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Advances and Technical Standards in Neurosurgery

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Volume 13

Springer-Verlag
Wien New York 1986

With 77 partly colored Figures

Softcover reprint of the hardcover 1st edition 1986

Library of Congress Catalog Card Number 74-10499

ISSN 0095-4829
ISBN-13:978-3-7091-7473-9 e-ISBN-13:978-3-7091-7010-6
DOI: 10.1007/978-3-7091-7010-6

Preface

As an addition to the European postgraduate training system for young neurosurgeons we began to publish in 1974 this series devoted to Advances and Technical Standards in Neurosurgery which was later sponsored by the European Association of Neurosurgical Societies.

The fact that the English language is well on the way to becoming the international medium at European scientific conferences is a great asset in terms of mutual understanding. Therefore we have decided to publish all contributions in English, regardless of the native language of the authors.

All contributions are submitted to the entire editorial board before publication of any volume.

Our series is not intended to compete with the publications of original scientific papers in other neurosurgical journals. Our intention is, rather, to present fields of neurosurgery and related areas in which important recent advances have been made. The contributions are written by specialists in the given fields and constitute the first part of each volume.

In the second part of each volume, we publish detailed descriptions of standard operative procedures, furnished by experienced clinicians; in these articles the authors describe the techniques they employ and explain the advantages, difficulties and risks involved in the various procedures. This part is intended primarily to assist young neurosurgeons in their postgraduate training. However, we are convinced that it will also be useful to experienced, fully trained neurosurgeons.

The descriptions of standard operative procedures are a novel feature of our series. We intend that this section should make available the findings of European neurosurgeons, published perhaps in less familiar languages, to neurosurgeons beyond the boundaries of the authors countries and of Europe. We will however from time to time bring to the notice of our European colleagues, operative procedures from colleagues in the United States and Japan, who have developed techniques which may now be regarded as standard. Our aim throughout is to promote contacts among neurosurgeons in Europe and throughout the world neurosurgical community in general.

We hope therefore that surgeons not only in Europe, but throughout the world will profit by this series of Advances and Technical Standards in Neurosurgery.

The Editors

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A. Advances

Present Status of Lasers in Neurosurgery

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The application of laser technology to medicine and surgery has lagged behind industrial, recreational and military development. Acceptance has been slow in neurological surgery until refined technology was developed and skilled investigative surgeons recognized the potential for this new technology when applied with microscopic principles. Creative approaches, applications and remarkably improved results have been achieved. Yet we are probably only in an infantile stage of development of the potential of the

myriad of applications of laser energy in Neurosurgery. In this chapter, we will review the currently accepted technology, applications and practical results which have been achieved.

History and Evolution of Laser Neurosurgery

The first laser was produced in 1960 by Maiman utilizing a ruby crystal[64]. Early investigators studied the effects of ruby laser energy on neurological tissues in experimental animals[12, 13, 26, 52]. Rosomoff used pulses of ruby laser energy in three patients with glioblastoma in 1966[53]. This laser was abandoned for the more powerful carbon dioxide laser developed in 1964 by Patel[45]. Stellar used the experimental carbon dioxide laser to define the characteristic histological lesions produced by various amounts of energy[56]. He reported the first application of the carbon dioxide laser in patients with glioblastomas in 1969[64]. In the same year, Takizawa began experimentation and development of carbon dioxide laser systems in Japan[60, 61]. Ascher and Heppner reported their first clinical experience with the carbon dioxide laser in 1976[3–5, 32] and Beck began experimentation and clinical application of the Neodymium : YAG laser in 1977[7, 8]. Laser neurosurgery education courses were initiated in the United States by Cerullo in 1980[11]. By 1984, the surgical laser had become an indispensible tool in many neurosurgery centres around the world[5, 7, 18, 28, 30, 33, 39, 40, 44, 51, 58, 62–64]. The carbon dioxide laser is now the most commonly used laser in neurosurgery. At the present time the Nd : YAG and argon lasers are not available for clinical neurosurgical use in the United States except by those individuals who have an investigational device exemption authorized by the Food and Drug Administration. Other lasers which are currently under experimental evaluation include tunable dye lasers and free electron lasers.

Principle of Laser Function and Application in Biological Tissues

Laser is an acronym which stands for Light Amplification by the Stimulated Emission of Radiation. Laser light is produced by electrical stimulation of the active medium, *i.e.,* carbon dioxide (gas), or Nd : YAG crystal (solid), which results in electron transitions to higher energy states in the molecules of the medium. These energized molecules spontaneously revert to an unenergized or ground state, in a decay process in which photons are emitted. These photons are captured, modified and form the laser beam (Fig. 1). The laser beam is transmitted either to the surgeon for free-hand application, or attached to the operating microscope where it can be manipulated by the surgeon or by a microprocessor[14]. The carbon dioxide laser has physical wavelength characteristics which currently proscribe transmission by a fibre-optic system. Thus the carbon dioxide beam is reflected via a series of interlocking hollow tubes and mirrors to the microscope. Inability to transfer the carbon dioxide beam is a practical

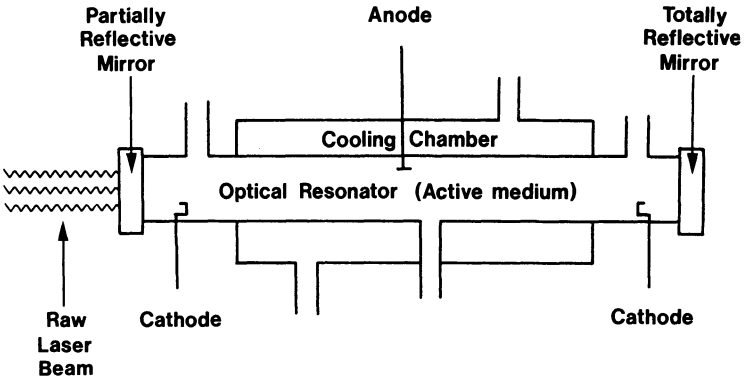

Fig. 1. Schematic illustration of gas laser. The active medium is contained within the optical resonator. High voltage stimulation results in molecular excitation. In the decay process these molecules emit photons and this process is called stimulated emission. The photons are captured and form the laser beam. (From Ref. 64)

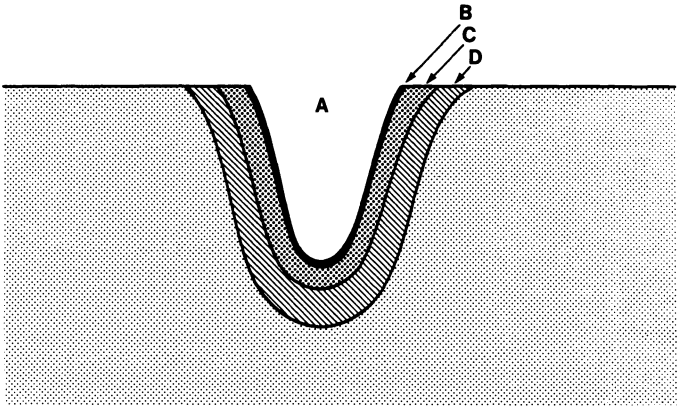

Fig. 2. Morphology of a laser lesion. *A* Central crater. *B* Charred mantle. *C* Dessication zone. *D* Oedema zone. The actual size and relative proportion of each zone varies according to power setting, mode of application, and laser. (From Ref. 64)

handicap which will probably be solved by the development of more efficient fibre bundles. The Nd : YAG laser and argon laser beams utilize quartz fibre-optic delivery systems[46–48, 55, 57].

Laser energy exerts its destructive effect on biological tissues by a thermal reaction created by excitation of vibrational and rotational levels of matter[46]. Concentric zones of tissue injury are formed by laser impact (Fig. 2). These include a central crater formed by the instantaneous superheating and vapourization of cellular contents where temperatures

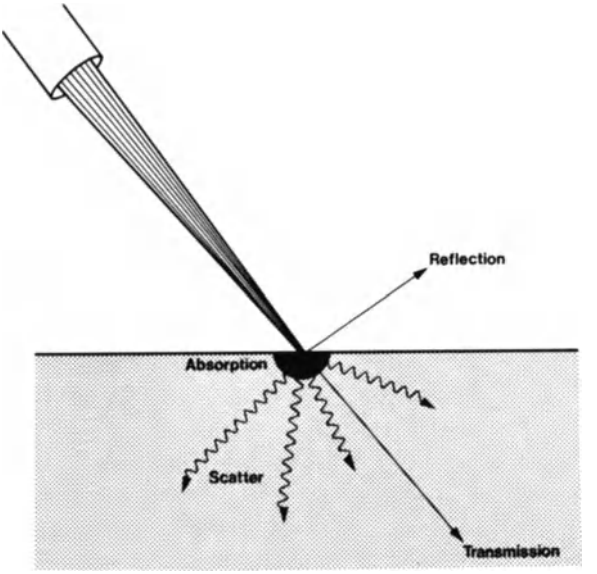

Fig. 3. Diagram of laser-tissue interaction. The tissue effect for the application of a specific laser will be one or a combination of reflection, absorption, scatter and transmission. The effect is determined primarily by the type of laser, and the biological properties of the tissue. The factors which influence tissue reaction are optical density, cellular composition, water content, temperature and pigmentation. (From Ref. 64)

reach several hundred degrees centigrade at the point of impact. The inner layer of damaged tissue consists of a charred mantle of cellular debris, surrounded by a zone of desiccated tissue, and the outermost zone consists of edematous but viable tissue[2, 6, 67]. Four characteristic reactions occur when laser energy is applied to biological tissue. These are reflection, absorption, scatter, and transmission (Fig. 3). The degree to which these effects occur varies with each laser and this characterizes the unique properties of the individual laser wavelength.

The nature of the lesion is also determined by the optical and biological properties of the target tissue. These properies are influenced by the cellular composition, water content, pigmentation and vascularity of the tissue. Current studies are evaluating the optical properties of pathological neural tissue[16, 20].

Neurosurgical Lasers

Carbon Dioxide Laser

Carbon dioxide laser energy has a wavelength of 10.6 microns which is located in the far infrared region of the electromagnetic spectrum (Table 1).

Table 1. *Characteristics of Commonly Used Neurosurgical Lasers*

	CO_2	Nd:YAG	Argon
Wavelength (microns)	10.6	1.06	0.488–0.514
Electromagnetic spectrum	far infrared	near infrared	visible (blue-green)
Power range (watts)	1–100	1–100	1–20
Pigment-dependent	no	yes	yes
Scatter (tissue)	low	high	medium
Absorption (tissue)	high	low	medium
Transmission (water)	no	yes	yes
Mode	CW, pulsed, super pulse	CW, pulsed, Q-switched	CW, pulsed
Delivery system	articulated arm micromanipulator	fiberoptic cables micromanipulator	fiberoptic cables micromanipulator

Therefore, the beam is invisible, and for clinical application these lasers must be equipped with a coaxial helium-neon pilot laser beam. Carbon dioxide energy is characterized by near total surface absorption, a fact which makes it a valuable instrument for ablative purposes (Fig. 4). The carbon dioxide laser is particularly applicable to neurosurgery because it efficiently vaporizes tissues. The effect is superficial; ablation is restricted to the tissue which the surgeon can directly visualize. Carbon dioxide laser energy is not selectively absorbed by pigmented tissue and therefore its biological effect is not enhanced by vascular or pigmented tissue. Because of superficial absorption of the carbon dioxide laser beam, it is rendered ineffective in a field flooded by water or blood. This property can be used to one's advantage to insure safe application of the laser. Water soaked cottonoids placed on important structures such as nerves and arteries serves to protect them while adjacent tissue is vapourized (Table 2).

