an ADHD Coordinator, who received, scored, and summarized packets of questionnaires sent by seven pediatric practices. Seven "research naïve" primary care offices in the San Diego area were recruited to participate. The pediatricians and their office staff were trained in the San Diego Attention-Deficit/Hyperactivity Disorder Project (SANDAP) protocol that was based upon the AAP practice guidelines and utilized the NICHQ Toolkit. More than 40% of the subjects demonstrated discrepant results on the Vanderbilt scales, with only the parent or teacher endorsing sufficient symptoms to meet DSM-IV criteria for ADHD. Significant barriers plague the primary care providers. One such barrier is that providers do not have the mechanisms for implementing the ADHD diagnostic guidelines. Also, without the study, ADHD coordinators, physicians' offices, and in some cases care providers would have to take the time to score questionnaires and summarize this data. At this time private primary care providers cannot take the amount of time that is required to diagnose and manage ADHD utilizing the AAP practice guidelines.

If primary care providers are to treat ADHD and ADHD associated mental health conditions, third-party payers will have to pay for the time

that it takes to do a competent job. Currently, there is no incentive for the loss of revenue that implementation of the AAP diagnostic and treatment plans will bring about. This requires significantly more time that the 10-minute office visit PCPs are reimbursed for by third-party payers.

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Educational Policy

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Children with attention deficit hyperactivity disorder (ADHD) experience significant academic and/or social difficulties in school settings (1). Approximately 90% of students with this disorder underachieve academically and about 30% have specific learning disabilities (2). Given these pervasive and chronic difficulties, school services (e.g., special education) may be necessary to enhance the academic and social functioning of students with ADHD. Over the past decade, the nature of school services available to children with this disorder has been shaped by educational policy related to education for students with disabilities. Educational policy starts with legislation but also includes what is largely neglected in the limited relevant literature (3), published interpretations by the administering agency.

Whether the clinician refers to ADHD as a "disability," the child's legal entitlement to accommodations or services in elementary or secondary school will depend on whether the child meets the criteria for "disability" under either the Individuals with Disabilities Education Act (IDEA) or Section 504 of the Rehabilitation Act (§ 504). The third pertinent federal law, the Americans with Disabilities Act (ADA), has the same definition as does § 504; its only additional relevance here is that it applies to private schools that do not receive federal financial assistance.

In this chapter, we will provide (1) an overview of the disability definitions and related information for the IDEA and § 504, (2) a chronological, stage-by-stage summary of the relevant policy interpretations under each of these overlapping statutory frameworks, and (3) a brief discussion of the clinical implications of educational policy related to identification and diagnosis.

IDEA AND § 504

The IDEA legislation dates back to 1975. It was basically a funding act, providing federal funds to school districts along with a set of detailed state and local requirements. Congress has amended the Act several times. The Office of Special Education Programs (OSEP) is the agency, which is part of the federal Department of Education that administers the Act, including the issuance of policy interpretations (4). In contrast, § 504 is a civil rights act—in parallel to Title VI for race and national origin and Title IX for gender—that succinctly prohibits organizations receiving federal financial assistance from discrimination based on disability. It is older than the IDEA, dating back to 1973, but its regulations were not issued until 1978. § 504 has remained largely unchanged, except for amendments in 1990, upon passage of its sister statute, the ADA, which changed the term "handicap" to "disability" and made revisions in terms of substance abuse. The agency charged with administering § 504 and the ADA in relation to schools, including the issuance of policy interpretations, is the Office for Civil Rights (OCR), which is another part of the federal Department of Education (5).

The IDEA regulations (6) define "child with a disability" in terms of two essential elements: (i) meeting the criteria of one or more of 13 specified categories, such as "other health impairment" (OHI) or "specific learning disability" (SLD); and (ii) needing, "by reason thereof," special education. Available in the form of a practical checklist (7), the IDEA criteria for OHI are (i) a chronic or acute health condition that results in (ii) limited strength, vitality, or alertness, having (iii) an adverse effect on the child's educational performance that (iv) necessitates special education (with or without related services).

In contrast, the amended § 504 legislation (8) defines "individual with a disability" in terms of three essential elements: (i) a physical or mental impairment, (ii) that substantially limits, (iii) a major life activity. The courts have clarified the meaning and measurement of these elements. For example, they have held that the measurement of "substantially limits" is with reference to other students in the general population and with, not without, the mitigating effects of medication (9). In relation to students with ADHD, the major developments in terms of the application of the IDEA's and § 504's statutory eligibility definitions have largely been, first, the regulations, and second, interpreting the ambiguities and filling in the gaps, OSEPs and OCRs policy interpretations of these respective laws. Courts generally defer to regulations and, to a lesser extent, to the policy interpretations that supplement them (10). In contrast, very few published court decisions have focused on the eligibility of ADHD students under the IDEA (11) or under § 504 (12,13). Moreover, the guidance that they provide, particularly those under the IDEA, has been limited, except that these decisions continue to reinforce the case-by-case "it depends" answer rather than the automatic

"yes" or "no" answer (14,15). These policy interpretations may be grouped into succeeding stages under the IDEA and § 504, respectively.

IDEA: STAGES OF POLICY INTERPRETATIONS

The policy interpretations under the IDEA are relatively frequent. They fit into four succeeding stages of policy evolution.

Stage 1

The first major policy change relating to students with ADHD was the Joint Policy Memorandum (16), jointly issued by the OSEP, the OCR, and the Office of Elementary and Secondary Education. This Memorandum, issued in the wake of a notice of inquiry soliciting public comment on the education of children with ADHD mandated by the 1990 Amendments of the IDEA, concluded that no change was necessary in the IDEA definition of disability. The explanation was that children with ADHD could qualify as OHI or under the other specified categories, such as SLD or emotional disturbance (ED), under the IDEA where they needed special education and related services. This policy interpretation further explained that when such children did not meet the IDEA requirements, they "may fit" (p. 118) under the broader definition of disability under § 504 depending on the severity of their condition. This alternative is discussed in the subsequent part of this chapter.

Stage 2

The second stage was an assortment of policy interpretations in the early and later 1990s, including another joint endeavor (17) that reiterated and supplemented the Joint Memorandum. One line of the policy letters during this period clarified when the IDEA eligibility evaluation must be conducted for a child who has or may have ADHD. Specifically, the OSEP has repeated that district's have an affirmative "child find" obligation to evaluate, without undue delay, all children who have or are suspected of having a disability under the IDEA (18). Parents may request such an evaluation at any time, but the district's obligation is only triggered if—based on the parents' request and/or other information—the district has reason to suspect that the child is eligible under the two-part test of eligibility under the IDEA (19,20).

Another line of the policy letters during this period addressed the roles of educators, including school psychologists, and physicians in the diagnosis of ADHD. First, the OSEP clarified and reiterated that a district may not refuse to evaluate a child for possible IDEA eligibility for the reason that the child has a medical diagnosis of ADHD (19,21). Second and more importantly, a physician is not necessary under the IDEA for the diagnosis of ADHD (17,21). Rather, when a district conducts an evaluation of OHI as a

result of ADHD, the multidisciplinary team must include "an individual who is knowledgeable about the possible adverse effects of ADD on a child's educational performance" (21, p. 964). Third, if state law or the local policy/practice opts to require a physician for this purpose, which is within their discretion (17,22), a physician's diagnosis of ADHD is not sufficient to establish IDEA eligibility (22); rather, the district must ensure that this diagnosis is at no cost to the parents (17,21) and that "any necessary evaluation by other professionals are also conducted and considered as part of the eligibility determination process" (21, p. 965).

Stage 3

The third stage was the express recognition in the 1999 IDEA regulations, in the wake of the 1997 IDEA Amendments, that ADHD was one of the chronic or acute health conditions in the definition of OHI and that the "limited alertness" in the same definition may be met by the "heightened alertness to environmental stimuli" attributable to ADHD. On one hand, this recognition effectively added more legal force to the possible eligibility of ADHD students under the IDEA, taking the form of a regulation rather than just policy interpretations. On the other hand, all that this recognition did was fulfill two of the essential elements of OHI. The IDEA evaluation process, including the impartial second and binding opinion of a hearing and/or review officer and, if appealed, one or more levels of the judiciary, must conclude not only that the child has ADHD but also that the child's ADHD meets the remaining criteria of adverse effect on educational performance and the need for special education.

Stage 4

In a final, postregulations stage, the OSEP has issued two further policy interpretations in response to the continuing inquiries of interested individuals and organizations in ADHD issues under the IDEA. Both revisit the issue of the respective roles of physicians and educators. In the first letter, the OSEP confirmed its long-standing position that the IDEA does not require a medical diagnosis of ADHD for purposes of OHI eligibility, allowing the district instead "to use qualified personnel other than a licensed physician to conduct the [eligibility determination] as long as all of the protections in evaluation procedures under IDEA are met" (23, p. 151). More interestingly, the second policy letter responds to the increasing concern about educators pressing parents to secure medication for their children with ADHD. Specifically, the OSEP endorsed the position of Rhode Island's department of education that districts may not condition educational services upon the parents' consent to medicate the child (24). Second and perhaps less obvious, the OSEP announced what it characterized as part of "its long-standing policy" that "[a]t parents' request and with their consent, educators may provide input

about a student's behavior that may aid medical professional in making a diagnosis, but it not the role of educators to attempt to medically diagnose or recommend medical treatment for students with ADD or ADHD" (23, p. 794). The two distinctions that are noteworthy in this policy statement are (i) the qualifier of a "medical" diagnosis and treatment, as compared to the IDEA, or a primarily educational, determination of eligibility or services; and (ii) the more subtle and arguably new qualifier of educators only providing such information "at the parents' request and with their consent" (23, p. 794).

SECTION 504 (AND THE ADA): STAGES OF POLICY INTERPRETATION

Although some districts use § 504 as, in effect, a consolation prize for students, including those with ADHD, who do not attain or whose parents oppose eligibility under the IDEA, the corresponding policy statements have been less frequent from the OCR. They appear to fit into two successive stages.

Stage 1

First, the Joint Memorandum (16) pointed out that "the protections of Section 504 extend to some children who do not fall within the disability categories specified in [the IDEA]" (p. 117) and, more specifically, reciting the three-part definition of disability under § 504, concluded that "depending on the severity of their condition, children with ADD *may* fit within that definition" (p. 118). Additionally, the memorandum traced the related § 504 requirements, including the obligation to evaluate the child "if parents believe that their child is handicapped by ADD" (p. 118); the parent's right to contest an adverse decision via a due process hearing; and the child's right, in the wake of a favorable eligibility determination, to appropriate education in the least restrictive environment. Finally, the memorandum stated that state and local education agencies "should" take necessary steps "to train regular education teachers and other personnel to develop their awareness about ADD and its manifestations and the adaptations that can be implemented in regular education program to address the instruction needs of these children" (p. 118). The specified examples of such adaptations included the use of behavior management techniques, modified test delivery, and tailored homework assignments. On the other hand, the memorandum also specified examples of more restrictive steps or strategies, including reduced class size, one-on-one tutorials, and classroom aides.

Stage 2

In the absence of any change in the regulations, the remaining stage has been the entire period after the Joint Memorandum, marked by three policy interpretations and a limited assortment of other pertinent legal developments. In the first policy interpretation, the OCR first qualified its statement in the

Joint Memorandum about triggering a district's duty to evaluate in terms of § 504 eligibility. More specifically, in tandem with the IDEA, the OCR clarified that the standard that triggers an evaluation for § 504 eligibility is "reason to believe," not parental suspicion or demand (25). The difference from the IDEA, however, is that this reasonable suspicion standard applies to a wider definition of "disability" and "appropriate education." This same policy interpretation also includes reiterations or clarifications that (i) children with ADHD are not automatically protected under § 504; (ii) districts may not refuse to evaluate a child with ADHD solely because the child did meet the eligibility criteria under the IDEA; (iii) districts may use the same or a different process from that of the IDEA for § 504 evaluation; and (iv) districts may use the same or different procedures from those under the IDEA for impartial due process hearings (25).

Soon thereafter, in a second policy interpretation, the OCR repeated even more emphatically that under § 504, for students with ADHD or other physical or mental impairments "there is no absolute right to an evaluation on demand" (26, p. 1128). Rather, based on the same "suspected disability" standard, applied to a broader criteria of physical or mental impairment that substantially limits a major life activity and needs special or regular education, the district is obligated to either evaluate the child or, if it refuses on the basis of no purportedly reasonable basis to do so, provide notice to the parents of their right to an impartial due process hearing to challenge that refusal (26). Second, in the same policy letter the OCR confirmed that the IDEA-eligible children are typically double-covered, which is also entitled to protection under § 504. Finally, pointing out that "appropriate education" under the § 504 regulations, is defined more broadly than it is under the IDEA as consisting of "special or regular education and related services," the OCR included these additional examples of students with ADHD covered by this entitlement:

- a student with ADHD who meets the three-part definition of disability under § 504 and who needs "what the district considers to be adjustments in the regular classroom (e.g., providing a structured learning environment, simplifying instruction about in-class and homework assignments, using behavioral management techniques, modifying test delivery, using audio-visual equipment)"
- a student with ADHD who meets the three-part definition of disability under § 504 and who needs "regular administration of medication to attend regular class" (26, p. 1128).