The carbon dioxide laser beam can be focused by lenses to a fine point of 250 microns concentrating the energy to a very high power density (expressed in watts/cm^2). The focused beam then functions as a scalpel to sharply incise tissues to any desired depth. Defocusing enlarges the spot size, diffuses the power and converts the laser to an ablative instrument which vapourizes tissue mass. A further increase in spot size and subsequent

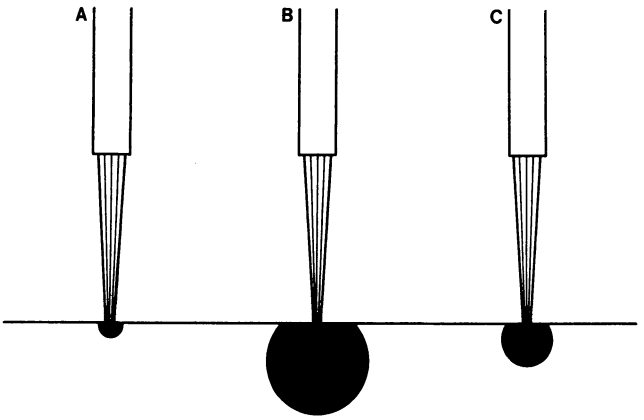

Fig. 4. Relative laser-tissue interaction. A) Superficial effects of absorption dominated, low scatter CO_2 laser. B) Deep tissue effect of the scatter-dominated low absorption Nd : YAG laser. C) Intermediate effects of the medium-absorption, medium-scatter argon laser. (From Ref. 64)

Table 2. *Advantages and Disadvantages of the Carbon Dioxide Laser*

Advantages	Disadvantages
High power for tissue ablation	lack of fibre-optic cables for beam transmission
No touch vapourization	non-transmission through water and blood
Precise microscopic control	requires co-axial pilot laser
Minimizes brain retraction	
Decreases blood loss	
Minimizes tissue manipulation	
No electrical interference with monitors	
Protective effect of water	
Micromanipulator attachment	

reduction in power density, enables coagulation of capillaries and small blood vessels. A finely focused beam at very low powers applied continuously, or intermittently, provides a precise microscopic tool capable of vapourizing minute fragments of tissue from vital nerves and vascular structures. Precise control of power density and manipulation of the beam is required to avoid undesired injury to critical structures. A power density that is too high may injure a vascular structure and cause uncontrollable haemorrhage. Considerable experience is required to develop a sense of stereoscopic control of the laser's potential destructive force. In neurosurgery, the principal application of the carbon dioxide laser is in microsurgical

procedures where access is limited, the tissue is calcified, vascular, or entangled by eloquent tissue. Micromanipulators which contain focusing lenses attach to the microscope and provide cursor control of the visible coaxial helium-neon beam. These microscopic attachments adapt to any operating microscope and do not significantly encumber the function of the equipment. The most advanced systems contain an infinitely variable spot size, variable focal length and analog-computed power density[15]. A microprocessor can be programmed in a multi-dimensional configuration of the target and the laser will precisely ablate the delineated structure under microscopic stereotaxic control[14].

Milliwatt carbon dioxide lasers are capable of generating very small spot sizes, of 150 microns yet are capable of achieving enormous power density. These small units can be directly attached to the microscope for reconstructive welding and ultra-precise surgical feats[41]. The theoretical basis for tissue welding can be explained by lysis of intermolecular collagen bonds, which occurs at precisely controlled, low temperatures. On cooling new bonds are formed and welding of tissue surfaces may be accomplished[64]. Apposition of divided ends of a vessel may facilitate anastomosis with a minimum number of sutures. This process can coapt neural and dural tissues. Conventional large carbon dioxide lasers lack the fine power control necessary in the lower ranges of operation for welding. A milliwatt laser can be purchased as a separate unit, or an attachment can be added to the carbon dioxide laser. The theoretical advantages of these milliwatt systems for anastomosis have not been substantiated in practical application, thus no significant body of human experience has accumulated in the application of this laser. The clinical effectiveness of these new applications are ready for documentation.

Nd : YAG Laser

The Nd : YAG laser is a solid state laser which emits invisible light with a wavelength of 1.06 microns and is located in the near infrared region of the electromagnetic spectrum (Table 1). This wavelength is associated with tissue scatter and minimal absorption (Fig. 4). Because of this, Nd : YAG energy penetrates more deeply into the target tissue producing a deep thermal effect which results in shrinkage, coagulation, and necrosis of tissue 4 to 6 mm below the surface. The coagulation effect is enhanced by the preferential absoption of the laser energy by pigmented, especially heme-pigmented, tissues. These properties combine to make the Nd : YAG laser a potent coagulative device. It has some ablative effect, but is markedly less efficient in vapourizing tissue than the carbon dioxide laser. Nd : YAG energy is thoroughly transmissible through water, so that it can be used effectively in a fluid filled cavity. Nd : YAG energy is transmissible through thin quartz fibres which greatly enhances its delivery to the tissue surface.

Because of these combined properties, neurosurgical endoscopy is possible with the Nd:YAG laser. Treatment of intraventricular tumours and stereotaxic surgery are currently under investigation with these techniques[27, 35, 49]. Nd:YAG lasers generate up to 100 W of power. The quartz fibres may attached to a micromanipulator or may be used free-hand under the microscope. The fibres may be directed through a conventional suction tip or focussed by a lens apparatus[59]. Absorption is greatest in vascular or pigmented tissue, a factor which enhances the removal of vascular lesions (Table 3).

Table 3. *Advantages and Disadvantages of the Neodymium: YAG Laser*

Advantages	Disadvantages
High power	precise depth of scatter is unpredictable
Potent deep tissue coagulation	poor ability to vapourize tissue
Fibre-optic transmission	requires co-axial pilot beam
Transmission through water	
No electrical interference with monitors	
Differential absorption by blood vessels	

The integrated use of the carbon dioxide and Nd:YAG lasers for simultaneous vapourization and coagulation has been reported[23, 24]. Combined carbon dioxide and Nd:YAG lasers are commercially available but have gained little clinical acceptance. Separate units can be easily used together during the same procedure.

Reports in the literature agree that the Nd:YAG laser is superior to the carbon dioxide laser for the surgery of haemorrhagic tumours, especially angioblastic meningiomas, haemangioblastomas, and glomus tumours[7, 27, 59, 63] but there is some controversey about the effectiveness of Nd:YAG laser for vascular malformations in contrast to the standard bipolar coagulation technique[22, 25, 68]. The accrued clinical experience is insufficient to render a judgment at this time, but we also believe that the use of Nd:YAG microsurgical techniques, in combination with neuroradiological interventional techniques with cyanocrylate or particulate embolization, will ultimately improve the outcome in the surgery of vascular malformations.

Further controversy exists in the literature about the safety of the application of Nd:YAG energy because of its unpredictable depth of

penetration[55, 64, 70]. This has led to the reluctance on the part of many to use this laser. One must certainly consider the effect of this laser if used in the para- and suprasellar regions, or in the posterior fossa where cranial nerves may be only millimetres from the target tissue. A recent report by Yamagami in 1984 attempted to address this issue by studying histological changes with the application of various amounts of Nd : YAG energy[70]. They report injury limited to 6–10 millimetres with standard amounts of energy one might use. But further caution is necessary since Toya *et al.* in 1980 demonstrated physiological disturbance beyound the extent of histological changes in the application of the carbon dioxide laser[65] and Boggan *et al.* in 1982 showed disruption of the blood brain barrier up to 2 mm from the margin of the laser lesion[10]. Such studies for Nd : YAG energy have not been published.

Contradictory reports in the literature and claims about the superiority of the carbon dioxide laser or the Nd : YAG laser may confuse the student of laser neurosurgery[5, 8, 31, 63]. Our assessment is that these lasers function in a complementary fashion. However, most institutions will not have the luxury of both the carbon dioxide and Nd : YAG laser for use. It is our opinion at this time, that the carbon dioxide laser has a broader clinical applicability for neurosurgical use if a choice is necessitated. While enthusiasm for the continued development of Nd : YAG laser application remains high, one must exercise extreme caution when using this laser near vital structures. It does not provide the precise microdissection capability possessed by the carbon dioxide laser. It is, however, a superior coagulation instrument.

The Argon Laser

The argon laser produces a visible blue-green light with a wavelength range of 0.488–0.514 microns (Table 1). This does not require a coaxial pilot beam. Production of this energy is more inefficient than carbon dioxide or Nd : YAG energy; maximum power output in present systems reaches a mere 20 watts. This laser is intermediate in function between the carbon dioxide and Nd : YAG lasers (Fig. 4). It possesses better coagulative abilities than the carbon dioxide laser, and can vaporize tissue better than Nd : YAG energy. Its absorption is pigment dependent, and therefore it is a more efficient laser when used on pigmented tissue. It is a very precise dissecting instrument because of its ability to achieve high power density and small spot size (Table 4). For example, both the argon laser and the carbon dioxide laser have been successfully used to create dorsal root entry zone (DREZ) lesions for pain relief[38, 50]. This laser may become a very valuable tool for endovascular-reconstruction. The literature contains a few excellent reviews of the argon laser in neurosurgery[18, 19, 29, 50].

Clinical Experience with Neurosurgical Lasers

The carbon dioxide laser was first used at our department in late 1981 and the Nd : YAG laser was added in early 1984. Our cumulative experience has reached 215 cases. In the majority of these cases, the carbon dioxide laser was the only laser used. Table 5 classifies our case experience thus far.

In evaluating a patient for laser surgery we assign each to one of three categories based upon our criteria of indication for laser application. These categories are: the laser is unequivocally necessary; helpful but not essential, and the last is one in which the laser provides no advantage to the patient. We have found that the laser is absolutely indicated in basal

Table 4. *Advantages and Disadvantages of the Argon Laser*

Advantages	Disadvantages
Coagulates and vapourizes	lower power
Fibre-optic transmission	inefficient
Small spot size	
No pilot beam required	
Transmission through water	
No interference with electrical monitors	
Precise microscopic control	
Micromanipulator	

tumours, including meningiomas, acoustic neuromas, chordomas, para- and suprasellar tumours. The carbon dioxide laser is absolutely indicated in very firm tumours which require significant manipulation for removal by other techniques. These tumours could be located anywhere in the neuroaxis. An example of this is a densely calcified meningioma of the convexity. The laser is also indicated in the removal of previously radiated, fibrotic pituitary tumours. The carbon dioxide laser, because of its precision, is indicated in the removal of all spinal cord tumours, especially intramedullary, intradural and foramen magnum region tumours. The Nd : YAG laser is absolutely indicated in the removal of vascular tumours, such as glomus tumours, haemangioblastomas, angioblastic meningiomas, and some metastatic tumours.

Relative indications for carbon dioxide and Nd : YAG laser are pituitary tumours. Hemostasis by coagulation of the dura by both lasers can be accomplished, but more easily with the Nd : YAG laser. In many cases, the laser facilitates pituitary tumour removal. In any patient where blood loss is a critical factor because of medical condition or religious beliefs, the laser may be of significant benefit.

Table 5. *Cumulative Experience with the Carbon Dioxide and Nd: YAG Laser in Tumours and Vascular Malformations over a Three-Year Period*

Intracranial tumours	
acoustic neuromas	32
glial tumours	24
meningiomas	48
metastases	14
miscellaneous	20
Transsphenoidal approach	
adenomas	44
craniopharyngiomas	3
chordomas	5
intrasellar cyst	1
Arteriovenous malformations	9
Spinal tumours	
meningiomas	3
extradural metastases	3
chordomas	2
haemangioblastoma	2
miscellaneous	5
Total cases	215

There is no indication for the use of the laser in the excision of superficial, non-vascular tumours. However, the inexperienced surgeon may first develop his laser skills with these less critical cases.

The following case summaries represent categories where we find the laser to be indispensable. The discussions further emphasize the salient features of laser application.