However, the double-covered case and the two additional examples require some cautionary warnings in light of more recent relevant legal developments. First, in relation to the double-covered child with ADHD, the OCR more recently issued the more general clarification that it is the district's decision whether to provide special education under the IDEA

individualized educational program and that if the district elects to do so and the parent insists instead on a § 504 plan, "the parent would essentially be rejecting" what they were entitled to under § 504 (27, p. 296). Second, although the entitlement of "appropriate education" is undeniably broader, because it attaches related services to regular education as an alternative to special education, the courts in more recent years have applied the definition of eligibility, particularly the criterion of substantial limitation, rather restrictively (9,12) and, in any event, § 504 is an "unfunded mandate," that is, it is triggered by the receipt of federal financial assistance but provides no funding itself. Third, it may be, based on recent case law, that some students with ADHD who require regular administration of medication and who have the requisite parental consent and medical prescription may not meet the definition of disability under § 504 in the first place (9).

Finally, in the second joint policy interpretation (15), the OCR reiterated that whether a child's ADHD is an impairment that substantially limits a major life activity must be determined on an individual basis. With regard to the overlapping definitions of disability, the OCR commented: "While it is possible that a child with ADD might be covered by Section 504, but might not be eligible for services under [the IDEA], the reverse—that the child is eligible for services under [the IDEA], but not covered by Section 504—is difficult to imagine" (p. 76). Based on the recent Supreme Court decisions about mitigating measures, such as medication (9), the reverse today is more possible to imagine—specifically, in the case where 1) the parents agree to medication for their child with ADHD, 2) the district obtains baseline data showing that with the medication the ADHD does not substantially limit learning, 3) the parents then decide to discontinue the medication, and 4) the ADHD, without the mitigating effects of the medication, so adversely affects the child's educational performance as to necessitate special education. On the other hand, for a child not covered by the IDEA, the determination must be careful and individualized, not absolute or stereotyped, particularly in light of the courts' imprecision in further defining and specifically applying the three elements of the definition of disability under § 504 (13).

The Williams letter (17) also clarified with respect to children suspected of having ADHD the OCRs more general position (28) that, "like the IDEA" (p. 77), § 504 does not require a school district to conduct a medical diagnosis, but that if the district determines that one is necessary in addition to or instead of alternative assessment methods, the district must ensure that it is at no cost to the parents.

CLINICAL IMPLICATIONS

The express requirements and policy interpretations of the IDEA and § 504 directly influence the process of identifying students with ADHD who may

require special education services and/or general education accommodations. Zirkel (7) has designed a checklist for determining the legal eligibility for special education services in accordance with the regulations enumerated above. Using this checklist as a guide, several steps should be followed in determining whether a specific child will require special education services for ADHD (for more detailed procedures, see Ref. 1).

The first step in the eligibility process is to conduct the IDEA evaluation of ADHD and related difficulties (1). Does the child meet the criteria for one of the IDEA classification categories and, as a result thereof, need special education services? The multidisciplinary team needs to pay special but not exclusive attention to the OHI category. Specifically, if the child is found to meet the criteria for ADHD, then, by definition, the child has a chronic condition that significantly limits alertness, thus satisfying two components of the "other health impaired" eligibility criteria. Two OHI criteria remain.

Next, does the child's ADHD-related behavior in the classroom significantly limit his or her educational performance? The team can determine a child's educational functioning by using academic performance data, such as norm-referenced achievement tests or, more preferably, curriculum-based measurement (29).

Finally, does the child need special education services because of his or her ADHD? This ambiguous criterion could be interpreted in a variety of ways. One way to reach a relatively objective decision regarding this criterion is through evaluating the efficacy of regular classroom interventions (30). Baseline data should be collected on a number of target behaviors prior to implementing a specific intervention (including medication). After implementing the recommended treatment(s), the clinician collects data on the same variables to assess behavioral change. If significant improvement in child functioning does not occur, the clinician can follow one of three possible courses of action. First, changes could be made to the intervention program in the general education classroom. Alternatively, the child could receive some form of special education programming. A third alternative would be to make changes in general education interventions and provide special education programming. The efficacy of both general and special education interventions should be evaluated on a continuous basis to determine when changes in programming and/or placement are necessary.

A similar data-based decision-making process should be followed to identify those students who may require accommodation in general education instruction under § 504. A clinician must first determine whether the child is suffering from "a physical or mental impairment which substantially limits one or more∗major life activities" (5) including learning. Thus, a multimethod assessment procedure (2,31) can be used to determine whether a child has ADHD (i.e., a mental impairment) and whether the symptoms of this disorder lead to substantial impairment in educational performance.

In particular, this assessment must include reliable and valid measures of academic functioning and should establish a connection between ADHD symptoms and decrements in educational performance. It is important to note that the framework is used for determining whether ADHD symptoms substantially limit learning in the "average" student in the general population, and, for those children who are medicated, the determination is made with medication, not without it (9).

CONCLUSION

Federal legal policymaking concerning eligibility of ADHD in elementary and secondary education has proceeded on two fronts during the same period—the IDEA and § 504. The primary action has been on the IDEA front, and it has proceeded through several stages marked by refinements rather than reversals in policy. The end results include (1) the recognition, on the elevated level of regulations, that ADHD may qualify under the OHI category; (2) the continuing recognition, in various policy letters, that ADHD may also qualify for other categories, such as SLD, but that the determination will be on an individual basis in terms of the remaining criteria, including the need for special education; (3) the refined recognition, in the second stage of policy letters, that the district's evaluation duty is triggered when it has reason to suspect that a child's ADHD is of sufficient severity to qualify under one of the IDEA categories, and (4) the recent recognition, in the final stage of policy letters, that the IDEA does not require a physician's diagnosis for determination of OHI eligibility and that educators may give their input but may not interfere with the parents' and physicians' roles regarding the medical diagnosis of ADHD for purposes of medication and other such treatment.

The activity under § 504 and, since 1990, its sister statute the ADA, has been less frequent but largely parallel within the context of a broader definition of "disability" and "appropriate education." At the first stage, the Joint Memorandum (16) formalized the recognition that a child with ADHD may meet the three-part definition of disability. During the more recent stage, the OCR clarified that (1) the same "reason to suspect," rather than parental demand per se, is the triggering standard for an eligibility evaluation, (2) the interpretation regarding medical diagnoses also parallels that under the IDEA, and (3) § 504 provides a parallel, albeit more streamlined, notice requirement for procedural safeguards, centering on the parents' right to proceed to a due process hearing.

Finally, clinicians must follow a data-based decision-making model in determining the eligibility of individual students with ADHD for special education services or accommodations to instruction in general education classrooms. Practitioners should use psychometrically sound assessment measures that include multiple sources and methods to evaluate whether guidelines under the IDEA and/or § 504 are met.

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Section VIII: New Directions

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Sluggish Cognitive Tempo: The Promise and Problems of Measuring Syndromes in the Attention Spectrum

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Sluggish cognitive tempo (SCT) is a term used to describe a syndrome of excessive daydreaming, sluggishness, drowsiness, and forgetfulness, hypothesized to accompany some cases of the inattentive type of attention deficit hyperactivity disorder (ADHD). The term SCT was introduced by Lahey et al. (1). Items describing "daydreams" and "seems sluggish or drowsy" were included in rating scales, e.g., Revised Behavior Problem Checklist (2) and Child Behavior Checklist (3), which were widely used in research in the 1980s. These symptoms were observed to be elevated in children with DSM-III attention deficit disorder without hyperactivity (ADD-WO) (4–6). These symptoms were present in data sets because of their inclusion in behavior rating scales used by these researchers. In those years, no concerted efforts were made toward gathering a more complete set of descriptors, or in more fully delineating SCT beyond those two items. The shift away from recognition of an inattentive type of ADHD in DSM-III-R hindered progress in studying the construct. A renaissance of interest in SCT began around the time of DSM-IVs introduction and has slowly continued, although progress continues to be limited by the lack of a psychometrically sound and generally accepted measure of SCT.

Daydreaming

Research in the 1960s from Jerome Singer's group (7,8) demonstrated that individual differences in daydreaming could be experimentally

manipulated, and furthermore that high frequency daydreamers exhibit marginally poorer vigilance in signal detection that sharply deteriorates over time, compared to low frequency daydreamers. This attention decrement was associated with an increase in self-reported daydreaming. Although individuals who frequently daydream are impaired from the viewpoint of sustained attention, it is not known whether children who appear to be daydreaming are actively engaged in processing off-task information (in which case, daydreaming may be associated with divergent rather than convergent thinking, with potential benefits in creativity and problem solving) or with episodic lapses in awareness (e.g., microsleep).

HYPOACTIVITY

Research in the 1970s from Roscoe Dykman's laboratory demonstrated that individual differences in activity level extended from hyperactivity to normoactivity to hypoactivity. Dykman et al. (1970) (24), divided children with learning disabilities (ages 8–11) on the basis of parent and teacher reports into hyperactive, normoactive, and hypoactive groups and tested them along with controls on a variety of conditioning and reaction time tasks. Although all clinical groups tended to perform worse than controls, the hypoactive group consistently displayed longer response latencies across experimental paradigms. Participant matching using chronological and mental ages did not eliminate these disparities. Follow-up data when the children were in their midteens suggests that hypoactivity is a stable characteristic. Behavioral ratings at follow-up found the percentage of participants who were "extremely slow moving" was 0% for the hyperactive and control groups, 20% for the normoactive group, and 65% for the hypoactive group. Some findings suggested that deviation from normal activity levels in either direction is pathognomonic. Neurological abnormalities and soft signs were observed in all three clinical groups at baseline but only in the hyperactive and hypoactive groups at follow-up. Social adjustment at follow-up differed little between normoactives and controls. Hyperactives had more conflicts with family and authorities, whereas hypoactives had more difficulties with self-esteem, social withdrawal, and internalizing symptoms.

PRIMARY DISORDER OF VIGILANCE

Weinberg and Brumback (9) reported six cases that exhibited what they called a primary disorder of vigilance (PVD), and they offered diagnostic criteria for classifying cases with PVD. These criteria included difficulty sustaining alertness and arousal, daydreaming, difficulty focusing attention, losing one's place in activities and conversation, slow/delayed/incomplete

tasks, susceptibility to boredom, fidgeting and other behaviors to improve alertness, and a "caring, compassionate, affectionate, kind temperament" (9, p. 721). The most detailed case report is what we consider to be the prototypical representation of SCT: teacher reports were "slow moving, a dawdler, a procrastinator, not competitive, immature, a daydreamer with poor attention, easily distracted, lazy and wanting to avoid work, kind, affectionate, compassionate, sensitive, a very good child who was never a behavior problem" (p. 721). The authors acknowledged an overlap of PVD and ADHD but argued in favor of considering PVD to be distinct in its unique cognitive impairments. Of considerable interest are their observations that (1) half of the reported cases were accompanied by clinical depression; (2) PVD impairment increases over the course of the life span; and (3) methylphenidate resulted in "excellent response" in all six cases. Among the diagnostic criteria for PVD was a requirement that the PVD symptom complex precede the onset of other disorders (including depression, narcolepsy, medication use, alcohol/drug abuse, hypothyroidism), which can cause secondary hypovigilance.

SCT IN DSM-III

DSM has always structured ADHD categories such that there were no cognitive symptoms that were unique to an inattentive type of attention disorder. Thus, DSM-III distinguished types solely on the basis of whether hyperactivity was present. Studies using DSM-III categories reported that the cognitive deficits in ADD-WO sometimes differed from those in ADD with hyperactivity (ADD-H). The chief difference was that some children with ADD-WO exhibited slow retrieval and information processing, low levels of alertness, and mild problems with memory/orientation (4–6). Clinically, there were reports of peers' calling these children "space cadets," a pejorative term that reflects their being briefly but frequently nonresponsive ("spacing out") during periods of daydreaming or wandering attention. In a review of studies of DSM-III defined cases (i.e., ADHD with and without hyperactivity), Barkley et al. (10) reported that both types share deficits on tests of frontal lobe functions, but that additional problems in perceptual-motor speed and processing may be specific to the ADD-WO group. In their review, Goodyear and Hynd (11) suggest that several neurocognitive deficits, including dysfunction of automatized information processing and slow cognitive speed, may be specific to ADD-WO.

Interestingly, the pattern of comorbidities seen with hyperactive and hypoactive learning disabled (LD) children (see above) was also observed in DSM-III. ADD-H was associated with oppositional and conduct problems, and ADD-WO was associated with social withdrawal and internalizing symptoms (12,13).

SCT IN DSM-IV

DSM-III-R did not distinguish types at all, thus curtailing research into that aspect of ADHD. When DSM-IV was being developed, two SCT items ("often daydreams" and "is often sluggish or drowsy") were included in the Field Trials for Attention and Disruptive Behavior Disorders. As symptoms, SCT items were found to have excellent positive predictive power (PPP) for the Inattention group of symptoms, meaning that their presence was highly associated with the presence of the remaining symptoms of Inattention. However, they demonstrated poor negative predictive power (NPP), meaning that when an SCT symptom was not endorsed, it did not provide much information about whether inattention symptoms were generally absent. This lowered the overall utility of the SCT items as symptoms of Inattention. In other analyses, the SCT items were found to be mainly associated with ADHD-I and not with the other types. The DSM-IV child work group chose not to include the tested items ("often daydreams" and "is often sluggish or drowsy") as DSM-IV Inattention symptoms, largely because of the group's intention to adhere to a set of cognitive symptoms that were common to both ADHD-I and ADHD-C (B.B. Lahey, personal communication).