Basal Meningioma

A 60-year-old surgeon developed temporal lobe seizures and was found to have a large, densely calcified, left sphenoid wing meningioma (Fig. 5). The surface of the tumour was easily exposed but very firm. Without any tugging or pulling, the tumour was vapourized in a no-touch technique. After partially debulking this tumour, a branch of the middle cerebral artery and, further medially, the M-1 trunk, were found to be encased by the tumour. Recognition of these vessels enabled preservation and vapourization of tumour from these vessels. The central portion of this tumour was rock-hard. The lesion could not be evacuated by mechanical force. The powerful carbon dioxide laser gently vapourized this tumour and its dural

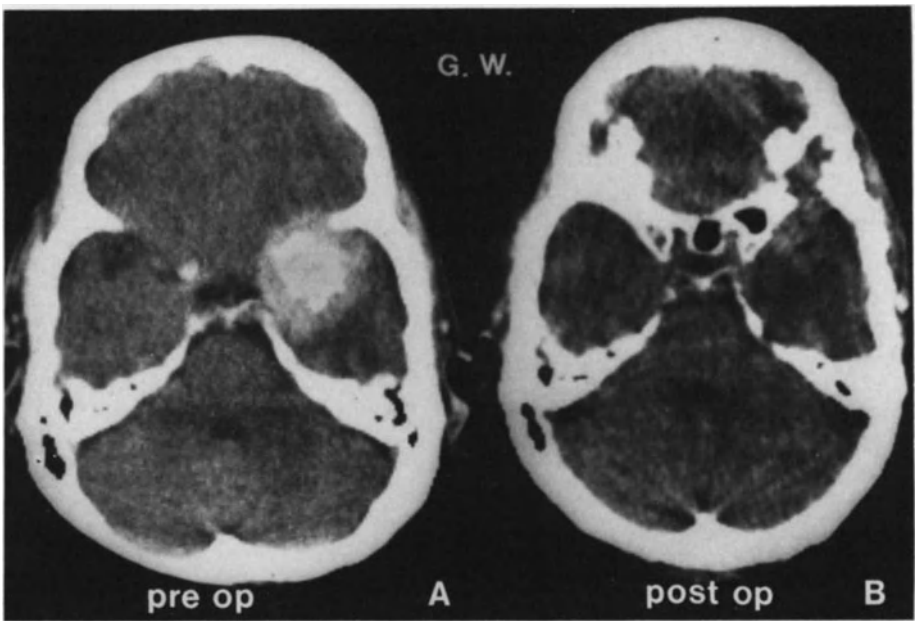

Fig. 5. Densely calcified sphenoid wing meningioma. A) Preoperative, note the densely calcified central portion. B) Post-operative

origin along the medial sphenoid wing and cavernous sinus. Post-operative CT demonstrates complete removal of the lesion (Fig. 5). The patient was neurologically intact post-operatively and there is no evidence of recurrence in two years.

A 28-year-old male noted progressive hearing loss in his left ear over a nine-month period. Two months prior to admission, he developed morning headaches and left facial paraesthesias. On examination, the patient had left facial hypalgesia, diminished left hearing, nystagmus and ataxia of tandem gait. CT scan disclosed a massive left cerebellopontine angle tumour (Fig. 6). Audiogram disclosed a moderate neurosensory hearing loss (Fig. 7). At surgery, a meningothelial meningioma was debulked using maximum laser powers of 80 watts in slightly defocused mode. The technique employed incision of the capsule, followed by application of a circular sweeping motion of the laser beam producing a coring effect in this tumour. The pressure of the tumour and compressed brain collapsed the tumour and its capsule inward and enabled progressive debulking and total removal. The cranial nerves were easily identified and separated from the capsule. The dural attachment was vapourized with the laser (Fig. 8). The patient's hearing improved; his nystagmus, headaches, and facial paraesthesias resolved (Fig. 7). It is important to be mindful of the unquantifiable effect of heat conduction during the continuous application

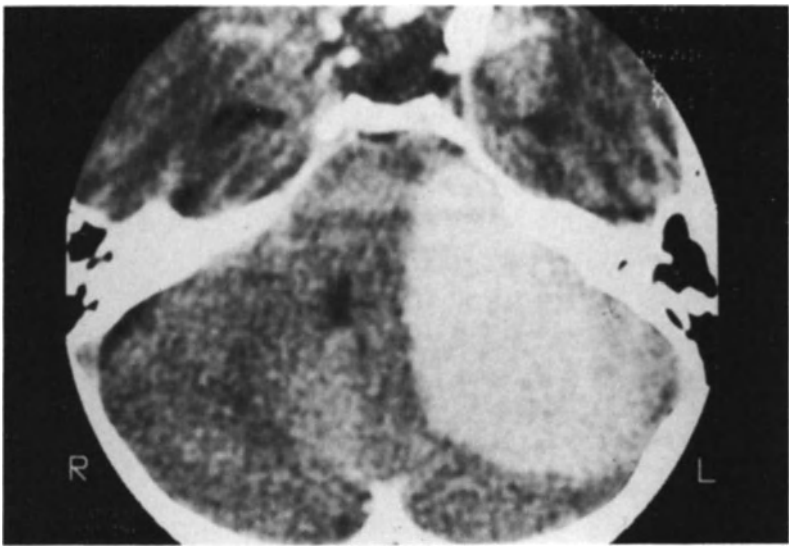

Fig. 6. Massive left cerebellopontine angle meningioma

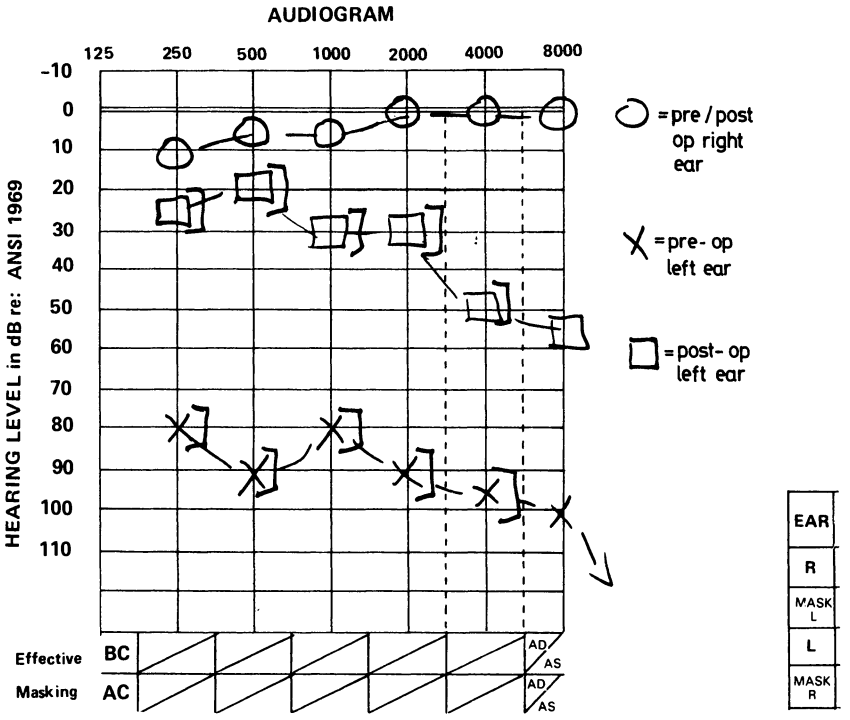

Fig. 7. Composite audiogram demonstrates post-operative hearing improvement

of laser energy in these large tumours. Therefore, we frequently pause and irrigate with saline to dissipate this heat.

A 25-year-old woman developed headaches and intermittent paraesthesias of the upper extremities. Examination disclosed hyperreflexia and clonus, but no other deficits. CT scan showed a large foramen magnum region tumour (Fig. 9) which was exposed by a lateral suboccipital craniotomy and upper cervical laminectomy. The vertebral artery was

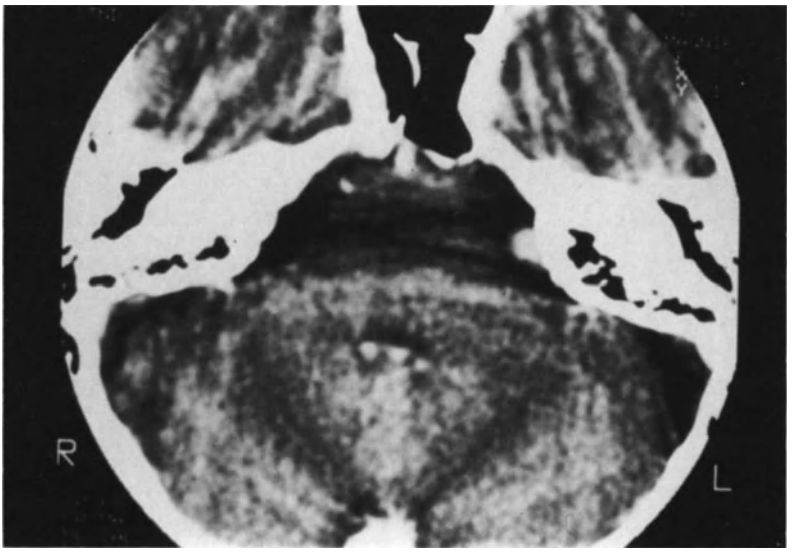

Fig. 8. Post-operative CT demonstration of complete tumour removal

encased and intentionally sacrificed. The dural attachments of the tumour anterior to the medulla and upper cord were vapourized with a finely-focussed, low-powered (3–5 watt) carbon dioxide laser beam. This meningothelial meningioma was easily separated from the cord and medulla, and completely removed with carbon dioxide laser vapourization. The patient has been symptom-free since surgery and CT scan indicates its complete removal (Fig. 9). The advantage of the laser in this case is its precision in vapourization of tissue in a region of narrow access. The no-touch laser eliminates the use of punches and dissectors in these small areas which interfere with vision and it also eliminates the risk of inadvertent manipulation of the cervical cord or lower medulla. Again, this meningioma was partially calcified and firm, making its removal by more traditional techniques highly risky. Recurrent meningiomas may be highly vascular, fibrotic and infiltrate the cord. Removal can be accomplished only with

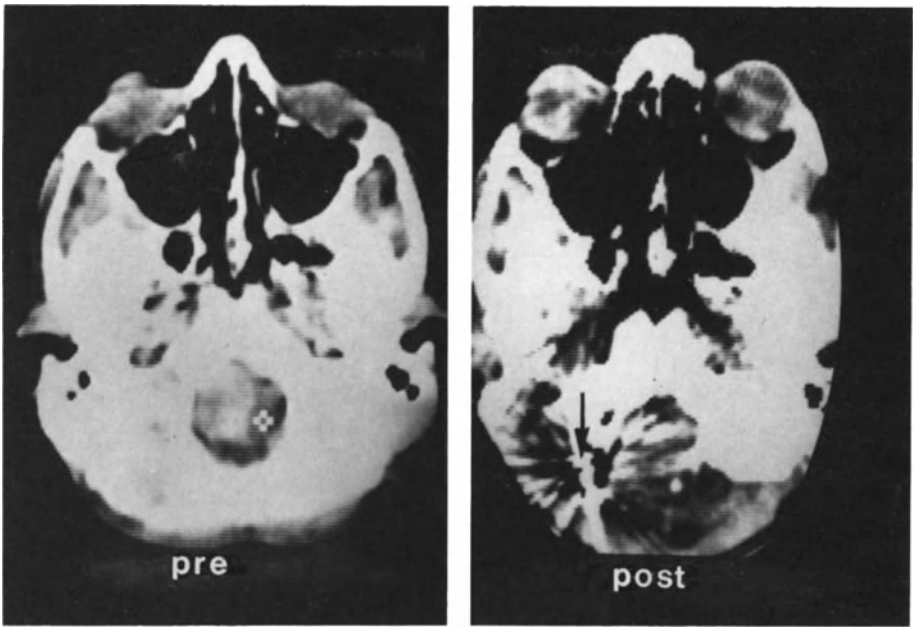

Fig. 9. Pre- and post-operative CT scans of foramen magnum meningioma. There is scatter artifact from metallic clips on the post-operative CT (arrow)

laser techniques. In contrast to our technique with the carbon dioxide laser, Beck *et al.* in 1984 review their experience with Nd : YAG laser in tumours of the forament magnum region[9].

Acoustic Neuromas

Surgical removal of acoustic neuromas is one of the major applications of laser technology. Rapid debulking can be achieved without traction or transmission of heat to surrounding nerves, arteries or the brain stem. Electrical interference with evoked potential monitoring is eliminated and delicate dissection of the tumour capsule from critical structures can be achieved with phenomenal ease. Many of our acoustic patients have been operated on because the referring surgeon was unable to totally remove the residual capsule from the brain stem. Moreover, haemostasis is no problem, even in the prone position, because of their usual modest vascularity where the carbon dioxide laser offers effective coagulation. Routine monitoring of brain stem evoked potentials and facial nerve function has remarkably aided our ability to preserve neurological integrity.