Nevertheless, evidence has accrued suggesting that the two major DSM-IV types do not share the same neurocognitive dysfunction. At least three studies have found higher rates of SCT symptoms in ADHD-I (14–16). Klorman et al. (17) found executive function deficits only for the ADHD-C group. Houghton et al. (18) found greater deficits in perseveration and response inhibition among the ADHD-C group. Bauermeister et al. (14) found deficits for ADHD-I on a factor measuring vigilance and persistence of effort. Studies by Weiler et al. (19) and Lockwood et al. (20) report slow information processing speed, possibly reflective of low arousal, in children with ADHD-I.

EXTERNAL VALIDITY

The presence of SCT appears to indicate difficulties beyond those that can be accounted for by ADHD. Carlson et al. (21) found that among children with ADHD-I, those with more severe SCT symptoms exhibited more unhappiness, anxiety/depression, withdrawn behavior, and social dysfunction. Mikami et al. (22) conducted an analog Internet chat room experiment with children with ADHD and normal controls. Even after controlling for DSM-IV diagnostic group, computer skill, IQ, and reading achievement, SCT symptoms predicted fewer total verbal responses; less perception of subtle social cues; less memory for the conversation, and a smaller proportion of hostile responses.

MEASUREMENT DIFFICULTIES

Progress in studying SCT is hampered by the absence of a good way to measure it. The measures of SCT that have been employed nearly equals the number of studies in this area: McBurnett et al. (16) used three items from the DSM-IV Field Trials symptom pool; Huang-Pollock et al. (25) used two of these but a different third item; Todd et al. (26) used two items similar to those used by McBurnett et al. in 2001; Bauermeister et al. used five items from the Teacher Rating Form and four from the Child Behavior Checklist; and Hartman et al. (15) used five items, including two used by McBurnett et al. (16). The lack of a consistent approach introduces ambiguity when comparing studies, and it is likely to be daunting to new investigators looking to expand this literature. Moreover, the paucity of SCT items hinders the investigation of latent structure (28). A final concern is that the symptoms of SCT are nonspecific and are likely to be secondary to other problems, particularly mood and anxiety problems.

FUTURE DIRECTIONS

Efforts are currently underway to assemble a large pool of items that may indicate an internally consistent latent construct resembling SCT. McBurnett and Pfiffner (27) developed a semistructured interview, the Kiddie-SCT (K-SCT) interview, which uses a format similar to that of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) (23). The instrument uses a stem-contingent format, in which clinicians first decide whether the item is present or absent for a given case. If present, follow-up questions are then asked which assess the duration and variability of the item, and its relationship to any anxiety or mood problems. The clinician then uses this information to decide whether the item is primary (relatively stable and characteristic of the individual) or secondary (highly variable and tending to resolve when emotional disturbance, anxiety, fatigue, etc. are not prominent). The hope is that primary symptom candidates can be reliably identified, and that latent structural analyses can be used to demarcate the relationship of SCT items to those of Inattention in ADHD.

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ADHD Pharmacogenomics: Past, Present, and Future

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INTRODUCTION

Clinicians who choose to prescribe a particular medication based on a family history of positive results are practicing a simple form of pharmacogenetics. Pharmacogenetics is the study of genetic variability in medication response (1). Pharmacogenetics had its formal beginnings in the 1950s when clinicians noted increased patterns of adverse reactions within certain families or ethnic groups. One example pertinent to psychiatry was the discovery that some patients receiving electroconvulsive therapy developed prolonged muscular paralysis after administration of succinylcholine due to a mutation within the gene coding for the enzyme succinylcholine esterase (2). Other early pharmacogenetic findings included attribution of peripheral neuropathy to slow acetylation of isoniazid in patients with tuberculosis, and hemolysis to glucose-6-phosphate deficiency in African-American males treated for malaria (1). The molecular genetic causes for these inherited differences were subsequently elucidated in the 1980s (3).

In contrast to pharmacogenetics, pharmacogenomics refers more specifically to the study of variations in genes and gene products and their relationship to medication response (4). Studies in pharmacogenomics have become much more practical with technological advances in gene

sequencing and complete mapping of the human genome. Obvious foci of pharmacogenomic investigations include drug metabolic pathways and drug targets, such as transporters and receptors (5). Although there remain many challenges, several established pharmacogenetic findings are likely to significantly impact mental health treatment.

At present, the most widely appreciated pharmacogenetic finding is that polymorphisms at the gene for hepatic cytochrome P450 2D6 (CYP2D6) isozymes lead to slow metabolism of many psychotropic medications in 5% to 10% of Caucasians and 0% to 19% of African-Americans (6) (see later discussion of atomoxetine). Polymorphisms are defined as variations in a single allele that occur in more than 1% of the population (7). Other recent association studies have demonstrated relationships between polymorphisms in the serotonin transporter (SERT) and response to antidepressant therapy (8), as well as associations between polymorphisms at several dopamine and serotonin receptors and increased likelihood for positive response or risk of side effects in clozapine treatment of schizophrenia (9).

Linkage studies, utilizing haplotype mapping, are also being conducted in attention-deficit/hyperactivity disorder (ADHD), and have potential relevance to pharmacogenomic study (10). A haplotype is a combination of alleles that are found together on the same chromosome. With increased identification of single-nucleotide polymorphisms (SNPs), tagging of common haplotypes can economically identify regions of interest which more fully represent common genetic variation in association with drug response (51). Consequently, pharmacogenomic studies might examine relationships between drug response and candidate polymorphisms and haplotypes.

ADHD has an estimated heritability in the range of 80% and is theorized to arise from the interaction of multiple genes and environmental factors (11). Molecular genetic findings for ADHD are among the most highly replicated of any psychiatric disorder (12). However, the majority of studies have utilized broad phenotype definitions of ADHD (52). Therefore, given the heterogeneity of ADHD samples as currently defined by DSM criteria, it is not surprising that only a small percentage of the variance in ADHD is accounted for by specific genes (13). Candidate gene investigations in ADHD have largely been guided by the recognition that stimulant medications have their putative targets of activity on catecholaminergic and serotonergic pathways (12,14). Candidate genes associated with increased risk for ADHD include the dopamine transporter (DAT1), the dopamine receptors (DRD2, DRD4, and DRD5), the serotonin receptor (5HT1B), dopa-β-hydroxylase (DBH), synaptosomal-associated protein (SNAP-25), catechol-*O*-methyltransferase (COMT), and others.

While knowledge about the presumed mechanisms of activity of ADHD medications initially informed searches for polymorphisms related to increased risk for the disorder, it is also reasonable to assume that these same polymorphisms might predict medication outcomes. Although stimulant medications have a large effect on ADHD symptoms in short- and

intermediate-term studies (e.g. the MTA study done in 1999), long-term prognosis has not been demonstrated to change significantly. Moreover, the high prevalence of ADHD, its significant heritability, variability in drug response, and the need to individually titrate doses, creates a compelling case for pharmacogenomic investigations of treatment response. In addition, the cost of failed treatment trials is significant as many families choose not to pursue pharmacotherapy for ADHD if the child does not respond to the first medication trial or displays significant side effects. The promise of ADHD pharmacogenomics is far reaching, and includes the potential to develop individualized medication regimens that improve symptom response, decrease risk of side effects, improve long-term tolerability, and thus contribute to long-term treatment compliance and improved effectiveness and general functioning. Pharmacogenomic studies of ADHD may also add to our understanding of the pathophysiology of the disorder, as the moderating effects of polymorphisms are increasingly utilized in psychopathology research.

PRELIMINARY STUDIES

Several preliminary reports indeed suggest that candidate genes related to catecholamines, such as dopamine or norepinephrine, predict response to ADHD medications. However, the nature, direction, and magnitude of these associations remain unclear. These early pharmacogenomic studies have utilized modest samples sizes and, not surprisingly, have yielded inconsistent results. The majority are limited to investigations of methylphenidate response, include retrospective reports and both open-label and placebo-controlled clinical trials, and emphasize ADHD symptom reduction as the primary outcome measure. Nonetheless, these early trials attest to the feasibility of pharmacogenomic studies of ADHD and provide a foundation for future research investigation.

Dopamine Transporter (DAT1)

DAT1 is located on chromosome 5. The gene contains a variable number tandem repeat (VNTR) of a 48-bp sequence within its 3′-untranslated region. Common allelic polymorphisms result from different VNTRs. Cook et al. (15) first described an association between the 10-repeat (480 bp) DAT1 polymorphism and ADHD. This association has been replicated in some (16,17), but not all studies (18) and explains a small percentage of the variance in ADHD symptoms (12).

Several reasons underlie interest in DAT1 as a candidate gene for ADHD treatment response. First, as noted previously, numerous studies suggest an association between variants at DAT1 and increased risk for categorically defined ADHD. More recently, Cornish et al. (19) reported an association between dimensional measures of ADHD symptoms,

response inhibition, and the 10/10 DAT1 genotype in a sample of non-referred children. Second, methylphenidate, and to some extent amphetamine, specifically targets and blocks the dopamine transporter (20,21). This results in an increase in extracellular dopamine in dopamine-rich brain regions, which project to the striatum, nucleus accumbens, prefrontal cortex, and hypothalamus. These brain regions are frequently implicated in the pathophysiology of ADHD (22). Third, several neuroimaging studies reveal increased dopamine transporter densities in striatal regions of adults with ADHD, giving rise to the hypothesis that blockade of the transporter in ADHD patients might correct underlying brain pathophysiology (23). Moreover, Durston et al. (24) recently demonstrated that DAT1 influences caudate volume.

In the first pharmacogenomic investigation of ADHD, Winsberg and Comings (25) reported that 86% of "poor" responders to methylphenidate (defined as less than a 50% reduction in ADHD symptoms on parent ratings) were homozygous for the 10-repeat allele (10/10) in a sample of 30 African-American children with ADHD. Roman et al. (26) and Cheon et al. (27) utilizing similar methodology described similar findings in Brazilian and Chinese samples respectively. In these studies, approximately 30–50% of the homozygous youth (10/10) responded positively to methylphenidate (MPH) as compared to a response rate of 70–100% in the predominantly 10/9 genotype groups.

It should be noted that the 10/10 and 10/9 genotypes are the two most common genotypes of DAT1. The Winsberg and Colleagues studies prematurely assumed that the 9-repeat allele was dominant. Two other studies that did not make this assumption found improved response to methylphenidate in patients heterozygous or homozygous for the 10-repeat allele. Based on retrospective recall of medication outcomes, Kirley and colleagues (13) reported that "very good" responders were more likely to have at least one copy of the 10-repeat allele, and that a linear relationship existed between number of 10-repeat alleles and degree of positive response. Similarly, Stein and colleagues (28) found that the presence of one or two 10-repeat alleles was associated with increased response rates in patients receiving 36 or 54 mg doses of OROS-methylphenidate as compared to those without a copy of the 10-repeat allele, who did not display a linear dose–response curve. Those individuals with the less common, 9/9 genotype of DAT1 not only displayed a different dose–response curve, they displayed more stimulant side effects and the majority remained impaired during MPH treatment. In contrast, methylphenidate treatment was associated with mild to minimal impairment in 80% of those with either the 10/9 or 10/10 genotype (Fig. 1).

The Stein et al. study (28) was the first pharmacogenomic study of ADHD to analyze the 9/9 group separately. Subsequent reanalysis of the Kirley study (13) also found a poor stimulant response rate (25%) for those

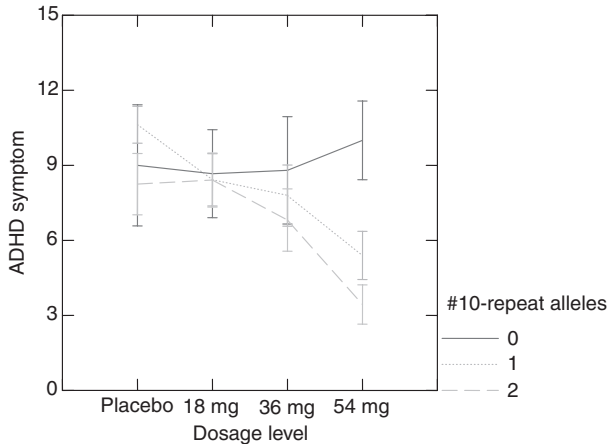

Figure 1 Total ADHD parent rating scale IV scores (with standard errors) by dosage level and by genotype. *Source*: From Ref. 28.

with the 9/9 genotype as compared to a robust positive response rate (65%) for those with one or two 10-repeat alleles.

Interestingly, a similar effect of the 9/9 genotype on amphetamine response was reported by Lott and colleagues (29). In this study, healthy college students homozygous for the 9-repeat allele were less sensitive to amphetamine effects in terms of subjective ratings and diastolic blood pressure. For example, individuals with the 9/9 genotype were less sensitive to the subjective effects of amphetamine as suggested by ratings of feels drug (Fig. 2).

Thus, three studies indicate that when the 9/9 is examined separately or not combined with the 9/10 genotype, there appears to be a clear difference in stimulant response. Although the statistical significance of the effect of the 9/9 genotype on methylphenidate response is robust, replication is necessary for the results to be more conclusive and to determine any clinical significance of this finding.

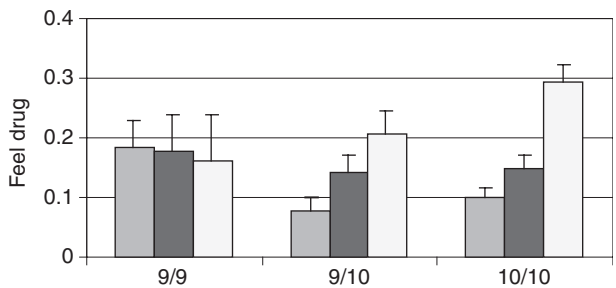

Figure 2 Visual analog scale of ratings of feels drug. *Source*: From Ref. 29.

Several studies are ongoing with the goal of determining clinical predictors of nonresponse, specific adverse events associated with DAT1 genotypes and other candidate genes, and neuropsychological or neurophysiological endophenotypes (30,31). In a National Institute of Mental Health (NIMH) sponsored study, Dr Jeffrey Newcorn, Dr Mark Stein and colleagues are testing whether those with the 9/9 genotype respond to nonstimulant treatment (e.g., atomoxetine). Additionally, Dr Chandan Vaidya and colleagues at Georgetown University are examining the relationship between DAT1 genotypes and striatal activity utilizing functional magnetic resonance imaging (fMRI).

Dopamine Receptors (DRD2, DRD4, DRD5)

DRD2, DRD4, and DRD5 are presumed targets of postsynaptic catecholaminergic activity. DRD2 is located on chromosome 11 and is involved in central reward-mediating mesocorticolimbic pathways. DRD2 has been implicated in risk for alcoholism and nicotine addiction. DRD4 is also located on chromosome 11. The 7-repeat (48 bp) VNTR polymorphism found in the coding region of DRD4 exhibits odd ratios for increased ADHD risk ranging from 1.4 to 1.9 in numerous studies (32). DRD5 is located on chromosome 4. The 148-bp allele of DRD5 has a pooled odds ratio of 1.24 for ADHD risk in meta-analysis, although the association is mostly confined to the inattentive and combined subtypes (12).

In vitro studies of the DRD4 7-repeat suggest that this allelic variant is functionally less responsive to dopamine effects (33,34). Consistent with this, one study demonstrated that patients with at least a single copy of the 7-repeat required higher doses of methylphenidate for optimal symptom reduction (35). In contrast, Winsberg and Comings (25) failed to demonstrate any relationship between DRD4, DRD2, and treatment outcomes.

Salee et al. (36) reported that ADHD children with at least one DRD4 4-repeat allele showed a trend toward improved response to the nonstimulant atomoxetine, in contrast to methylphenidate response, which was unaffected by DRD4 genotype. Furthermore, improvement on the ADHD-Rating Scale hyperactivity subscale was maximized by the absence of the 7-repeat allele. The results of this study suggest an interaction between atomoxetine and DRD4 genotype, supporting a role of the dopamine D4 receptor in ADHD, and also suggest possible relevance of pharmacogenomic factors associated with atomoxetine treatment.

Norepinephrine Transporter (NET) Protein 1

NET is located on chromosome 16 and has been implicated in susceptibility for orthostatic hypotension. NET is a likely candidate for studies of medication outcome as the NET is also targeted and blocked by methylphenidate. NET blockade is also the presumed mechanism of activity for atomoxetine (37).

Bobb et al. (38) reported an association between NET and ADHD. In addition, one study in Han Chinese evaluated the relationship between the G1278A polymorphism at NET and medication response (39). These investigators found that individuals homozygous for the less common A/A genotype had decreased symptom reductions compared with the G/A or AA groups. The authors noted that, since the G1278A allele has no known functional activity, the allele might be in linkage disequilibrium with another allele responsible for outcome differences.

Cytochrome P450 2D6 (CYP2D6)

Atomoxetine metabolism is regulated by the CYP2D6 enzyme system. In one of the first examples of pharmacogenomics applied during ADHD drug development, the effects of CYP2D6 polymorphisms were evaluated for atomoxetine. Whereas most individuals are extensive metabolizers (EMs), approximately 7% of the U.S. population are poor metabolizers (PMs) (40). Atomoxetine has a plasma half-life of approximately 5 hr in EMs. In PMs, atomoxetine has a longer plasma half-life of approximately 22 hr (Eli Lilly, personal communication, July 2005). In a review of several studies, PMs displayed greater symptom improvement than EMs and were more likely to continue treatment (41). Not surprisingly, decreased appetite and insomnia were reported more frequently in PMs taking any dose of atomoxetine. PMs also displayed a greater increase in pulse and diastolic blood pressure compared with EMs, while EMs gained more weight than PMs. Thus, both efficacy and adverse events to atomoxetine appear to be moderated by the CYP2D6 enzyme system.

GENOME-WIDE INVESTIGATIONS

An alternative to candidate gene studies is the whole genome or genome-wide scan approach. Several genome-wide scans have importance for ADHD risk (12). A genome-wide scan makes no a priori assumptions regarding the potential functional significance of particular genes, but examines the entire genome to identify possible regions of functional importance. A similar approach has been proposed to identify regions in the genome with implications for ADHD treatment outcomes. In one study, investigators used quantitative trait analysis to test for linkage with methylphenidate response in a genome-wide scan (42). The authors found regions of moderate significance on chromosome 7, with additional regions on chromosomes 3, 5, and 9. With the development of high-density SNP genotyping arrays, whole-genome association studies are now technically (if not financially) feasible for study of pharmacogenetic response (or study of etiology).

CLINICAL RELEVANCE

Although stimulant medications are regarded as effective first-line ADHD therapies, the majority of treatment studies are short-duration trials with long-term efficacy being much more modest (43). In a 5-year prospective study, 50% of children did not continue methylphenidate into the second year, and many who remained in treatment reported clinically meaningful side effects (44). Moreover, in two open-label studies of both methylphenidate and amphetamine, fewer than 60% of previously stabilized patients remained on medication after 12 months of treatment (45,46). At 14 months follow-up in the ADHD Multimodal Treatment Study (MTA), only 56% of patients assigned to intensive medication management continued to meet criteria as excellent responders (47). In one community study, 49% of children who were receiving stimulant medications met full symptomatic criteria for ADHD (48). In most longitudinal studies of ADHD, although ADHD symptoms tend to decline with age, impairment tends to persist or worsen. Thus, impairment as well as ADHD symptoms should be studied as outcome measures in pharmacogenomic investigations (28).

ADHD pharmacogenomics might ultimately lead to individualized medication prescriptions based on a patient's own genomic information. More individually tailored ADHD treatments could conceivably lead to improved tolerability, enhanced symptom reduction, and associated improvements in patient compliance. Alternatively, pharmacogenomics might identify patients at increased risk for certain side effects, allowing physicians to minimize exposing individuals at risk of adverse events. Pharmacogenomics might also play a role in the development of new ADHD medications.

FUTURE DIRECTIONS

There is growing international interest in ADHD pharmacogenomics. Future studies will consider an expanded range of treatment outcomes, including variability in tolerability and side effects, symptom change, pharmacokinetics, and metabolic pathways (49). These studies are likely to consider individual variation in responses to multiple medications, such as amphetamine, atomoxetine, guanfacine, buproprion, and other compounds deemed selectively useful in treating ADHD and related disorders, symptoms, or dimensions. Research is apt to consider a broader set of candidate genes, with samples large enough to examine gene–gene and gene–environment interactions.

Larger controlled clinical trials will require multisite collaborative networks of clinicians and researchers working with the support of government agencies and the pharmaceutical industry. In this regard, there is much to be learned from other illnesses, such as cancer, in developing

infrastructures to promote pharmacogenomic studies of ADHD. Such collaborations will increase the speed of findings, reduce research costs considerably, and also increase the rate at which findings are translated into clinical practice. Consideration of pharmacogenetics early in drug development might promote identification of new drug targets as well as subsets of patients likely to respond to a specific treatment. Conversely, subjects with increased risk of side effects could be excluded from clinical trials, allowing others to benefit from medications that might have otherwise been rejected during early development.

The goal of ADHD pharmacogenomics is to be able to individualize medication based on a patient's own genomic information. More individually tailored ADHD treatments could conceivably lead to improved tolerability, enhanced symptom reduction, and associated improvements in patient compliance. Alternatively, pharmacogenomics might identify patients at increased risk for certain side effects, allowing physicians to minimize exposing individuals at risk of adverse events. Advances in pharmacogenetics may also lead to increased understanding of ADHD pathophysiology, which may also have implications for diagnosis and treatment. Finally, pharmacogenomic studies might also play a role in the development of new ADHD medications with more specific drug targets.

SUMMARY

Pharmacogenomic studies of ADHD are in a relatively early stage, but hold considerable promise for improving treatment of this disorder. Several studies suggest differences in stimulant response between individuals with DAT1 genotypes. Children with the much less common 9/9 genotype do not benefit from usual clinical methylphenidate doses and might be less sensitive to stimulant effects. Larger samples are needed to clarify inconsistent findings and to determine the magnitude of pharmacogenetic effects in different samples. There are also promising leads with other candidate polymorphisms, such as NET and the CY2D6 enzyme system and atomoxetine.

Pharmacogenetic and pharmacogenomic studies have progressed from small samples looking at single genes and ADHD symptom reductions, to larger studies looking at a broader phenotype of clinically relevant stimulant response and various neurophysiological and neuropsychological endophenotypes (30). As noted by Cook (50), replication of positive findings with adequately powered samples and determination of the positive and negative predictive value are the next steps.

Being able to predict which individuals are likely to respond positively or which individuals do not tolerate a particular medication or class of medications would alter the trial and error approach to stimulant treatment of ADHD. Ultimately, it is hoped that further understanding of the genetic

variability in ADHD treatment response may shed light on both genetic and nongenetic factors which contribute to the outcome.

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Endophenotypes in ADHD: Rational and Progress

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Twin, family, and adoption studies provide compelling evidence that genetic risk factors contribute substantially to attention deficit hyperactivity disorder (ADHD) (1,2). Twin studies show high genetic contribution regardless of whether ADHD is defined as a category, as a continuous trait, or as an extreme of a trait ($h^2 = .64$ to .9) (3,4). Genetic linkage and association studies have proven remarkably productive in ADHD identifying a number of genetic risks for the disorder (3). Progress in ADHD was swift because scientists were forearmed with considerable knowledge about the probable role of neurotransmitter dysfunction based on the dramatic effect of stimulant medication in ameliorating behavioral and cognitive manifestations of ADHD (5,6). There have now been over 30 association reports for candidate genes including the genes for the DA transporter (DAT1), DA receptors D4 and D5, the serotonin receptors 1B and 2A, calcyon, EKN1, G(olf), and the gene for the synaptic vesicle docking fusion protein, synaptosomal-associated protein of 25 kDa (SNAP25) (3,7). Furthermore, there have been four genome wide scans on relatively small, independent samples (8–11), which are suggestive of linkage signals in the distal region of chromosome 5p.

Despite this progress, not all findings have been replicated. For example, of the many studies of DRD4, almost half have failed to replicate association or linkage (12). Moreover, the effect size of observed risks has been small. Meta-analysis of DAT1 and DRD4 linkage and association findings (12,13) indicate that the average increase in risk for ADHD

associated with replicated genetic findings is approximately 1.5-fold. Similarly, a recent large joint meta-analysis of DRD5 by Lowe et al. (14) showed an overall odds ratio of 1.2. The lack of consistency in genetic findings is also evident in the largely nonoverlapping areas of linkage identified in genome scans conducted to date.

In response to the problem of nonreplication, there has been a call for application of novel strategies to facilitate gene discovery. The goal of this chapter is to detail the logic for the utility of nonclinical endophenotypes in facilitating genetic research and to propose a priori criteria by which endophenotypes should be evaluated before they are applied in molecular research. As an illustration, we summarize evidence bearing on one putative ADHD endophenotype for which considerable evidence is available—motor response inhibition—in order to illustrate the validation of an endophenotype.

SOURCES OF VARIATION IN GENETIC RESEARCH

There are various explanations for the apparent difficulty in replicating genetic association and linkage in ADHD. The first relates to the apparent complexity of the relationship between causative genes and the behavioral phenotype. ADHD is clearly not a single-gene disorder with Mendelian inheritance. One-to-one correspondence between genes and specific aspects of a disease or a syndrome as a whole is unlikely. Rather, ADHD conforms to a multifactorial polygenic threshold model of heredity. This model holds that a complex trait results from the action of a number of genes each of which exerts a small effect. These genes contribute individually or interact with other genes from the moment of conception or at any time during development and may do so in conjunction with various environmental factors. Together, these factors generate a continuous phenotypic distribution. When these contributions reach a certain threshold on this continuum, pathological manifestations occur (15) (Fig. 1). Any allelic variant or environmental risk factor can therefore be present among individuals located anywhere in the phenotypic distribution, and no single variant is either sufficient or necessary to cause individuals to cross the threshold between affected and nonaffected. If this model is correct, it is easy to see that the current categorical approach to diagnosis wastes much of the information present in the underlying distribution, and will inevitably result in nonreplicable genetic association findings. Another reason for nonreplication is genetic heterogeneity: different genes might contribute to ADHD risk in different populations.