An elderly 66-year-old female with deafness, fifth nerve palsy and severe ataxia was found to have a large acoustic neuroma indicating a tumour extending from the tentorial incisura to the foramen magnum (Fig. 10).

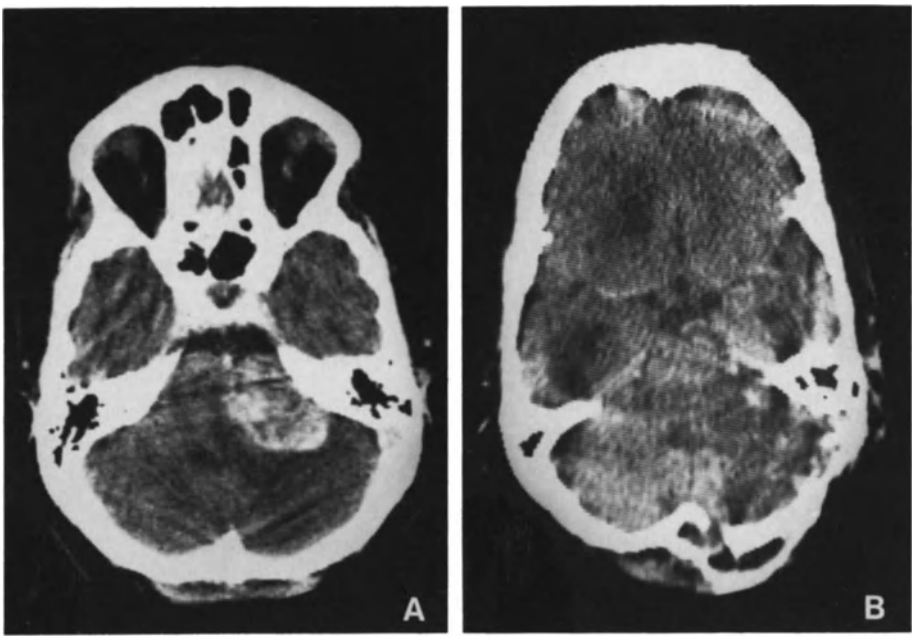

Fig. 10. A) CT scan demonstrates left acoustic neuroma. B) Post-operative tumour removal

Exposure was gained laterally through a suboccipital craniectomy. Small capsule vessels were easily coagulated by the laser. A suction was used to aspirate the laser plume, which contains vapourized debris but no viable tumour cells, and cerebrospinal fluid which intermittently enters the tumour bed. Importantly the suction also functions as a palpating instrument. This helps one to recognize the deep margin of the tumour so that unintentional laser perforation of a critical deep structure may be avoided. In this case, the tumour capsule was dissected from the brain stem and the post-operative CT shows no residual tumour (Fig. 10).

Transsphenoidal Approach to Sellar and Midline Basal Tumours

Both the carbon dioxide and Nd:YAG lasers are effective in the transsphenoidal approach because of the deep and limited access associated with this technique. The ability to vapourize and coagulate tissue without instrumentation is a valuable feature of this procedure. Vapourizing the floor of the sella and coagulating the dura is a helpful technique. The laser is most valuable for removal of fibrotic pituitary tumours which have been previously radiated, calcified intrasellar craniopharyngiomas, and chordomas of the clivus. Avoidance of traction on a tumour capsule is reduced

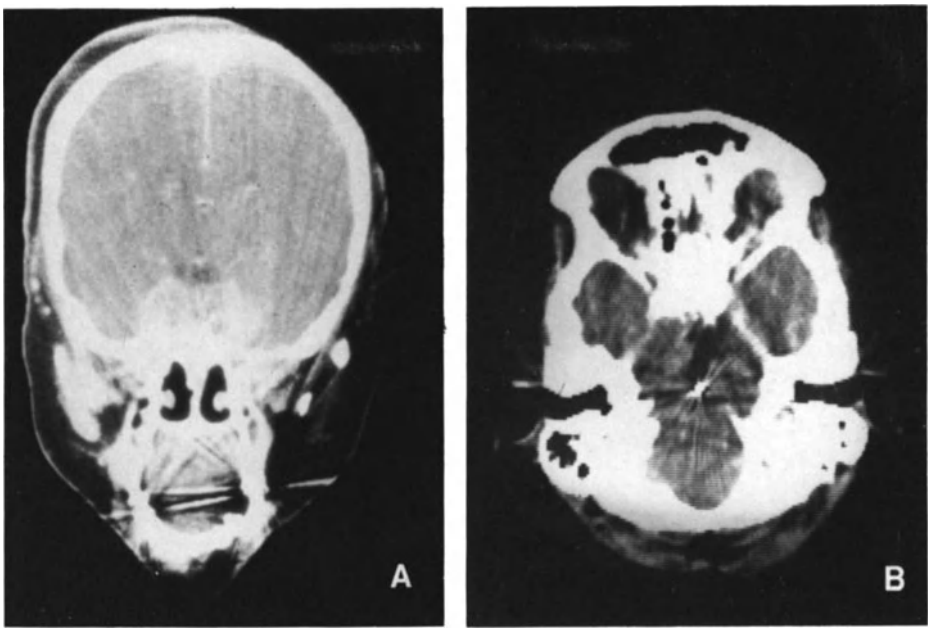

Fig. 11. A) Clivus chordoma. B) Post-operative CT shows no residual tumour

and debulking of massive tumour is possible. Haemostasis is often difficult and is only obtained by the laser in this location.

Fig. 11 shows the pre- and post-operative CT of a middle-aged lady with a large clivus chordoma removed by this approach with the carbon dioxide laser. Haemostasis would have been better obtained with the Nd:YAG laser had it been available to us. Oeckler *et al.* in 1984 reported improved outcome in 30 patients with intrasellar tumours treated with Nd:YAG laser[42].

An elderly female who underwent transsphenoidal hypophysectomy and radiation returned with increasing visual loss due to recurrent tumour (Fig. 12). This tenacious fibrotic tumour could not have been removed by other methods, but an adequate decompression was obtained with the carbon dioxide laser (Fig. 12). This patient experienced improved vision post-operatively and has had no recurrent symptoms in three years of follow-up.

A young ten-year-old child underwent a frontal craniotomy for a calcified craniopharyngioma, but the intrasellar portion could not be removed due to adherence to a prefixed chiasm and to both carotid arteries. A gross total excision was achieved via the transsphenoidal approach with the use carbon dioxide laser (Fig. 13).

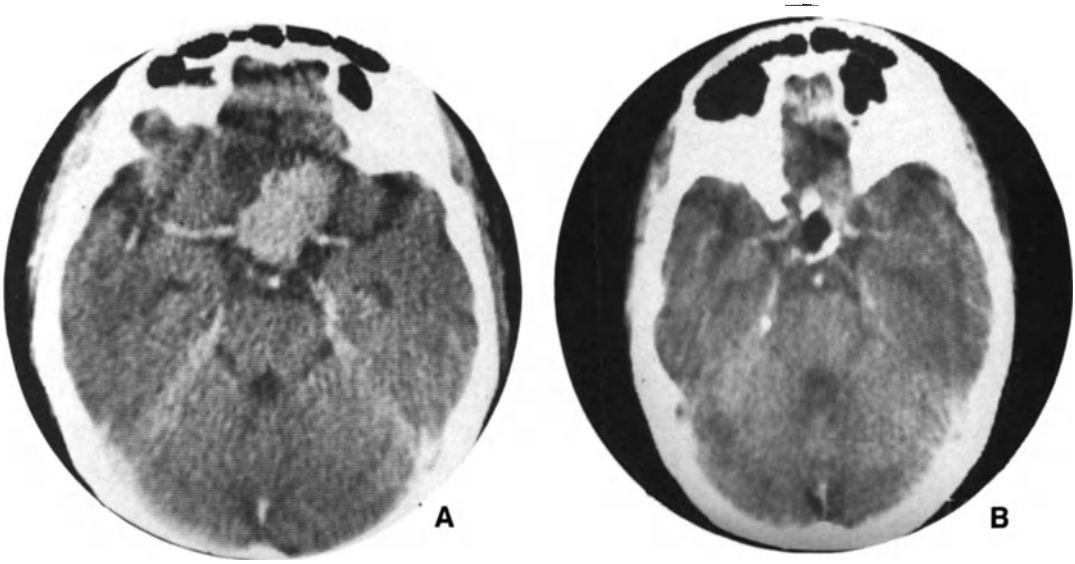

Fig. 12. A) Fibrous, radiated adenoma. B) Post-operative CT demonstrates tumour decompression. Low attenuation area is fat in the tumour cavity

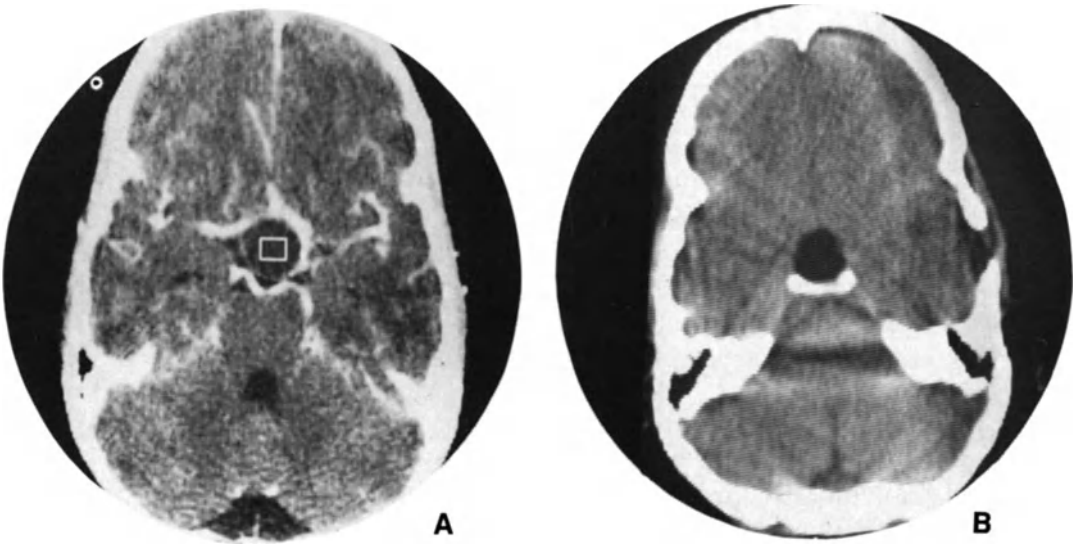

Fig. 13. A) Cystic craniopharyngioma. B) Post-operative CT shows total removal of calcified cyst and fat filling the surgical defect

Transcallosal Approach to Intraventricular Tumours

We have used the laser in 15 patients in an anterior transcallosal approach to intraventricular tumours, of the lateral and third ventricle, and the posterior transcallosal approach to pineal region tumours. The laser is