Heritability rates for ADHD vary from 50% to 90% (7,16). Therefore, a substantial component of variance is due to environmental risks (including measurement error). These environmental factors could contribute to ADHD independently or through interactions with genetic factors. A range

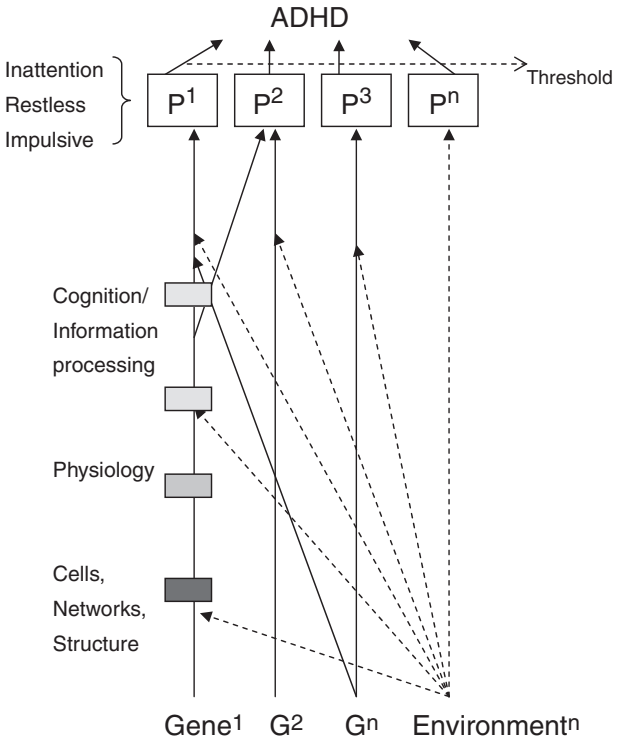

Figure 1 Locating endophenotypes with the multifactorial, polygenetic threshold model of ADHD. *Note*: Figure 1 shows various hypothetical pathways from genes (G^1,..., G^n) and environmental risks (E^1,...,E^n) to the behavioral manifestations of ADHD (Phenotype, P^1,...,P^n). The lowest level shows the effects of various genes and the highest level shows individual behavioral manifestations such as restlessness, inattentiveness, and impulsiveness. For the sake of simplicity, the figure does not include separate genetic or environmental risks for home versus school behavior, although this is a possibility. As one ascends from the level of genes toward the level of the clinical manifestations of the disorder, a greater number of genetic and environmental factors come into play and interact in the genesis of each manifestation of the behavioral outcome of ADHD. In addition, as one ascends from the level of genes to that of overt clinical manifestations, the overall effect of any single genetic or environmental risk factor becomes diluted by the contribution of other factors. A range of neurobiological processes and structures are traversed as one moves from the level of genes toward overt behavior, such as, proteins (*red bars*), cellular networks and structures (*green bars*), neurophysiology (*yellow bars*), and cognition and information processing (*blue bars*). By contrast, as one descends from the behavioral level toward the genetic level the relationship between any specific clinical manifestation and any specific genetic cause is strengthened although less of the variation in overall clinical manifestation might be explained. Putative endophenotypes such as cognitive deficits (*Caption continues on next page*)

of environmental risks are thought to contribute to ADHD including maternal smoking, perinatal insult, head injury (17–20), and psychosocial adversity (poverty, low-income housing, single-parent families, parental psychopathology and early severe deprivation; 21). Environmental factors might even be capable of generating nongenetic phenocopies of ADHD. The converse is also possible: environmental protective factors could yield cases in which genetic risks are present but disorder is absent. The genetic and nongenetic factors which contribute to ADHD could differ across populations and families, making replication difficult.

The prevailing diagnostic approach is based on clusters of symptoms, clinical characteristics, and natural history (22). The resulting ADHD diagnosis may be clinically informative although it may not describe homogenous and genetically relevant subtypes. It is not yet possible to distinguish subtypes of ADHD that arise from different combinations of genetic and/or nongenetic factors. For example, ADHD occurs following traumatic brain injury in approximately 20% of injured children (19). No research to date has identified specific markers of these two ADHD variants.

Phenotypic variation across genetic studies could also derive from disparities among informants, variation in the way ADHD subtypes are handled, or the inclusion of comorbid conditions. There is only modest agreement between parents and teachers in their report of ADHD symptoms (~.4) and different informants identify different children as disordered (23). Twin studies indicate that both parent and teacher ratings of ADHD behaviors are highly heritable (24–27). Yet, there is evidence that parents and teachers may be identifying genetically unique traits (25,28,29). ADHD cases vary considerably in the nature of their behavioral manifestations—some have a predominance of inattentive symptoms, some a predominance of hyperactive and impulsive symptoms and some exhibit both of these clusters to approximately equal extents. It is not yet known whether genetic and environmental factors operate in the same way across these subtypes (4,30,31). There may be distinct sets of genes involved at various levels of ADHD severity and with various subtypes, or, subtypes and severity could reflect variable manifestations of a common set of genes (pleiotrophism) as is seen in conditions such as Marfan's syndrome (32). Another source of

(*blue bars*) are genetically informative because they are closer to the expression of a smaller set of underlying genes. The model represents the complexity of the possible relationships, one gene (G^1) may contribute to multiple subphenotypes (P^1, P^2), or any single subphenotype (P^1) may be influenced by multiple genes (such as, $G^1 \times G^3$; $G^1 + G^2$, G^1 or G^2). Moreover, in the case of ADHD a range of more complex models are likely, involving multiple genes and environment factors (such as, $G^2 \times G^1 + E^2$ results in P^3) that may be interacting or functioning in an additive way.

genetic heterogeneity could arise from the various "subtypes" that are delineated by the presence of a comorbid disorder. Comorbidity with conduct, learning, and emotional disorders is very common in ADHD (33). ADHD and conduct disorder (CD) and ADHD and reading disorder share common and unique genetic influences (34,35). Treating ADHD as a quantitative trait does eliminate the issue of the arbitrary threshold that is imposed on the diagnosis of ADHD, however it does not mitigate other sources of error such as those introduced by the presence of comorbidity.

THE POTENTIAL OF ENDOPHENOTYPES

Genetic risks in complex medical and psychiatric diseases may be more clearly and reliably expressed in nonclinical endophenotypes (from the Greek *endo* meaning within and *phainen* meaning to show) than they are in clinical phenotypes as presently defined (36–39). Endophenotypes are manifestations of gene action that are in the same genetic pathway linking genes to complex clinical manifestations of disorder, but are closer to the mechanism of action of the genes involved in the disorder (36–39). The closer one gets to the immediate effects of genes and the farther one is from the clinical phenotype, the fewer the number of genetic and nongenetic factors that are likely to affect the trait. The interplay among genetic and environmental risk factors and phenotypic variation is illustrated in Figure 1.

A valid endophenotype should be more strongly associated with specific susceptibility genes than other complex clinical endpoints even if it is not associated with all of the alleles that confer risk for the broader ADHD phenotype. Linkage and association could be stronger in a subgroup of individuals who show a particular endophenotype. Even if endophenotypes are themselves multifactorial and multigenic, as is likely to be the case, they could nevertheless be useful in genetic research if they are influenced by a smaller set of genetic and environmental factors than the clinical manifestations of the disorder (39). Accordingly, endophenotypes could increase the power of genetic linkage and association analyses by identifying individuals with particular genetic susceptibilities across samples, subtypes, situations, levels of severity, and presence of comorbidity.

Endophenotypes could be used to identify individuals at genetic risk even in the absence of overt disorder (spectrum phenotypes) (40). Some individuals with the disease genotype might not express the disease phenotype per se but rather might exhibit subclinical or alternative phenotypes because of incomplete genetic penetrance, pleiotropy, or the absence of necessary interacting genetic or environmental risks. This pattern is thought to be at work in other psychiatric disorders such as schizophrenia where nonschizophrenic monozygotic twins may not exhibit schizophrenia per se but manifest schizoid personality disorder. Both twins have an equal tendency to transmit the disorder to their offspring indicating that the schizoid

personality is a marker of similar genetic risk (41,42). In the case of autism, unaffected siblings tend to exhibit language learning disorders more often than expected (43). We do not yet know the phenotypic spectrum of ADHD: there might be a range of behavioral and nonbehavioral (including endophenotypic) expressions of the various genotypes (pleiotropy). In addition to identifying spectrum phenotypes, endophenotypes could delineate subgroups with increased etiological homogeneity (affected individuals with the endophenotype). Finally, endophenotypes could be used as a quantitative trait with a wide range of scores in place of a binary diagnosis as is typical employed in research into the genetics of psychiatric disease. The net effect of a valid endophenotype could be an increase in statistical power to detect linkage or association.

There is considerable optimism that valid and useful endophenotypes can be identified because a good deal is known about the pathophysiology of ADHD. A wide range of potential endophenotypes are currently proposed and many twin and genetic studies include a panel of putative endophenotypes (what we call "candidate" endophenotypes to mirror the concept of a candidate gene). However, few if any of these candidate endophenotypes have been tested to see if they meet a priori criteria for a valid endophenotype. Ultimately the validity of a candidate endophenotype will be evident in its ability to increase the power to detect functional genetic variants in ADHD. But, given the limitations and expense of clinical research, it is not possible to include in any particular study every measure that has a purported relationship to ADHD. Moreover, poorly chosen measures could yield associations that prove to be false positives or false negatives. Next, we review the criteria by which a candidate endophenotype should be evaluated before inclusion in genetic research (36–39) (Table 1).

CRITERIA FOR GENETIC ENDOPHENOTYPES

Sensitivity and Specificity

An endophenotype should be common in affected individuals (i.e., sensitive), relatively if not completely unique to the disorder (i.e., specific),

Table 1 Criteria for Genetic Endophenotypes

Sensitivity and specificity
Heritability, genetic sensitivity, and genetic specificity
Familial aggregation
Presence in unaffected family members
State-independence
Biological plausibility
Sound psychometric properties
Feasibility

and relatively uncommon among unaffected individuals in the general population (44). However, there is an important limitation to this criterion that it concerns only phenotypic sensitivity and specificity. Phenotypic sensitivity to ADHD may not be high for a candidate endophenotype if some apparently unaffected individuals are carriers of risk genes with reduced penetrance. Given the high prevalence of ADHD in the general population it is likely that common allelic variants are involved in ADHD. Therefore, we can expect that many unaffected individuals will carry susceptibility genes without manifesting the ADHD phenotype at a diagnostic level. ADHD may also share some genetic risks with other psychiatric disorders. Genetic risks that are shared among disorders could contribute to the elevated rate of comorbidity that is evident in ADHD (45,46). It is easy to see how this could be the case for ADHD and reading disorder, for example, where both disorders could share common genes affecting cognitive processes such as temporal processing, working memory, or inhibitory control. In ADHD, these cognitive deficits could result in behavioral manifestations (e.g., inattention), whereas in reading disability the deficit could result in impaired phonological decoding. In such cases, the specificity of an endophenotype would not be high although it might still increase power for detecting genetic risks for each disorder. Although nonspecific genetic risks for child psychopathology may be quite common, the ideal starting point for ADHD genetics should be the identification of endophenotypes that are both genetically sensitive and specific to ADHD.

Heritability, Genetic Sensitivity, and Genetic Specificity

Endophenotypes should be heritable, meaning that the endophenotypic variation in the population should be partly caused by genetic variation between individuals. Typically, when endophenotypes are discussed, it is said that "…the endophenotype must be as heritable as or more heritable than the behavioral phenotype" (31). This criterion for the validity of an endophenotype is only partially correct. It is not likely that any endophenotype can be more heritable than ADHD (approximate $h^2 \approx 80\%$) (7,16). However, putative endophenotypes do have to be heritable otherwise they would not be useful for genetic studies. What is crucial is that the genetic structure of the putative endophenotype be simpler than the clinical "exophenotype" that it is meant to dissect. If an endophenotype is sensitive and specific to a disorder, has even moderate heritability ($\approx 50\%$), and is genetically simpler (i.e., affected by fewer loci), it could lead to significant increases in power to detect disease alleles for the associated disorder.

To determine whether an endophenotype is valid and useful for increasing power in molecular genetic research, a decisive criterion would be that the phenotypic covariance between the ADHD phenotype and the putative endophenotype at least partly be due to shared genes. Multivariate quantitative

genetic modeling (i.e., simultaneously analyzing two or more traits) can be used with twin data to estimate the degree of genetic correlation between traits (47). The genetic correlation measures the extent to which two phenotypes are influenced by the same genetic factors regardless of their respective heritability (48). The higher the genetic correlation between a candidate endophenotype and a disorder, the more likely it is that identifying polymorphisms for the former will amount to finding disease alleles for the latter. If ADHD is a genetically heterogeneous disorder as is likely, then endophenotypes that have high genetic correlation with some subsets of ADHD symptoms or dimensions but not others may be useful in the genetic "dissection" of ADHD.

Finally, multivariate genetic modeling between a genetically sensitive ADHD endophenotype and disorders that are comorbid with ADHD (e.g., reading and CDs) can allow us to assess the "genetic specificity" of the endophenotype to ADHD. For example, a genetically specific endophenotype to ADHD would be one that shows strong genetic correlation with ADHD, but only weak or no genetic correlation with reading and/or other disorders.

Familial Aggregation

A candidate endophenotype should be evident in relatives of affected individuals. Full siblings, for example, share 50% of their genes on average. If the endophenotype is influenced by shared genetic factors, then the deficit should be found in at least some relatives of affected probands. Of course, the fact that a trait is familial does not ensure that it is heritable because shared environmental influences can generate familial similarity. Twin or adoption designs are required to assess heritability.