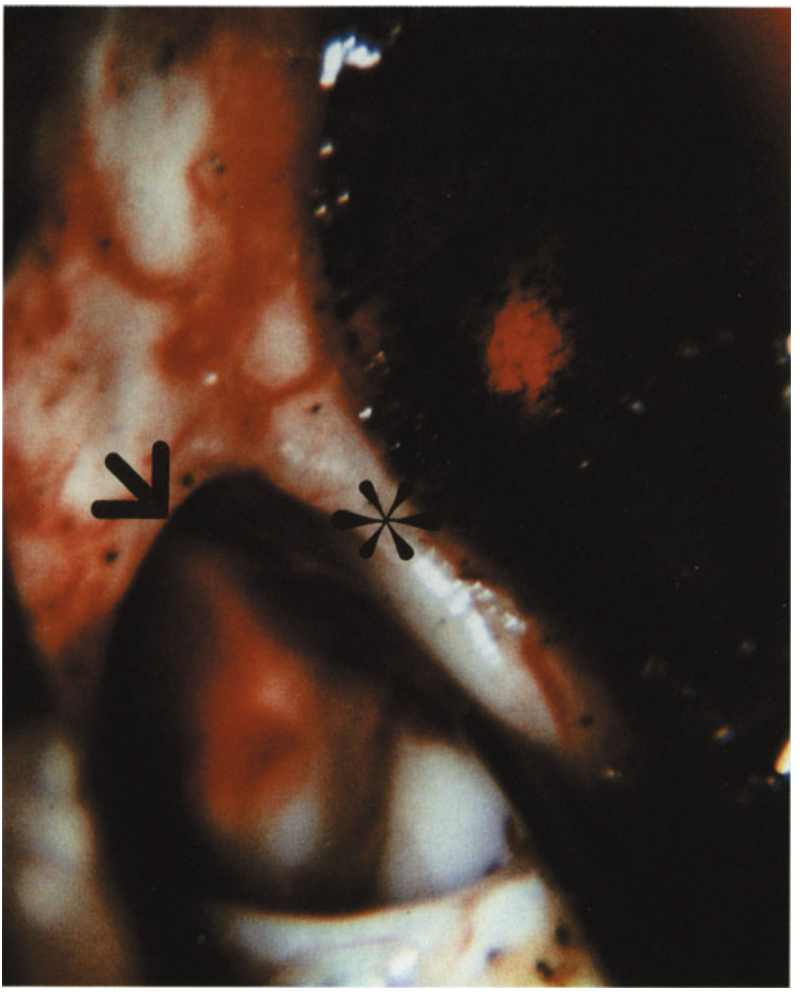

Fig. 14. Coagulating highly vascular oligodendroglioma of the right lateral ventricle with the Nd : YAG laser. The tumour is infiltrating the septum pellucidem (asterisk). The left lateral ventricle is visualized (arrow)

effective for incissing the corpus callosam and increasing access deep in the third ventricle because of the elimination of instrumentation. We are able to limit the opening of the corpus callosum to 2.0–2.5 cm to avoid disconnection symptoms[1,69]. Both the Nd : YAG and the carbon dioxide lasers are useful in these deep tumours. The Nd : YAG laser is shown coagulating this vascular intraventricular oligodendroglioma, resulting in near bloodless tumour excision (Fig. 14).

A 25-year-old male with a one-year history of hemicranial headaches and a one-month history of ataxia was found to have mild short-term memory loss, mild lethargy, and papilloedema. CT disclosed a large,

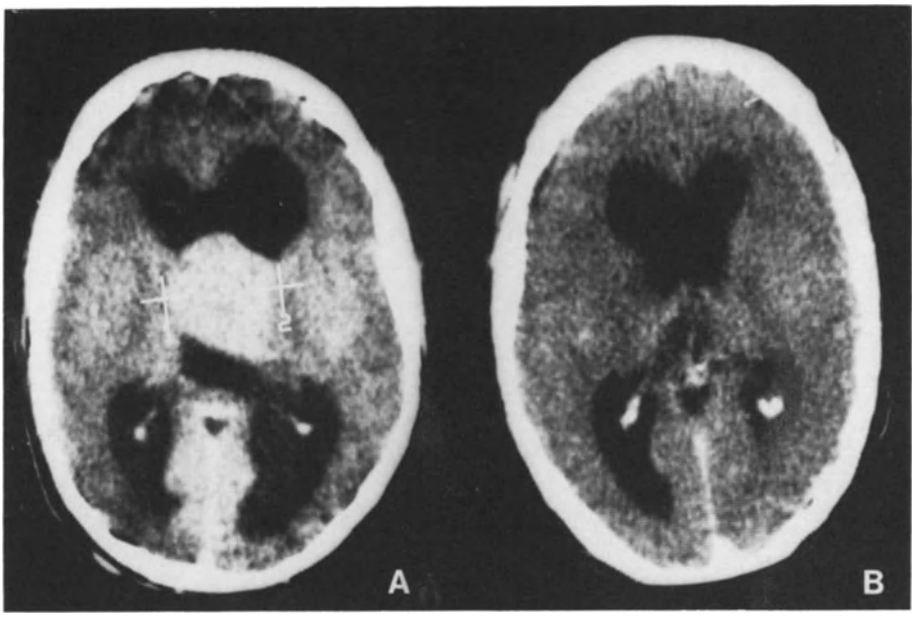

Fig. 15. Oligodendroglioma of right lateral ventricle. A) Pre-operative CT. B) Post-operative CT

enhancing tumour in the right lateral ventricle (Fig. 15). At surgery this tumour was soft and could be aspirated with the suction; however, it infiltrated and was firmly attached to the floor of the lateral ventricle and the column of the fornix. The tumour was effectively and completely vapourized from its attachment to the floor and to the column of the fornix with the carbon dioxide laser. There was no evidence of residual tumour on the post-operative CT scan (Fig. 15). The patient exhibited an increased but temporary short-term memory deficit but no evidence of a disconnection syndrome.

The laser has been most helpful in the deep, narrow exposures required for third ventricular tumours. With careful microdissection the tela choroidea and the internal cerebral veins can be retracted to gain access to the third ventricular regions where the tumour attachment to the lateral walls and floor of the third ventricle may be safely vapourized with the laser.

Spinal Cord Tumours

Perhaps the most dramatic application of carbon dioxide laser technology is in spinal cord tumours. Nowhere is the demand for precision in microdissection greater.

A 50-year-old man underwent a cervical laminectomy twelve years prior to referral to us, for biopsy of an intraspinal tumour identified as a

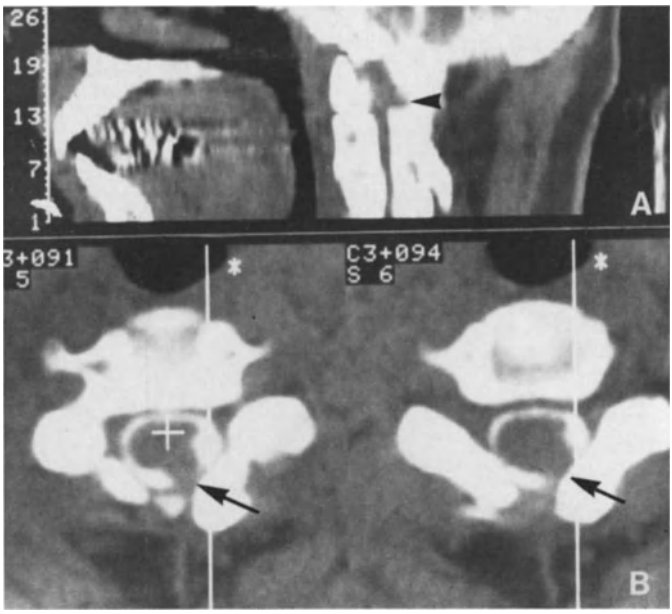

Fig. 16. Intramedullary and intradural angioblastic meningioma. Filling defects at arrow demonstrate the intradural extramedullary portion of tumour. A) Sagittal reconstructions. B) Axial sections

neurofibroma. Repeat exploration for increasing symptoms one year prior to referral to our institution disclosed a highly vascular lesion at the level of C_{1-2}, which infiltrated the dorsal cord, and could not be removed by the referring surgeon. He was referred to us for laser excision. Metrizamide CT scan disclosed an extraaxial, intradural mass invading the spinal cord at C_{1-2} (Fig. 16). A cervical laminectomy exposed a highly vascular tumour which was largely intradural but infiltrated the dura and spinal cord. The tumour was completely removed with a focused 3 watt laser beam, including the portion invading the cord. Blood loss was negligible. The Nd : YAG laser should not be used for this type of lesion because of less precise control of its absorption. Evoked potentials were monitored from the right side and demonstrated no change during the procedure. The lesion was an angioblastic meningioma and the patient's neurological condition has improved since the procedure.

Haemangioblastoma

These vascular lesions can be more easily controlled by the exquisite coagulation properties of the Nd : YAG laser. These tumours, especially the solid haemangioblastomas, have been associated with mortality rates as high as 50% [36,43].

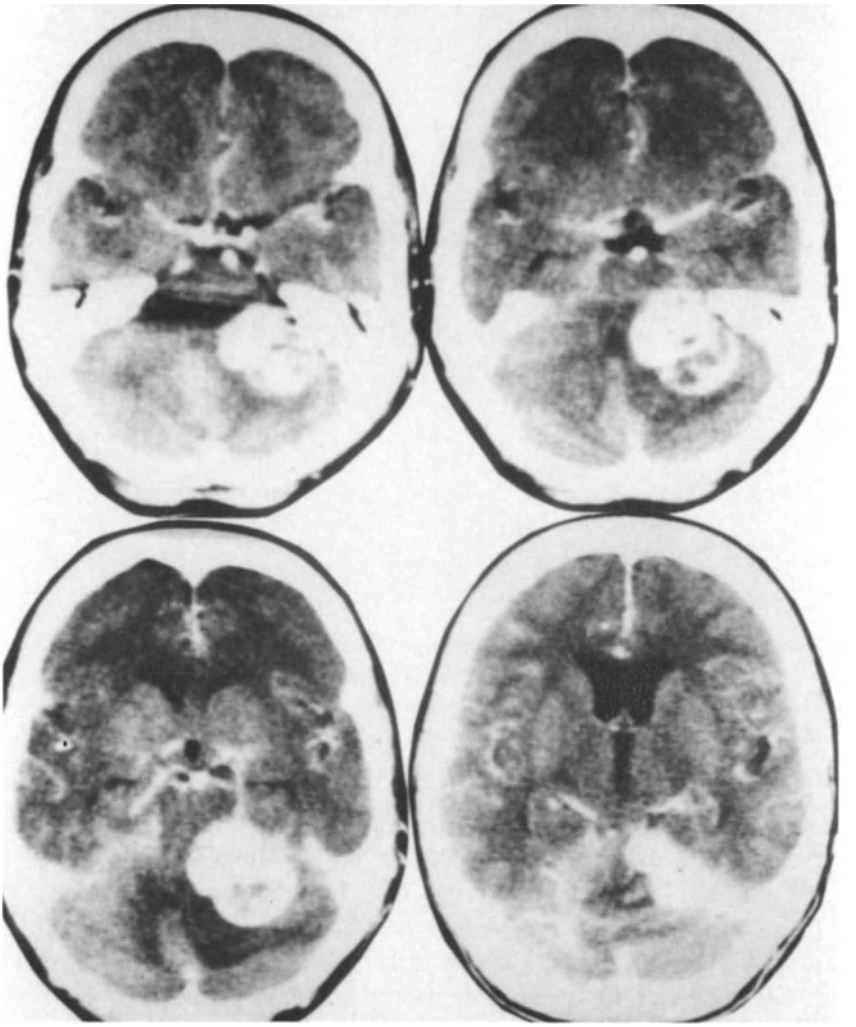

Fig. 17. Extremely vascular solid left cerebellar hemisphere capillary haemangioblastoma

A 57-year-old female developed occipital region headaches and ataxia over a four-week interval. On examination, she had bilateral lateral nystagmus, truncal and left appendicular ataxia. CT scan disclosed an enhancing left cerebellar hemisphere mass (Fig. 17) and angiography disclosed prominent vascularity (Fig. 18). At surgery, this tumour was beefy-red in colour and bled profusely when palpated with a dissector. The tumour was radiated with the Nd : YAG laser, then vapourized with the carbon dioxide laser in alternating fashion until complete removal was obtained. The haemostasis provided by the Nd : YAG laser was excellent

and enabled vapourization to be carried out rapidly, in a dry field. Complete excision of this tumour was obtained (Fig. 19). The carbon dioxide laser alone would have been inadequate for haemostasis in removal of this capillary haemangioblastoma. This case also illustrates the limitation of the carbon dioxide laser as a coagulative instrument. A dry field probably could not have been achieved to allow the carbon dioxide laser to be an effective

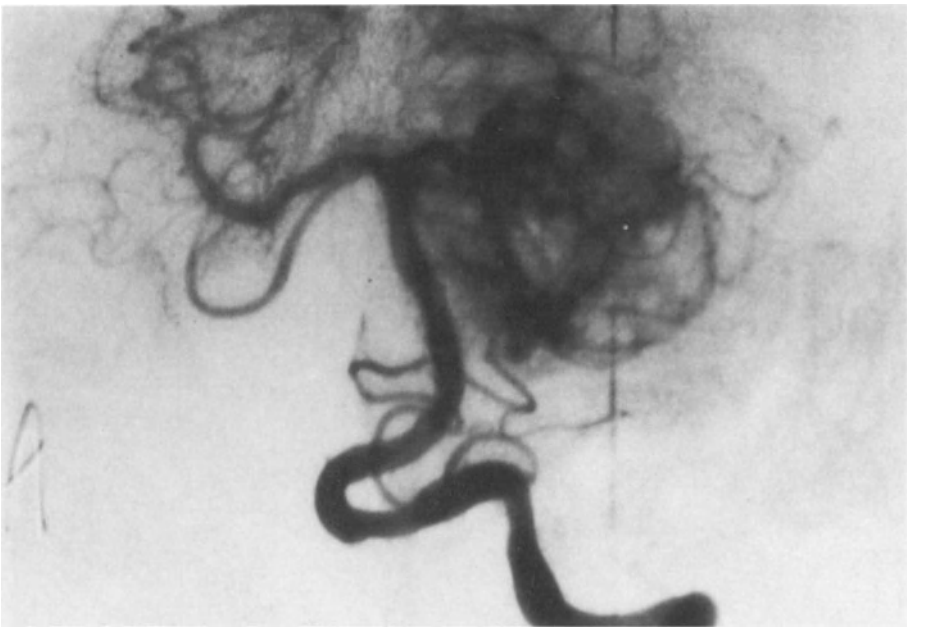

Fig. 18. AP vertebral angiogram verifies vascularity of the capillary haemangioblastoma

vapourizing instrument. The addition of the laser to the surgeon's armamentarium will likely lead to dramatic improvements in surgical outcome of this class of tumours.

Haemangiopericytoma

This tumour is similar if not identical to the more commonly known angioblastic meningioma[54]. This is a tumour composed of minute vessels; the Nd : YAG laser is indicated in surgical treatment.

A 19-year-old female presented with a right third, sixth and partial fifth nerve palsy and headaches. CT disclosed an enhancing mass in the right posterior cavernous sinus region (Fig. 20) which was highly vascular on angiogram (Fig. 21). At surgery there was a reddish fungating mass found invading the cavernous sinus. With low powers the fungating portion of this

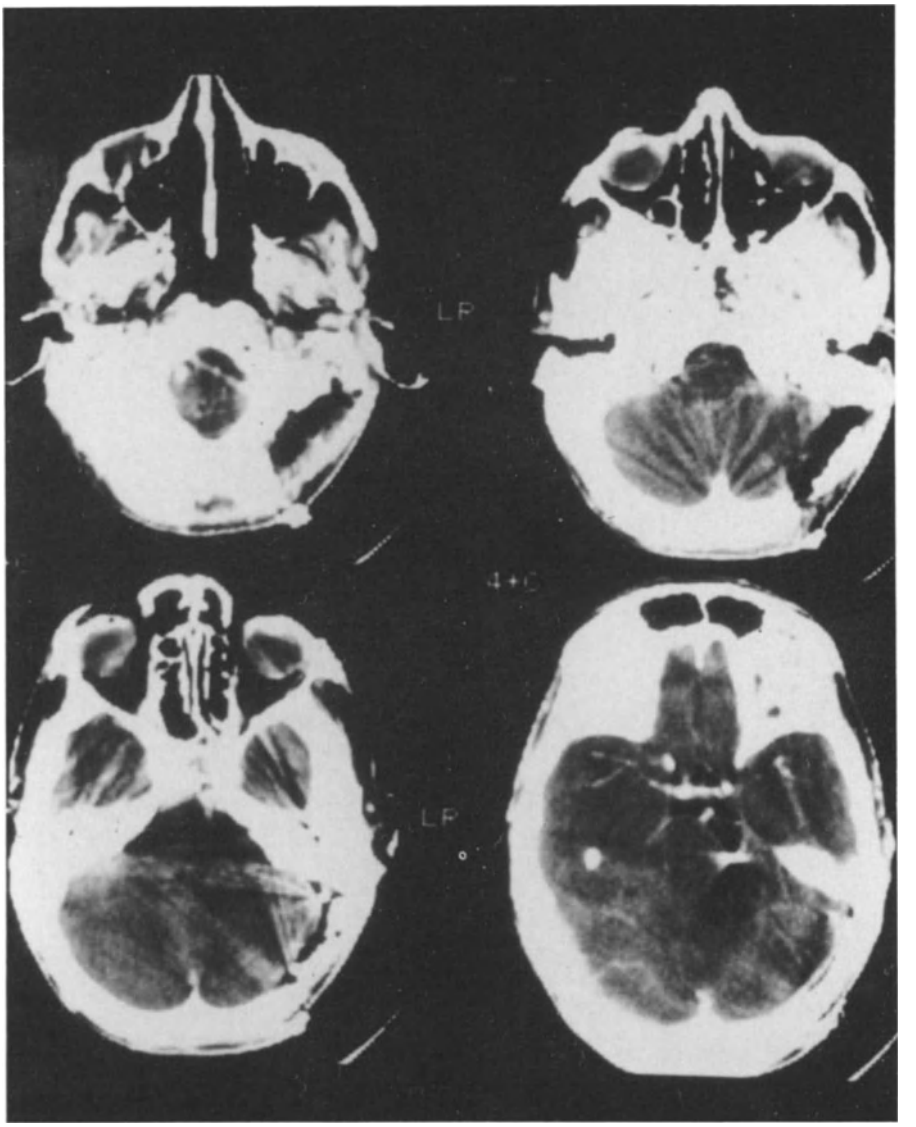

Fig. 19. Post-operative CT shows complete removal of solid haemangioblastoma

lesion was vapourized with the Nd : YAG laser. The base of the tumour in the sinus was radiated with Nd : YAG energy. Prior to the availability of the Nd : YAG laser, surgical excision or biopsy of this lesion carried a greater risk of serious blood loss and neurological complication. The patient has undergone a course of radiation therapy and is currently free of symptoms and neurological deficit. Post-operative CT shows no residual tumour mass (Fig. 22).

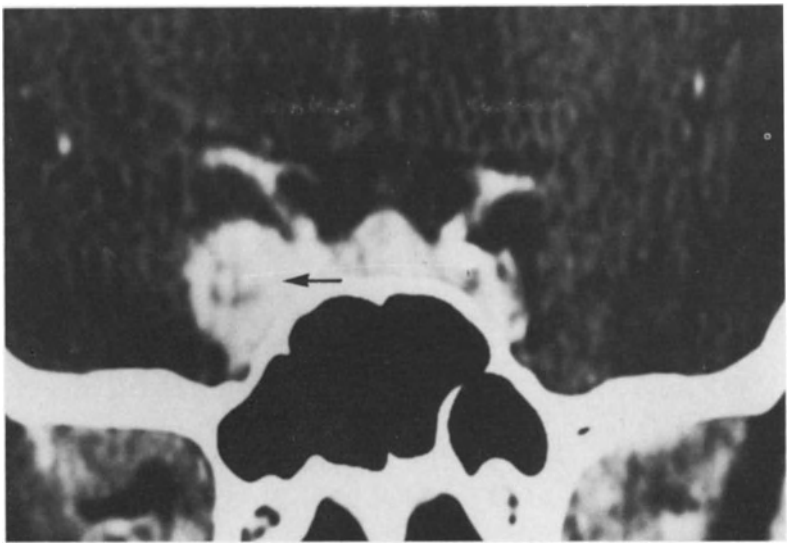

Fig. 20. Coronal CT discloses vascular haemangiopericytoma invading the right cavernous sinus (arrow)

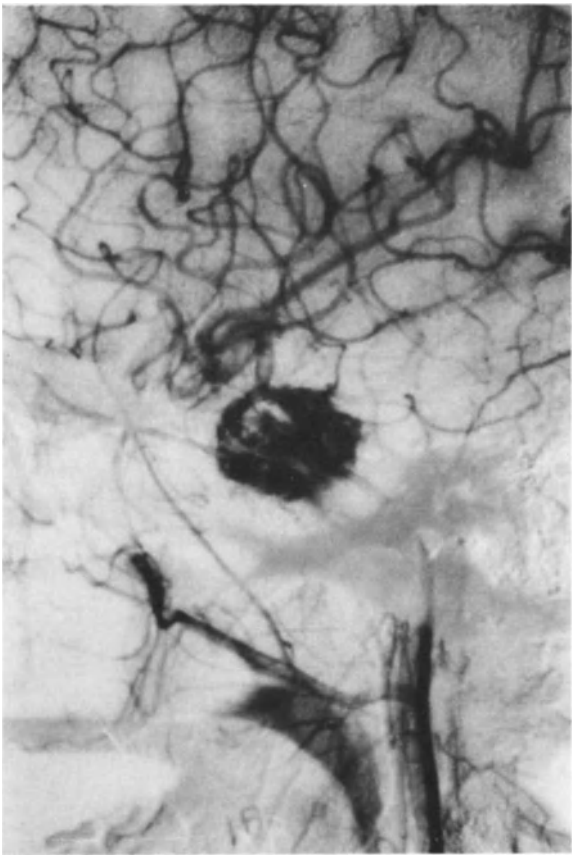

Fig. 21. Vascular blush of cavernous haemangiopericytoma demonstrated by angiography

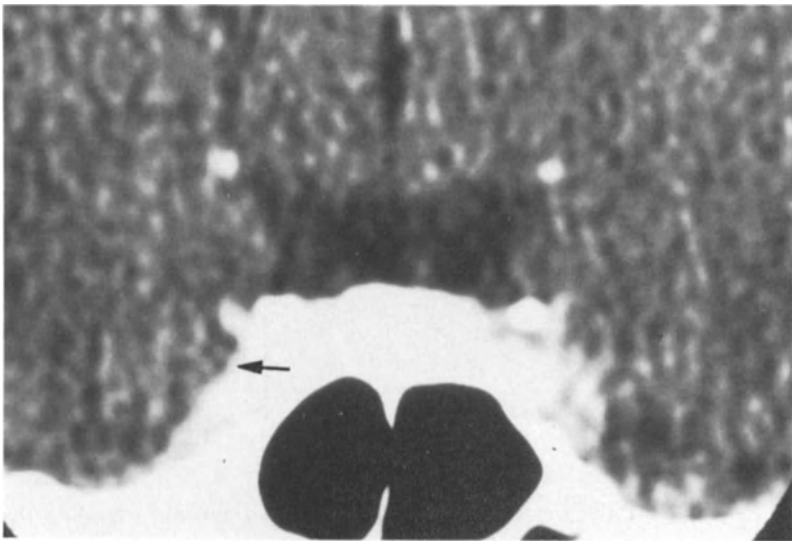

Fig. 22. Post-operative CT shows no residual tumour

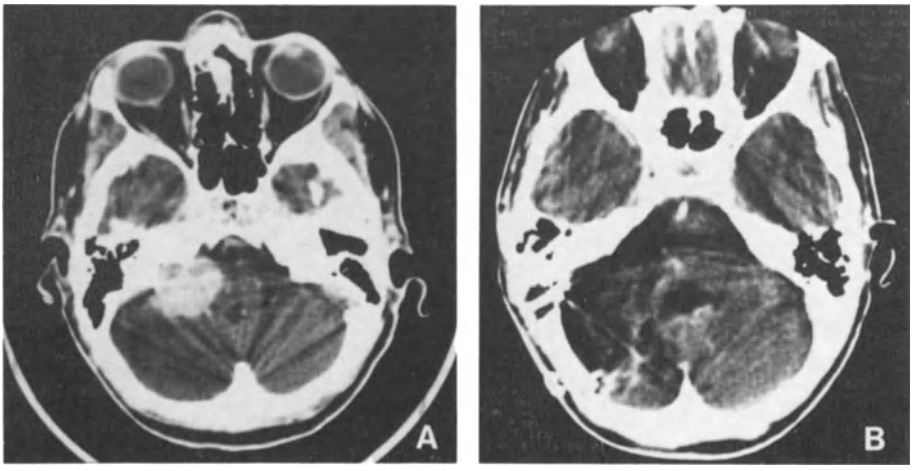

Fig. 23. A) CT demonstrates glomus jugulare tumour. B) Post-operative CT shows no residual tumour

Glomus Jugulare Tumours

These tumours are in the most difficult category of surgical challenge because of their highly vascular nature and diffuse infiltration of the skull base.