Presence in Unaffected Family Members

A corollary of familial aggregation is that an endophenotype should be present even in the unaffected relatives of affected probands. If the severity of overt clinical symptoms and the extent of the endophenotype are independent it would demonstrate that the endophenotype has the capacity to detect asymptomatic genetic carriers or those with incomplete penetrance of the disease-causing genotype (49). One would also predict covariance for the endophenotype among relatives. That is, the relatives of ADHD individuals with a particular endophenotype should be more likely to manifest the endophenotype than relatives of ADHD individuals who do not manifest the endophenotype, whether they are affected or not.

State-Independence

A valid endophenotype will not vary with disease progression or treatment and will not vary with measurement technique. If such an endophenotype

marks genetic risk despite fluctuations in overt manifestations of the disease, then one would expect that individuals of all ages would exhibit the genetic marker pre- and postonset of the disease. In addition, individuals who once manifested the endophenotype would continue to do so even if they had "outgrown" the overt disorder due to treatment or to altered environmental circumstances (unless these also affect the endophenotype) or if the original disorder had morphed into another disorder (heterotypic continuity).

Biological Plausibility

Biological plausibility, i.e., a functional relation between a putative endophenotype and the disorder, is a vital feature of a putative endophenotype. A good deal is known about the biological basis of ADHD from which to generate predictions about the nature of a potential endophenotype. Imaging and pharmacological studies indicate that structural or functional abnormalities in cortical–subcortical pathways supporting executive function are central to the disorder. Individuals with a diagnosis of ADHD have smaller prefrontal cortical volumes than controls particularly in the right inferior prefrontal cortex, corpus callosum, caudate, and cerebellum (50–52) and there is a relationship of prefrontal morphology and the clinical characteristics of ADHD (53,54). Functional imaging studies in ADHD show less activation compared to controls in frontal and cingulate regions (55,56) and there is a correlation between activation and clinical characteristics in ADHD (52,57). Subcortical structures are also implicated. Most studies show smaller caudate and globus pallidus volumes in ADHD (55,58,59) and there is a demonstrated link between volume and asymmetry of caudate nucleus and performance on executive function tasks in ADHD (60,61). Functional neuroimaging studies report differences in the amount of activation in the caudate, putamen, and globus pallidus during performance of executive function tasks (62). Dopamine transporters are particularly common in subcortical structures that are otherwise implicated in ADHD and in executive function. As a result, genes in the dopamine system have been targeted with success in molecular research. Therefore, a logical choice for an endophenotype would be any neuropsychological process, neurochemical, or structural abnormality that is affected by variation in these neurotransmitters, that responds to stimulant administration or that activates brain regions presumed to be abnormal in ADHD.

Sound Psychometric Properties

Candidate endophenotypes should be reliable if they reflect enduring traits. Standardized measures would be particularly helpful especially if the endophenotype varies with age or sex in a systematic way as is likely to be the case for cognitive processes. Furthermore, it would be advantageous for

statistical analyses for the putative endophenotype to be quantitative rather than categorical.

Feasibility

The biology of ADHD reviewed above suggests that structural brain abnormalities might be fruitful candidate endophenotypes. Durston et al. (105) investigated the validity of markers of brain structure in ADHD by comparing individuals with a confirmed diagnosis of ADHD and their unaffected siblings. They found reduced prefrontal gray matter and left occipital gray and white matter in both children with ADHD and their unaffected siblings. Despite the promise of this research, it seems highly unlikely that structural imaging can be incorporated easily and economically in most genetic designs. Candidate endophenotypes should be easy to measure and noninvasive in order to facilitate research in affected children, their relatives, and the general population.

EXECUTIVE FUNCTIONS AS CANDIDATE ENDOPHENOTYPES

There is a strong case to be made for the importance of executive function deficits in ADHD. Executive functions refers to those neuropsychological processes that are necessary to organize, integrate, and influence perceptions, emotions, and responses across time in order to meet the needs and goals of the organism (63,64). Executive function comes into play when one is required to prepare, withhold, inhibit, or switch responses, to monitor one's performance for errors, to manage delay, and to maintain and manipulate information held temporarily in memory. Executive functions are important to behavioral self-regulation, academic achievement, and development of cognitive skills (65,66). Various aspects of executive function are involved in overlapping and sequential ways in the performance of most tasks (67). Yet, each component appears to be somewhat distinct judging from their unique developmental trajectories (68–71), the limited intercorrelations that are observed among functions (72) and their dependence on partially segregated, although functionally inter-related, frontal-subcortical circuits (64,69,73).

Deficits in executive functions are readily apparent and reproducible in ADHD (74) and several theories posit that these deficits are central to the disorder (66,75,76). Executive functions depend on the same neural circuits and transmitters that are implicated in ADHD (77) and improve with administration of methylphenidate (78–80). The few twin studies published suggest that some executive function measures are heritable (81,82).

Various executive functions distinguish ADHD from controls (83) and could serve as potentially valid endophenotypes. While few have been evaluated formally as candidate endophenotypes, there is considerable

evidence pertaining to the validity of a proposed executive function endophenotype in motor response inhibition. We now review this literature from the perspective of the validity criteria proposed above.

INHIBITORY CONTROL AS A CANDIDATE ENDOPHENOTYPE FOR ADHD

Motor response inhibition is a crucial executive function that comes into play when one tries to withhold or interrupt an ongoing or planned response. The stop signal task a commonly laboratory paradigm used to study this type of inhibition. In the paradigm, participants perform two concurrent tasks—a primary or go task and a secondary or stopping task. The primary or go task involves a choice response: e.g., if an X appears, a right-hand response is made; if a Y appears, a left-hand response is made. The secondary task involves a stop signal on a subset of go trials. When the stop signal appears, the participant instructed to stop their response on that trial. In the stop signal task (Fig. 2), the stop signal is typically a tone which follows the presentation of the go signal. The delay between presentation of the go and the stop signals is dynamically adjusted. If a participant stops successfully on a given trial, the delay is increased for the next trial making it more difficult to stop. If the participant fails to stop, the delay is decreased making it easier to stop on the next stopped trial. As dynamic tracking proceeds, it converges on the delay at which the participant is able to stop 50% of the time. With knowledge of the latency of the go response and of the delay between go and stop signals at which the two processes are tied, one can estimate the latency of the unobserved stopping process known as stop signal reaction time (SSRT; 84). Longer SSRT indicates poorer inhibitory control.

Sensitivity and Specificity

Deficient inhibitory control, manifest in significantly longer SSRT, is a replicated deficit in ADHD (76,85–88). Willcutt et al. (83) reviewed a number of cognitive tasks and found that differences between ADHD and normal control groups in SSRT was a consistent finding; 22 of 27 studies in which ADHD and control groups were compared yielded a significant group difference ($p < .05$) with a weighted mean effect size of 0.61. The task has been shown to have an effect size of .74, sensitivity of .80, and specificity of .67 (86). Moreover, differences between ADHD and normal controls is not a function of associated CD, anxiety, or learning disability, and is independent of age or intelligence (83,86). Leblanc et al. (106) studied motor response inhibition in a group of children who suffered traumatic brain injury while controlling for preinjury history of ADHD. Inhibition was impaired by head injury whether it was associated with secondary ADHD or

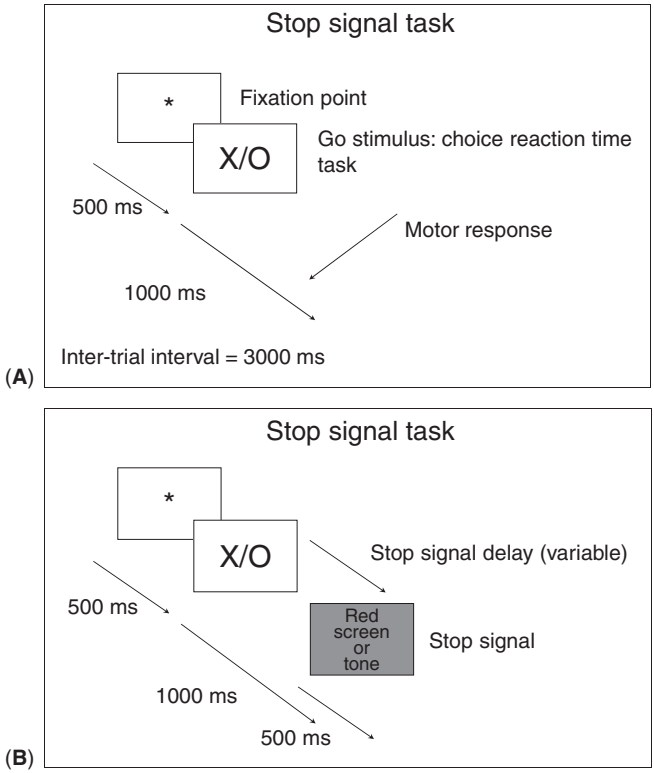

Figure 2 Stop signal task. The stop signal task involves two component tasks. In the go task (**A**), participants must respond as quickly and as accurately as they can to either an "X" or an "O" presented on a computer screen. In the stop task (**B**), a stop signal (e.g., tone), instructs the participant to cancel their response on that particular trial.

not. Moreover, deficit in inhibitory control discriminated between primary and acquired ADHD. More importantly, initial inhibition deficits normalized within 2 years postinjury.

Heritability, Genetic Sensitivity, and Genetic Specificity

Although there is preliminary evidence that various executive functions in normal control individuals are heritable (89), the heritability of motor response inhibition in the stop task or of other candidate ADHD endophenotypes has not been investigated extensively. Kuntsi and Stevenson (90) obtained evidence for genetic influence for several indices of performance on the stop signal task but did not report heritability for the primary index of inhibitory control (SSRT). Groot et al. (91) studied

heritability of performance in a go no-go task but found that it was not possible to distinguish between genetic (A), shared environmental (C), and unique environmental (E) effects, thus leaving unanswered the question of heritability. There is, however, evidence for the heritability of the neural substrate of inhibition and those brain regions implicated in ADHD. Pennington et al. (92) reported heritability of .56–.97 for subcortical and cortical volumes, left and right neocortex, and total cerebral volume (93). Furthermore, Durston et al. (105) found reduced prefrontal gray matter, left occipital gray, and white matter in both ADHD and their unaffected siblings.

Familial Aggregation

Crosbie and Schachar (107) found that deficient inhibition in ADHD children delineated a particularly familial subgroup of ADHD. They observed that ADHD children with poor inhibition were four times more likely than those with good inhibition to have a first-degree family member affected with ADHD regardless of comorbidity with CD or reading disability (RD), symptom severity, or level of impairment. By contrast, good and poor inhibition groups did not differ in history of neurobiological risk, psychosocial adversity, symptom severity, or intelligence.

Presence in Un-Affected Family Members

Further evidence of the familial nature of inhibitory control deficit was reported by Schachar et al. (108). They compared five groups of participants. Groups one and two were rigorously diagnosed ADHD participants and their ADHD siblings. Groups three and four were ADHD participants and their unaffected siblings. The fifth group consisted of normally developing participants. The probands and their affected siblings both showed significant inhibition deficit compared to normal controls. Unaffected siblings of ADHD probands showed an intermediate deficit in inhibition that was not attributable to the severity of their ADHD symptoms, or by the extent of exposure to neurobiological risks or psychosocial adversity. Moreover, ADHD participants in Groups 1 and 3 with inhibition deficit were more likely than those without to have a sibling in Groups 2 or 4 with inhibition deficit. Slaats Willemse et al. (109) also observed clustering in ADHD siblings of response inhibition as measured in the go no-go task as well as performance on measures of attentional control and fine visuomotor skills. These studies indicate that unaffected siblings of affected ADHD probands show deficits in executive function.

State-Independence

Deficient inhibition has been detected in ADHD individuals at every age indicating that it is a trait that does not disappear despite the usual

diminution over time in overt ADHD behaviors. Deficient inhibition has been detected in children, adolescents, and adults with an ADHD diagnosis although the effect was weaker in ADHD adults (94,95). We tested a group of nonmedicated ADHD children repeatedly over the course of a day using the stop task and measured their behavior at the same time. Not surprisingly, we found that the children became progressively more restless, less cooperative and less attentive as the day wore on. Nevertheless, performance on the stop task was stable, indicating that inhibition can be measured independent of concurrent behavior (96). In addition, inhibitory control improves along with behavior when stimulant medication is administered (97).

Biological Plausibility

Aron and Poldrack (110) conducted a meta-analysis of all functional MRI studies of motor response inhibition that have used either the go no-go or stop signal tasks. These studies indicate that the right inferior prefrontal cortex is critical to response inhibition. fMRI evidence converges nicely with lesion-deficit studies which show that the amount of damage to the right inferior prefrontal cortex is significantly correlated with SSRT in patients with unilateral frontal damage (98). The striatum is also involved in inhibition (99) as would be expected from current theories of motor control (100,101). The striatum is a critical relay station in the corticostriatal motor loop involved in controlling ongoing movement both in human and primates and is strongly influenced by dopaminergic and glutamaturgic neurotransmission. Human electrophysiological studies confirm the role of the dorsolateral prefrontal cortex in inhibitory control (102).

Sound Psychometric Properties

Soreni et al. (96) studied 14 nonmedicated children once a week in the morning for three consecutive weeks using the stop task to measure response inhibition. Interclass correlations showed high reliability and stability of this measure.