A 57-year-old female underwent a posterior fossa craniectomy and biopsy of a glomus tumour in 1959, when she developed pain and cranial

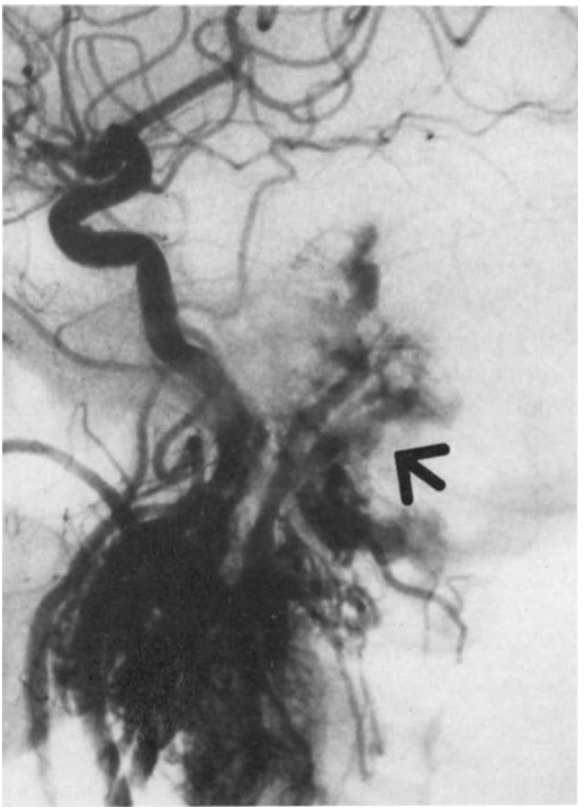

Fig. 24. Common carotid angiography demonstrates intense vascularity of glomus jugulare tumour of the posterior fossa (arrow) and concurrent glomus vagale tumour

nerve palsies. Surgical excision was not attempted. In 1976, the patient underwent craniotomy for section of the ninth and tenth cranial nerves for intractable vagoglossopharyngeal neuralgia. At that time cranial nerve palsies from seven through twelve were present. She presented in January 1984 with progressive headaches and loss of facial sensation. CT disclosed a large cerebellopontine angle tumour (Fig. 23), and angiogram disclosed feeding vessels primarily from external carotid branches (Fig. 24). The patient underwent particulate embolization of the tumour, which significantly decreased blood flow to the tumour prior to craniotomy. The Nd : YAG laser was used to coagulate this tumour, and in a nearly dry field it was vapourized with the carbon dioxide laser. Gross total excision was achieved, and the basal attachments, particularly the extension into the jugulare foramen were treated with Nd : YAG energy (Fig. 23). The patient has done well post-operatively, but has persistent cranial nerve deficits. A word of caution with this type of tumour is necessary. We were able to more

safely use the Nd : YAG laser in this case because of the non-functional state of the lower cranial nerves prior to surgery. One would be forced to exercise a greater degree of caution in such a case when these cranial nerves are functional.

Vascular Malformations

Uncertainty exists about the efficacy of lasers for arteriovenous malformations[22, 25, 68]. We continue to use the Nd : YAG laser for these lesions and express optimism regarding benefit of this method. The Nd : YAG laser is able to shrink and coagulate the small and serpentine vessels of a malformation. This is more easily achieved when flow through the malformation has been decreased by prior embolization. Neither the Nd : YAG or carbon dioxide laser can coagulate the larger, high flow vessels usually found on the deep side of the malformation. Careful microsurgical technique and use of bipolar coagulation are still required to deal with these difficult lesions.

A 25-year-old male awakened with headaches and experienced multiple seizures and was found to have a left parietal haematoma that required surgical evacuation. An initial angiogram did not disclose a vascular malformation but repeat angiography four months later disclosed a discreet malformation in the periventricular region fed by choroidal arteries (Fig. 25). At surgery the malformation was found in the lateral ventricular wall and it was vapourized completely with the Nd : YAG laser. The laser was not absolutely indicated in this particular case; however, it demonstrates the ease of a no-touch surgical technique. Further, it shows that even in more difficult cases the haemostatic and shrinking properties of the Nd : YAG laser may at least facilitate removal.

The discussion of these summaries has attempted to illustrate the ideal cases for carbon dioxide and Nd : YAG lasers. In certain cases, we believe the carbon dioxide laser is better suited; in others, the Nd : YAG laser is more appropriate. In many cases they are complementary, and in some either laser is effective. We have described the techniques which have been developed and refined through experience. Unquestionably, our ability to treat a broader range of vascular, fibrous, calcified, remote and difficult tumours has been expanded. Whether the laser improves long-term survival, or decreases incidence of tumour recurrence, will not be known for several years. In our series of 51 meningiomas, which includes six in the foramen magnum and spinal canal, we have only had one case of symptomatic recurrence. In five cases of falx meningioma the dural attachment to the sagittal sinus was radiated and none of these have shown evidence of recurrence in up to three years of follow-up. There were no wound infections in any of these cases. There were three peri-operative deaths in this series. One elderly female died of adult respiratory distress syndrome. The second death was due to direct laser injury of the carotid

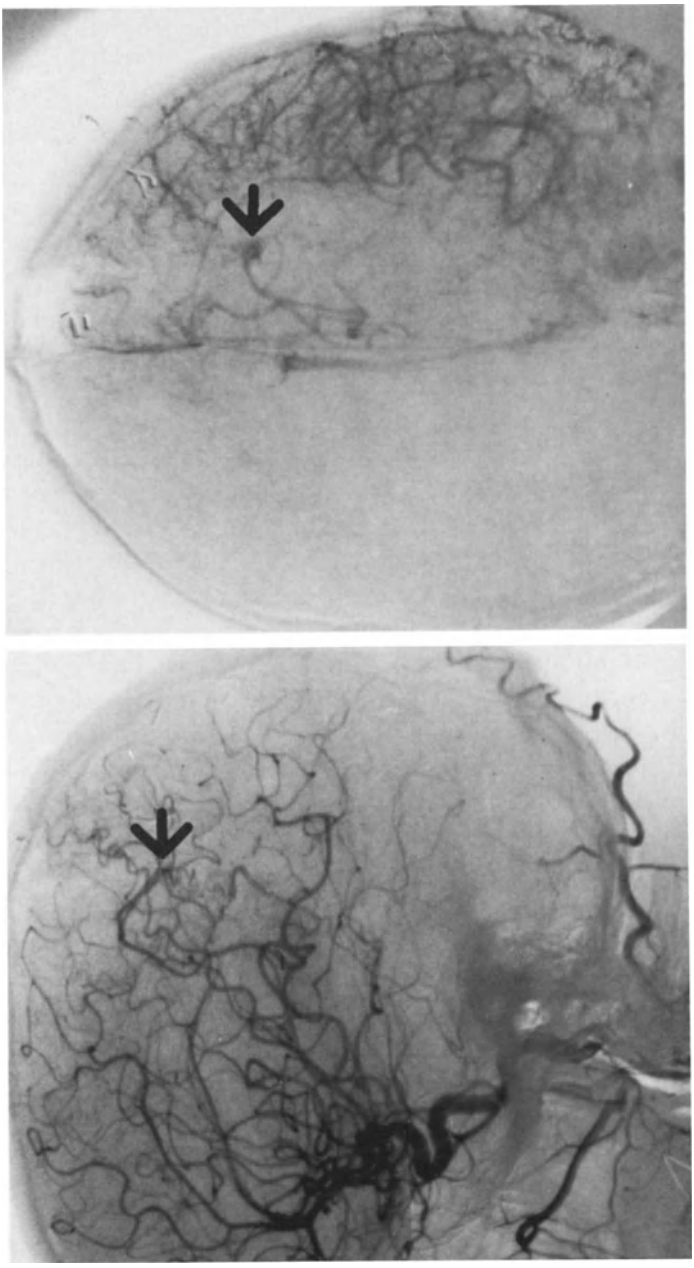

Fig. 25. Left parietal arteriovenous malformation (arrows) prior to obliteration with the Nd : YAG laser

artery which was encased by a meningioma. The defect was repaired with a clip-graft, however, the patient developed post-operative carotid occlusion and massive hemispheral infarction. The third death was due to middle-cerebral artery infarction in a subtotally resected meningioma which encased the carotid and middle cerebral arteries.

There we no other complications in this series attributable to the laser. It is our conviction that the results and ability to achieve gross removal of benign basal tumours has been vastly improved with the laser.

Ultrasonic Aspirator

Seeking to achieve atraumatic removal of normal neoplastic tissue, an ultrasonic surgical aspirating device was developed. The cavitron ultrasonic surgical aspirator (CUSA®) device emulsifies tissue by a high frequency (23,000 cycles per second) oscillatory mechanical motion. This hand-held device conducts irrigation and aspiration through a long slender tube. The system is very effective for rapidly removing large masses of tissue, and can be used in a complementary fashion with the laser. It does not transmit vibrations to adjacent tissue and therefore may be used near delicate structures, but is less precise than the carbon dioxide laser. The CUSA® is an expensive instrument comparable in price and operation to the laser. It does not induce haemostasis and it is unable to remove very firm or calcified tumours. Recent modification in construction improved the bulkyness and awkwardness encountered under the microsope but interfered with its effectiveness. It is our judgment that CUSA® is an important tool for those who choose not to develop the applications of laser technology to its maximum potential. Further refinements may make the CUSA® a more valuable addition to our surgical armamentarium[21,66].

Conclusion

Future development of laser technology will undoubtedly occur which will ultimately improve our methods of treatment. Hematoporphyrin derivative and laser photoradiation techniques currently under extensive research provide fascinating treatment possibilities[17,37]. Laser welding technology has been developed but at this time has not been widely used[34,41]. Aneurysm treatment with lasers has also been investigated and endo-vascular procedures are currently being pursued[25,39]. Laser technology holds unknown potential which may ultimately change neurosurgical treatment from what we know today.

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B. Technical Standards

Selective Amygdalohippocampectomy: Indications, Investigative Technique and Results

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With 39 partly colored Figures

Contents

Introduction

The modern era of surgical epilepsy therapy probably began with the work of Victor Horsley in 1886, yet the role of surgery in the treatment of the epilepsies is only now becoming more widely accepted and is still underutilized. One reason for this is that only a limited number of epilepsy centres are engaged in such treatment; this is perhaps because some epileptologists and neurologists are afraid of the neurosurgeons' encroachment into what they regard as a non-surgical domain. They then continue to neglect the good surgical results obtained if the patients are well screened. The major aspects of reporting this series are to discuss the criteria which must be met before considering surgery, the need to establish a proper diagnosis and the need for immaculate surgical techniques. These three factors provide the basis for a successful outcome following operation.

Sound judgements regarding surgical resective therapy require a broad knowledge of the problem and a flexible and sophisticated approach to diagnosis and management. Such a therapeutic approach must involve multiple disciplines in the neurological sciences. An amicable relationship between neurologists, neurosurgeons and the other representatives of the different subspecialities within the neurosciences provides for fruitful collaboration which is *imperative* in epilepsy surgery.

This follow-up study is the result of such a fruitful collaboration. It summarizes the experiences and results obtained using a new operative approach in an admittedly small subgroup of the general seizure population, *i.e.*, those patients suffering from drug-resistant recurrent complex partial seizures of the *mesiobasal-limbic type*.

Many years of refined investigations with systematic depth recordings in potential candidates for surgical epilepsy therapy, led to our dividing complex partial seizures into five comparatively distinct types (Wieser 1983 a). The most important is the (1) temporal mesiobasal-limbic, and within this a subtype involving (2) temporal pole and amygdala, could be discerned. The other types are: (3) frontobasal-cingulate, (4) opercular-insular, and (5) posterior neocortical temporal ictal constellations.