Feasibility

The stop signal task could be easily administered to individuals of ages 7 to 80 years (103). The function relating age to SSRT is basically "U" shaped: inhibitory control improves through childhood and adolescent and peaks in early adulthood, following which there is a slow increase into old age even though inhibitory control is well preserved even in old age. The results of the Williams study (103) serve as basic norms.

PUTTING ENDOPHENOTYPES TO WORK IN GENETIC RESEARCH

Only a few studies have applied inhibitory control or other endophenotypes in the search for genetic risks in ADHD. Crosbie et al. (in preparation)

investigated the relationship of three candidate genes in ADHD: the dopamine transporter (DAT1), dopamine receptor D4 (DRD4), and synaptosomal-associated protein of 25 kDa (SNAP25) and two candidate endophenotypes inhibitory control (measured with the stop task) and working memory (measured with digit span). The 4-repeat allele of the 48 bp repeat located in the third exon of DRD4 was associated with better inhibitory control and SNAP25 was associated with poor inhibition. No relationship was found between inhibitory control and DAT1. Langley et al. (111) observed that children with the 7-repeat allele had shorter mean reaction times for incorrect responses on the stop signal task (116.6 vs. 134.1 msec) than children without the allele, but did not report the relationship risk alleles and inhibitory control. Children with the allele also displayed higher activity levels. The children with and without the allele did not differ significantly in number of ADHD symptoms when the symptoms were split into the areas of inattention and hyperactivity/impulsivity.

CONCLUSIONS

The primary goals of this chapter were to describe the ways in which endophenotypes might advance research into the genetic basis of ADHD, to lay out criteria for validation of an endophenotype prior to its use in molecular genetic research, and to illustrate, using the example of motor response inhibition, the progress that has been made in validating and applying endophenotypes in the search for genetic susceptibility to ADHD. The commonly mentioned criteria of familial aggregation and presence in nonaffected family members are merely corollaries of the truly indispensable criterion of heritability. The criteria of phenotypic sensitivity and specificity are not enough, because genetic sensitivity and specificity are truly what matter for the genetic usefulness of an endophenotype. Finally, the other commonly recognized criterion of biological plausibility was discussed, arguing that it is a desirable although not a necessary characteristic of a valid endophenotype.

Motor response inhibition meets many of the proposed criteria for a valid endophenotype and has already proved useful for refining the search for genetic risks in ADHD. Inhibition has a well-established neurological basis which overlaps considerably with the proposed biology of ADHD. Deficient response inhibition measured in the stop signal task is a replicated and fairly specific deficit in ADHD. Inhibitory deficit is a marker for a particularly familial form of ADHD and the deficit is found in siblings of affected individuals whether they have ADHD or not. Inhibition is a reliable and stable trait that is found in affected individuals of all ages. The measure is easily administered and is feasible for use in general population studies. However, there are notable areas for further research. Twin studies are needed to determine whether putative endophenotypes such as inhibition are

heritable and genetically correlated with aspects of the clinical phenotype, and not with other disorders.

No claim is made that deficient motor response inhibition is the sole or the most important potential marker of genetic risk for ADHD. There most certainly are other cognitive deficits in ADHD such as in delay management, error detection, and working memory. These cognitive deficits may divide ADHD into etiologically meaningful subtypes. Sonuga Barke (112) has proposed a dual pathway model of ADHD in which some cases arise from dysfunctions that affect mesocortical pathways and motor inhibition and other cases arise from genetic influences on mesolimbic pathways that affect motivation, reward, and capacity to tolerate delay. Support for this hypothesis derives from a study showing that both deficient inhibition and delay aversion, a putative marker of mesolimbic pathway dysfunction, were both present in a group of ADHD cases, but that these deficits were found in different individuals to a considerable extent. Together, delay aversion and deficient inhibition accounted for the majority of ADHD cases (104). Similarly, Schachar et al. (108) measured performance monitoring, another proposed marker of mesolimbic pathway function, in a group of ADHD children. They found abnormality in both inhibition and performance monitoring and a nonsignificant correlation between the two. Given the proposed polygenic influence on ADHD it is likely that various genetically informative executive function deficits will be identified. If multiple, etiologically distinct deficits are evident in ADHD then it may not be correct to aggregate performance measures in an attempt to increase statistical power, as has occasionally been proposed (74). On the other hand, if clusters of cognitive deficits can be found, then aggregated measures may increase power over that achieved with a single measure.

Endophenotypes will not be the panacea that will overcome all problems in genetic research into complex disorders. Not every gene involved in ADHD may be expressed in a cognitive deficit and not every deficit in ADHD may serve as an indicator of an underlying genetic mechanism. Some performance deficits in ADHD could be manifestations of the disorder itself while others may reflect environmental influences rather than being steps along a pathway from genes to phenotype. Variation in executive control might be attributable to a subset of ADHD genes and still have a considerable amount of genetic heterogeneity. Some cognitive deficits may be highly influenced by environmental factors. Nevertheless, executive function deficits could be useful markers of genetic risk in ADHD given the importance of these processes in ADHD, their association with the proposed biological basis of ADHD, and the ease with which these markers could be exploited in clinical and general population samples. There will still be a need to test putative endophenotypes of different kinds such as functional deficits derived from neuroimaging studies, variation in life course, presence of comorbidity, or treatment response.

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35

Can Attention Itself Be Trained? Attention Training for Children At-Risk for ADHD

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WHAT IS ATTENTION TRAINING?

Attention training (ATT) is based on the concept that efficiency increases after repetitive practice of specific cognitive operations of attention (1) because practice produces adaptations in the underlying neuroanatomical networks linked to these processes (2). This concept has origins in the field of cognitive rehabilitation where attention process training (APT), using tasks such as listening for descending number sequences, shifting set, and visual cancellation, has been used to activate and train sustained, alternating, and divided attention (3). It should be noted that the term "ATT" has also been used to refer to different approaches, including (1) neurofeedback or biofeedback, (2) electronic equipment designed to give the child feedback

when he/she is off task, and (3) cognitive training techniques, which involve training the child to self-talk to keep themselves on task and paying attention. We do not review these approaches in this chapter. Instead, we specifically refer to ATT methodologies as those using adaptive tasks specific to attentional functions thought to have certain corresponding neural bases which are changed through repetition and practice.

Several randomized controlled trials have been conducted to investigate the efficacy of ATT in different populations, including traumatic brain injury and stroke. The majority of these studies report positive findings and demonstrate transfer of improvements on untrained assays of attention components such as sustained attention and executive function (4–10).

One criticism that has been levied against ATT methodologies is that they have not been based on a theoretical model or framework of attention (7). Some ATT approaches have focused on training sustained attention, while others focus on alternating or divided attention or executive conflict, making it difficult to compare results. Posner and colleagues have suggested a framework by which to understand attention based on neuroanatomical and neuroimaging evidence (1). This model suggests that attention includes three major functions: alerting, orienting, and executive control, associated with specified neuroanatomical networks (i.e., different networks of interconnected brain areas). The alerting network is involved in establishing a vigilant state and maintaining readiness to react. Imaging studies show that the alerting network depends largely on frontal and parietal areas of the right hemisphere (11,12). Orienting involves selectively focusing on one or two items out of many candidate inputs. The orienting network utilizes superior and inferior parts of the parietal lobe in conjunction with frontal and subcortical structures related to eye movements (13). The executive control network has been related to the control of goal-directed behavior, target detection, error detection, conflict resolution, and inhibition of automatic responses. The executive control network involves frontal areas including the anterior cingulate and lateral prefrontal cortex (14). Each of these neuroanatomical networks appears to undergo intense postnatal development (15). Individuals with attention deficit hyperactivity disorder (ADHD) tend to show specific deficits in these functions, especially in alerting and executive control (16).

Efforts to develop an assessment measure of these three functions has resulted in the attention network test (ANT) with versions for adults (17), school-aged children (18), and preschool children [CHOC-UCI Initiative for the Development of Attention and Readiness (CUIDAR), described later in the chapter]. The ANT task is a combination of a cued reaction time and flanker task (17). Studies suggest that performance on the ANT task follows a roughly normal distribution (19), and that performance is stable within normal adult subjects across a wide age range with no gender differences.

It has also been shown that practice or previous experience has little impact on the attentional measures although overall reaction time is somewhat reduced (19), making it a good candidate as an outcome measure for ATT of alerting, orienting, and executive control.

Posner (20) proposed testing the utility of the idea that implementing ATT early in development may actually enhance attention and executive control networks. Neuropsychological studies suggest extensive development of attention and executive control functions between the ages of 3 and 5, which correlate with developments in brain structure and function. Although the neurological basis of the effect of ATT is not yet understood, evoked potential measures and fMRI evidence suggest that ATT is impacting brain function (7,21). Implementing ATT with preschool-aged children may have a long term impact on the functional development of these systems. Further, implementing ATT with children at risk for the development of attention and behavior problems may prevent or arrest impairments of attention. Evidence suggests that computerized gamelike tasks can be utilized to assess and/or train attentional functions in preschool-aged children (22). Thus, researchers have adapted ATT materials to be developmentally appropriate for both typically developing and "at-risk" preschoolers.

APPLICATIONS OF ATT FOR ADHD POPULATIONS

Since ADHD is by its very nature a disorder of attention, ATT has been considered as a possible nonpharmacological alternative to treatment with stimulant medication. There are few studies investigating the utility of ATT in the ADHD population, however. Williams (23) utilized adult-based ATT materials with a group of six ADHD children. Forty hours of ATT yielded significant improvements in pre- and post-measures of attention. In a somewhat larger study ($n = 33$) by the same researcher, latency-aged children (8 to 12 years of age) diagnosed with ADHD were tested before and after an 18-week period, during which children were divided into a no-treatment control (NTC) group and an treatment group that received 36 sessions of ATT using materials augmented with problem-solving activities developed for adults. Significant treatment group effects were reported for measures of both sustained and executive attention. A cancellation task that involved discriminating between several potential targets showed a 32% improvement for the ATT group versus an 8% increase for the NTC group. An auditory discrimination target counting task showed a 56% ATT improvement versus an 18% improvement for the NTC group. These results represent an average treatment group and pre- and post-assessment effect size of 1.01. Despite the lack of age-appropriate materials, their findings suggest that ATT shows promise as form of treatment for children diagnosed with ADHD.

Thomson and colleagues (24) recognized the need to adapt attention assessment and training materials to the specific needs of children in an age-appropriate fashion. Kerns, et al. (2) used child-appropriate adaptations of the adult APT materials (3) and conducted a randomized active treatment control study of the effects of training sustained and executive attention skills in ADHD children (7 to 11 years of age; $n = 14$). Half the subjects were assigned to APT for 16, 30-min sessions per week over 8 weeks, and half were assigned to a video game control (VGC) group that was assigned to play age-appropriate video games with social praise from the experimenters for an equivalent amount of time. On a measure of sustained attention (Underlining Boxes test) the APT group improved by 32% whereas the VGC group improved only 6%, and on a measure of effortful processing (a Math Efficiency measure based on the number of age-appropriate problems completed within a fixed time), the APT group showed a 55% improvement compared to 20% for the VGC group. At the level of generalization, the APT group showed a greater reduction in teacher ratings of ADHD symptoms than the VGC group, but this difference was only marginally significant ($p < .066$). At the cognitive level, this study demonstrated significant treatment-specific benefits of APT in tasks related to sustained attention and executive attention measures.

Klingberg et al. (25) developed a version of ATT with a central focus on nonverbal working memory skills. Their study evaluated the impact of 25, 30-min sessions of ATT on a group of children with ADHD ($n = 14$, 11 ± 2.5 years of age). The treatment was delivered by computer in an adaptive fashion (i.e., each trial was dynamically adjusted to each child's ability to preserve high success and an element of challenge). In a randomized controlled study in which the assessment team was blind to assignment to "high" dose (experimental) or "low" dose (control) groups, the experimental group ($n = 7$) produced significantly greater gains on cognitive measures of sustained and executive attention reflecting performance on visual-spatial working memory, digit span, and Stroop tasks. Also, the treatment effects were significant for a measure of restlessness: the number of head movements was reduced by 74% in the experimental group, yet increased by 8% in the control group (an effect size of 1.75), which is comparable to the 62% reduction in head movement typically reported following 0.4 mg/kg methylphenidate in a similar paradigm and population (26). However, treatment effects on reaction time latency or variability did not reach statistical significance. An imaging study showed that the working memory treatment was effective in improving activation of brain areas related to working memory (21).

Shalev et al. (27) conducted a study of a version of ATT designed to adaptively challenge children in tasks that required sustained attention, selective attention, spatial orienting, resolving conflict, and dual task management. The study included children diagnosed with ADHD from

6 to 13 years of age randomly assigned to 16 sessions of ATT using the progressive attentional training (PAT) system ($n = 24$) versus a VGC ($n = 17$). Performance on an effortful, timed, passage copying task demonstrated a 48.7% improvement for the ATT group in the number of words copied, whereas the VGC group demonstrated a nonsignificant increase of 1.8%. Most strikingly, parental rating scores for the ATT group were reduced for ratings of inattention (by 23%) and hyperactivity (by 19%), but no significant reduction was found for the VGC group on these pre- and postmeasures assessed by raters blind to treatment condition.

Taken together, these studies provide significant support for the notion that adaptive training of executive function skills and sustained attention skills may positively impact the developing attention skills of elementary school-aged children with ADHD, and such increases may, under some circumstances, generalize to ecologically valid assays of real-world effortful task performance and expression of ADHD symptoms.

ATT FOR PRESCHOOL CHILDREN

Posner and colleagues have recently completed a three-year project funded by the McDonnell Foundation to investigate the impact of ATT on typically developing preschool children (28,29). ATT activities were adapted from a nonhuman primate study by Rumbaugh and Washburn (30) that demonstrated significant gains in attentional abilities of primates following adaptive (i.e., progressive increases in the amount of challenge on sustained attention and other attention skills) computer-based activities. Adapting these procedures for use with preschool children involved creating animated animal characters, and gamelike motivational schemes for a battery of interactive exercises. For example, one activity that required planning and maintaining information over a delay period was reconceptualized as a game of tag between a duck and a cat character, in which the child controlled the cat character, and the duck character would present challenges such as disappearing into a pond in a way that required the child to remember the duck's path, and anticipate and plan for the duck's return. Difficulty was adapted by manipulating the duration of the delay and the relative speed of the two characters in the "tag" game.

To evaluate the impact of these activities on typically developing preschoolers, Rueda and colleagues (18) conducted a randomized controlled trial with two groups of children aged 4- to 5-years old. The study contrasted the impact of 5 days of ATT ($n = 24$) with a randomly assigned control group ($n = 24$) that watched videos with an interactive component. Following training, children in the ATT group showed more adultlike performance in the conflict network of the ANT task than the control children and this performance was also reflected in an event-related

potentials component associated with the ability to resolve conflict. In addition, the ATT group showed a significantly greater pre- and post-change in a preschool analog of the Raven's Progressive Matrices Test, the Kaufman Brief Intelligence Test (K-BIT) Nonverbal IQ score (31), when compared to controls.

This preliminary research demonstrates that computer-based ATT activities developed for adult- and school-aged children can be adapted for use with preschool children. It also provides support for the hypothesis that such training can influence relevant behavior, generalize beyond the training tasks, and influence the underlying attentional network. Thus, it is plausible that ATT might be utilized as a possible intervention for preschoolers with attention problems.

Dowsett and Livesey demonstrated that some forms of ATT might be effectively adapted for preschool children at risk for attention difficulties (32). They studied 47 children (age 3 to 5) that had significant difficulties inhibiting responses during an age-appropriate go/nogo task. Children receiving three sessions of executive function training (dimensional card sort task, change task) demonstrated significant improvements on the go/nogo task, in contrast to both a no-intervention control group and a practice control group that received no training but three sessions of practice on the same go/nogo task.

ATT AND THE CUIDAR PROGRAM

New developments from the cognitive neurosciences about brain plasticity (33) set the stage for a collaboration of investigators at University of California, Irvine (UCI) and the Sackler Institute to investigate ATT, which challenged the consensus views (34). The traditional view has been that ADHD symptoms are due to fixed biological differences (e.g., a dopamine deficit) and that effective treatments (e.g., pharmacological intervention with stimulant medication or even behavioral interventions with token systems) offer "symptomatic relief" but have no carryover benefits and thus must be used chronically.

A new hypothesis purports that ADHD symptoms may be due to inefficient neural networks that could be strengthened during early development by specific experiences delivered by adaptive training (35). A fortunate collaboration between clinicians and scientists at the UCI, Child Development Center, and the Children's Hospital of Orange County (CHOC) provided an opportunity to test the cognitive neuroscience vision of ATT in preschool children at risk for ADHD. In 2000, California Proposition 10 imposed a statewide tax on tobacco products, with the proceeds specifically designated to fund service delivery programs to enhance school readiness. In 2001, a group of clinicians from UCI and CHOC proposed a service delivery program for preschool children at risk

for ADHD, which was labeled the CHOC-UCI Initiative for the Development of Attention and Readiness (CUIDAR), funded by the Children and Families Commission of Orange County.

Parent Groups

CUIDAR is based on application of an early intervention and prevention model for preschoolers with behavior problems suggesting risk for later diagnosis of ADHD. The primary intervention is a once-a-week, 10-session community parent education (COPE) program, which is supplemented by concurrent social skills/child care for the preschool children. After completion of the COPE program, an optional medical clinic evaluation of ADHD is provided. Thus, CUIDAR provides service via a psychosocial intervention (COPE) before diagnosis and consideration of pharmacological intervention. Over the past three years, this approach has been used with over 1500 families, and has been well-regarded by participating families, pediatricians, and schools. The program has been especially well received by the Spanish-speaking Latino/Hispanic population, a group that underutilizes behavioral health services. A discussion of issues related to designing and implementing the CUIDAR model is provided by Tamm et al. (36). Preliminary information from the start-up experience (rather than a controlled clinical trial), show that parents report overwhelming satisfaction with the program, significant gains in parenting skills, and a reduction in child behavior problems.

Parent education was selected as the main method of intervention because it has a long history of demonstrated efficacy in reducing child behavior problems (37–42). This psychosocial intervention is also more acceptable to parents and professionals than pharmacological intervention, in part due to the weaker evidence base for the efficacy of medication at this age, and the potential of greater side effects of medication in young children (38,40,42). While many different approaches to teaching parenting skills have been shown to be effective, most approaches teach a similar curriculum based on behavior modification and social learning principles.

In the COPE model (43,44) parenting skills are taught in a unique, interactive approach to a group of 20–25 parents. The large group is subdivided by the COPE facilitator into small discussion groups of 4–5 parents, and these groups are systematically led through the COPE curriculum that focuses on teaching the following parenting strategies: (1) praise and attending, (2) rewards, (3) planned ignoring, (4) transitional warnings, (5) when-then statements, (6) planning ahead, (7) point systems, (8) time out, (9) time out from reinforcement—loss of privileges, and (10) problem solving. A primary feature of each COPE session is watching a videotaped vignette of a parenting error related to a topic of the curriculum, followed by a discussion within the small groups to identify the error and to offer

suggestions for more appropriate parent–child interaction in that context. The COPE facilitator uses the group-generated solutions (1) to model appropriate parent behavior, (2) to demonstrate situations in which the strategies could be applied, (3) to practice in role-playing exercises, and (4) to propose homework for home implementation of the strategy before the next session.

Child Groups

The CUIDAR program provides a social skills intervention for children while their parents participate in the evening COPE parenting groups. The child groups follow a specific structure with a focus on prosocial behaviors. Components of the group structure include: (1) settling activity (story/coloring), (2) circle time (games/songs), (3) introduction of a social skill (using puppets), (4) role play of social skill (also using puppets), (5) activity time, (6) snack time, (7) movie. Throughout, a reward-based point system is used to promote positive behavior. The social skills covered in the 10-week program include following the rules of the "red sign" (observing a "red sign" for silence or required hand-raising to speak), listening and participating, ignoring, sharing, saying nice things, "calm body," and helping others. Debriefing with an experienced COPE facilitator occurs after each group to facilitate communication between the childcare/social skills providers and group leaders, and to allow problem solving for managing more difficult children.

ATT in CUIDAR

CUIDAR delivers services annually to about 700 families with preschool children at risk for ADHD (see www.CUIDAR.net). This provided an infrastructure to work directly with the children in these child care groups (while their parents attend the traditional COPE parent training groups) and created an opportunity to develop materials for ATT. Our goal was to develop and refine ATT materials to make the "games" appropriate for at-risk preschool children, and eventually to test the hypothesis that neural networks of attention (i.e., alerting and executive control as defined by Posner) can be strengthened by targeted adaptive training, as proposed by McCandliss for an intervention for children with reading disorders (35). The Sackler Institute and the Orange County Proposition 10 Commission provided start-up funding to adapt the materials initially developed for ATT in normal toddlers (28) for use with the preschool children at risk for ADHD, and a grant from the National Institute of Child Health and Development (NICHD) provided funds to conduct a pilot project with the CUIDAR families. Subsequent NIH applications have not been well received, perhaps due to the perception that this approach to implement and evaluate a program to prevent or "cure" ADHD is too radical.

The CUIDAR team focused on modifying the ANT task to be appropriate for preschoolers, since their performance was at approximately chance levels on the school-aged ANT (18). A preschool-appropriate ANT version was developed that assesses alerting, orienting, and executive control, and that has good test–retest reliability. This allows the ANT to be employed as a "probe" task of functioning levels of the attentional network components.

As part of an integrated development plan to create a more direct link between targeted cognitive skills and ATT modules, our team designed new training tasks to impact alerting and executive control. We created prototype versions of computer applications to reinforce and challenge preschoolers' ability to sustain attention and resolve conflict.

Alerting

The alerting activity involves a simple goal of attempting to wait and remain in a ready-to-respond state for an extended period of time, in order to rapidly respond to an infrequent and very brief event. In adapting this paradigm for children we created a "fly-catching" character, "HippityHop, the frog." Children are instructed to help "HippityHop" by pressing the space bar to catch as many flies as fast as they can from a jar, but they must also follow two rules: (1) the button can only be pressed when the flies exit the jar, (2) the child must wait for the fly despite an auditory cue (buzzing) on some trials. Children are told that in some trials they will hear a buzz before the fly exits the jar but they are still to withhold their response until after the fly exits the jar. The game is adaptive in that the "catch" time changes to maintain a success rate of 50% for the uncued (nonbuzzing) flies. It also slowly lengthens the wait time as children successfully catch the flies at a higher rate.

Executive Control

Similar adaptations and programming were used to produce a conflict resolution task based on the dimensional change control task (DCCT) paradigm (45). The DCCT paradigm was used to design a preschooler's game, using a character called Monster Zoo Keeper whose task it is to feed the monsters. On each trial the child is given an object and must decide which of two monsters should eat it, a truck-eating monster that likes red things, or a flower-eating monster that likes blue things. The rules whether the monsters are hungry for colors or hungry for shapes vary (i.e., during the day, the monsters are hungry for colors, and during the evening for shapes). Adaptive algorithms adjust the frequency of the rule change and the number of items that pose a direct conflict between the stated rule and recently reinforced, but currently inappropriate, decision responses.

We performed a pilot study to investigate the feasibility of implementing a randomized clinical trial with children of parents participating in the

CUIDAR COPE groups, as well as to test the feasibility of using the initial modules we developed for our version of ATT and a control task. We screened commercial video games from the Children's Software Review database (www.childrenssoftware.com), which reviews over 2500 video games, and chose Atari's "Tonka Firefighter" as an appropriate VGC example for comparison to ATT (e.g., "Hippity Hop" frog game and monster zoo game). In the Tonka Firefighter game, children play the role of a firefighter and help save the day by choosing and controlling a vehicle such as a fire truck, chopper, pump truck, or fire dozer. Children chose from a variety of activities such as saving stranded kittens, putting out blazing fires, cleaning up parks, and creating a fireworks show. Children were randomly assigned to an ATT group ($n = 14$, 5 sessions with the Alerting task) or a VGC group ($n = 13$, 5 sessions with the Tonka Firefighter game). The preschool version of the ANT task was administered pre and post.

The outcome of our initial feasibility study confirmed our experience and those of others of the benefits of ATT over VCG, and demonstrated that our ATT intervention in preschool children results in improvements after just 5 sessions that are about the same magnitude as those reported in the literature on elementary school-aged children with ADHD. The results of our initial pilot study will be presented in a later publication by our group. We utilized our experience with the feasibility study to modify and refine the prototypes of the alerting and executive control tasks. For example, additional "skins" and related "cover-stories" were developed so that the key task elements and paradigm are preserved, but the surface level of the task modified to be interesting for a child performing the task several times.

We are now conducting a randomized clinical trial to investigate the specificity of the alerting and executive control tasks. Preschool children in the CUIDAR childcare groups have been randomly assigned to an alerting training (AT) group ($n = 9$) or an executive control (EC) training group ($n = 8$). Each group is receiving 6 ATT sessions with the alerting task or the executive control task, respectively. The preschool ANT task and the KBIT administered pre and post will serve as primary outcome measures, and we anticipate that the ANT alerting scores will be improved for the AT group and the ANT executive control scores will be improved for the EC group. We are also exploring whether these tasks can be adapted upwards to be age appropriate for a school-aged population (ages 7 to 12), and utilized as a treatment for ADHD.

CAN ATTENTION BE TRAINED?

Although far from conclusive, it does appear that attention can be trained. Further, it appears that ATT can be adapted successfully for preschoolers,

and has promising evidence as an intervention for children at-risk for or diagnosed with ADHD. Future studies should examine the specificity of ATT tasks, utilize imaging techniques to explore the impact of ATT on brain function, and investigate whether attentional gains are generalizable to other settings.

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Psychiatry

McBurnett and Pfiffner bring you the most wide-ranging and up-to-date compilation of current knowledge and opinion in ADHD. From a 21st century perspective, the collection covers the basics but emphasizes new ideas and diverse viewpoints.

about the book...

Compiling the expertise and research of many of the most widely cited opinion leaders in the field, ***Attention Deficit Hyperactive Disorder: Concepts, Controversies, New Directions*** is insightful and thought-provoking. Written as an intermediate-to-advanced text, it explores the essential topics of this disorder including: neuroscience, medication and psychosocial treatments, special populations, controversies, and public policy.

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- presents emerging treatment innovations such as attention training, organizational skills training, and specialized treatment for ADHD, Predominantly Inattentive Type

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