Since 1975 we have felt that the "classical" anterior two-thirds temporal lobe (TL) resection is too crude a surgical operation in those patients in whom the presurgical stereoelectroencephalographic (Stereo-EEG, SEEG) evaluation has shown a narrowly defined seizure origin within the mesiobasal-limbic structures. More selective surgery specifically tailored to a given seizure constellation seemed necessary. Stereotactic procedures proved generally unsatisfactory [apart from lesions made in the amygdala in the relatively rare cases of pure amygdalar seizure (Hood *et al.* 1983)], and so newer open microsurgical techniques were developed. Microsurgical operations for mesiobasal-limbic TL epilepsy have been performed in Zurich since 1975. In the first cases of this series, however, the temporal pole was removed in order to gain access to the entire hippocampal formation. Although this type of operation already represented considerable progress, we were not entirely satisfied until the technique of "selective amygdalohippocampectomy" (Wieser and Yaşargil 1982 a, b) had been developed and stood its practical test. This operation is now a more or less standardized procedure. However, individual variability of the general and vascular anatomy of the brain has been quite large, and especially of the temporal lobes in our patients with proven mesiobasal-limbic epilepsy, necessitating slight technical modifications from patient to patient.

To date, 127 patients have been operated upon using this selective microsurgical approach, and another seven patients are awaiting surgery following careful preoperative studies. Allowing for a minimal post-operative follow-up of 1 year, this report includes 103 patients. The

rationale for including some patients with such a short follow-up may be derived from comparing the current results with the intermediate results of our earlier publications. Although the first preliminary report (Wieser and Yaşargil 1982 a, b) was based on only 27 patients and the following report (Wieser and Yaşargil 1984; published only in abstract form) was based on 56 patients, the overall outcome data have remained essentially unaltered.

As details of our presurgical evaluation protocol have been reported elsewhere in great detail (Wieser 1981 a, 1983 a), only the most essential and the more recently developed steps in evaluating a candidate for selective amygdalohippocampectomy are discussed here. These include measurement of mesiobasal temporal lobe herniation using metrizamide enhanced CT scanning (Bolender and Wyler 1982), the use of a recently developed new recording technique with electrodes placed through the foramen ovale, detailed pre- and post-operative neuropsychological results (Birri *et al.* 1982, Gonser 1983, Gonser *et al.*, in press, Nadig *et al.* 1985), tachistoscopic examination of higher brain functions during unilateral mesiobasal-limbic status epilepticus, and pre- and post-operatively performed detailed visual field examinations using the OCTOPUS.

Whereas others (Schwartzkroin *et al.* 1983) have already accumulated considerable experience by the *in vitro* studies of human chronic epileptic cortex, our attempts to examine the resected brain tissue by *in vitro* electrophysiology using slice techniques (Haas *et al.* 1983) and modern immunohistochemistry are at an early stage and have not as yet provided any relevant conclusions. This work may yield new insights when more detailed studies are possible, especially with respect to possible transmitter-linked pathological causes of hippocampal hyperexcitability. Gamma-amino-butyric acid (GABA) and glutamate (as well as aspartate) probably represent the most important inhibitory and excitatory antagonists (Fariello *et al.* 1984).

This article is divided into two main sections. In the first we present the rationale for operation as well as the screening protocol and the prerequisites for selective microsurgical intervention. The main aim during the diagnostic steps is to identify and localize, as exactly as possible, the epileptic focus. The essential points are evidence of a possible structural lesion, careful analysis of the clinical and electrical attack pattern and information from other "functional" studies.

The second section summarizes the patient data and the results. The hard core of data is presented by use of a coloured master-table (Fig. 25) in order to facilitate a synopsis of different variables which might influence the post-operative results. This figure serves as a basis for a further breakdown of the post-operative data, including general clinical, epileptological, neuropsychological and EEG results. Finally, a comparison is made of the results obtained in this selectively operated series with results of temporal lobe

surgery using "classical" anterior two-thirds resection or stereotactic approaches.

The operative anatomy and surgical technique are described in a separate chapter (Yaşargil *et al.* 1985).

1. Rationale for Performing "Selective Amygdalohippocampectomy"

1.1. Some Basic Considerations Relevant to Hippocampal Epileptogenicity

It has long been known that different areas in the human cortex have varying degrees of epileptogenicity. For example, a varying incidence of epilepsy as a result of penetrating head wounds at various cerebral loci was noted, the sensorimotor cortex being most susceptible. Today we know that the mesiobasal temporal lobe structures share this same enhanced tendency towards epileptogenicity. Theoretically such differences could be due either to different properties of local neuronal circuitry, or to local differences in the membrane properties of the neurons in the various cortical areas, or to both. Almost all current hypotheses of epileptogenesis suggest an inextricable relationship between circuity and intrinsic cell properties (Schwartzkroin 1983, Speckmann and Elger 1984). Basically, cortical hyperexcitability may be due to decreased inhibition, an increase in excitation, and increased synchronization of cellular discharges. One hypothesis, the "*release from inhibition concept*", advanced for hippocampal pyramidal cell regions, will be outlined (Wong and Prince 1978), Schwartzkroin and Wyler 1980). Inhibitory post-synaptic potentials (IPSPs), primarily at the level of the cell soma, but also in the dendrites (Andersen *et al.* 1980 a), exert a tonic inhibitory influence on pyramidal neurons. Excitatory afferent input is terminated abruptly by both feed-forward and feedback inhibitory mechanisms which prevent the cell from being appreciably depolarized.

Loss of inhibition [reduction in GAD terminals has been reported for epileptic cortex (Ribak *et al.* 1978, Lloyd *et al.* 1981)] results in excitatory events with much more potent effects. In particular, the intrinsic burst potential of hippocampal pyramidal cells is "released" and cells are more depolarized for a longer period by synaptic input, so the high threshold calcium spike mechanism can be triggered. In this model the long-lasting hyperpolarizing potentials following the burst prevent these cells from bursting continuously, when IPSPs are lost. The hyperpolarizations are due, at least in part, to calcium dependent potassium conductances (Alger and Nicoll 1980) that repolarize the cells and set up rhythmic depolarizing-hyperpolarizing oscillations of membrane potential.

The literature relating to kindling (Goddard *et al.* 1969, Goddard 1983) and potentiation provides data indicating that there are mechanisms to

increase excitatory post-synaptic potential (EPSP) amplitude and efficacy (Lynch and Schubert 1980). Some of these studies suggest that *increased synaptic excitation* is due to changes in intrinsic post-synaptic cell characteristics (Yamamoto and Chujo 1978, Andersen *et al.* 1980 b, Lynch and Schubert 1980). Large EPSPs may occur independently of IPSP alterations in these experiments. Such augmented EPSPs could conceivably be attributed to increase in transmitter liberation (as in post-tetanic potentiation) or in excitatory transmitter supersensitivity. The latter mechanism has been of particular interest since it has been hypothesized that epileptic cortex is, in a sense, partially deafferented cortex (Ward 1969).

Apart from a simple increase in excitation or decrease in inhibition, cortical hyperexcitability can be effected by *increased synchronization* of cellular discharge. In fact, epileptiform activity is, almost by definition, characterized by synchronous activity in a large number of neurons. The mechanisms that account for this synchrony were, until recently, rather neglected. Synchronous discharges, however, can be initiated and maintained by several factors. Altering of EPSP and particularly IPSP efficacy can affect oscillatory after-discharge phenomena (Mates and Horowitz 1976, Leung 1978). Increasing inhibitory feedback can increase after-discharge oscillatory activity, as is clear from thalamocortical spindling generation (Avoli *et al.* 1984). However, since IPSPs blockage is a major factor in the "*loss of inhibition theory*" of epileptogenesis, another means for synchronizing cell discharge, such as the burst-afterhyperpolarization, must be accorded greater importance. Although intrinsic to a single cell, it may play a part in such a synchronization mechanism since it produces an approximately equal period of functional inhibition in many neurons. Moderate excitatory inputs to the population might be all that is needed to maintain synchrony.

Other mechanisms that could contribute to population synchronization are the direct EPSPs from pyramidal cell to pyramidal cell in hippocampus (MacVicar and Dudek 1980) and non-synaptic mechanisms, in particular field interactions between pyramidal cells of CA 1 region (MacVicar and Dudek 1981, Haas and Jefferys 1984).

Recent modelling of a simplified hippocampal network, with neuronal elements having pyramidal cell properties, indicates that synchronized bursting in a penicillin-treated preparation (with IPSPs blocked) could develop with relatively few direct excitatory chemical synaptic connections between cells, but that some such connections are necessary (Traub and Wong 1981 a, b). The model further indicates that electronic coupling could modify discharge characteristics. However, it is neither necessary nor sufficient to produce epileptiform activity.

In summary, intrinsic burst discharges, disinhibition, and excitatory synaptic coupling are important mechanisms underlying development of

focal epileptiform discharges (Prince 1983). The intrinsic burst-generating mechanisms in hippocampal pyramidal cells are very similar to those in a variety of invertebrate burst generating neurons and depend on a net inward current which appears to be carried predominantly by Ca^{2+}. Rectifying K^+ currents have an important role in controlling or terminating burst discharge. Bursting can be modulated by iatrogenic or intrinsic mechanisms that alter K^+ currents, such as transmitters and modulators, and changes in extracellular ionic concentrations (Haas *et al.* 1984). Disinhibition is a critical factor in epileptogenesis that results in release of intrinsic burst generation and contributes to synchronization of populations with excitatory interconnections. Different populations of neurons, by virtue of both their intrinsic membrane properties and differences in excitatory synaptic coupling, have different capacities for epileptogenesis.

The augmented proclivity towards epileptogenicity of the limbic system probably is a reflection of at least three factors: first, the intrinsic proclivity towards epileptiform-like burst discharges of hippocampal CA3 pyramidal neurons following mild alterations in calcium conductances in their dendritic trees (Schwartzkroin and Wyler 1980); second, the excitatory nature of serial synapses within the hippocampus and the synaptic potentiation which occurs at these sites following tetanic or repetitive stimulation (Andersen and Lomo 1968); third, the high degree of associational connections within the hippocampus (Raisman *et al.* 1965, Swanson *et al.* 1978) as well as between the hippocampus and the other limbic structures (Swanson and Cowan 1977), as emphasized by anatomical tract-tracing studies, explain why seizure discharges starting in one part have ready access to the whole system.

A major challenge in the future must be to determine how various pathological processes affect these particular components to give rise to epileptogenesis, and to correlate morphological changes that have been described for cells in chronic epileptic foci. These consist of loss of spines and fine dendritic branches (Westrum *et al.* 1964, Scheibel and Scheibel 1973, Scheibel *et al.* 1983), cellular distortion as a consequence of gliosis (Ward 1978), and changes in the "patterns" of synaptic connectivity, such as partial deafferentation or more excitatory synapses directly on the dendritic shaft.

1.2. The Mesiobasal-Limbic Focus Concept

The rationale of surgical therapy for epilepsy depends on the concept of the "epileptic focus". Surgical excision of the focus containing a mass of "highly explosive cells" (Hughlings Jackson, 1890) might be expected to be therapeutically beneficial, and this in a rather causal sense. However, from the foregoing discussion it should be clear that the concept of the "epileptic focus" is a functional and dynamic one, in the sense that the pathological,

hyperactive, and more or less autonomic "epileptic pacemaker neurons" (Ward 1975) are intermixed with other neurons whose firing patterns may fluctuate between varying degrees of epileptic burst firing and normal firing rates, depending on the degree of recruitment. Some seizure precipitating factors, such as certain sleep stages or specific sensory inputs ("reflex epilepsies"), are well recognized clinically. Seizure preventing mechanisms used by many epileptics, and often consisting of "forced concentration", are equally well-documented (Wieser 1982, 1984). Depending on actual background synaptic activity and synchronizing factors, the size of the epileptic focus can expand and shrink. When the extent of the "focus" is widened, a critical mass is reached, at which point clinical manifestations and/or propagation of the pathologic cellular activity is apparent. The circuits of spread obviously depend on the cells of seizure origin and thus on the prewired hodology and connectivity of the brain. Thus, anisotropic seizure propagation should be expected. In certain instances, as in graded focal seizures, one can indeed observe stepwise involvement of synaptically related ganglionic stations.

In experimentally induced epileptic foci in the entorhinal cortex of the rat, Collins *et al.* (1983 a, b) using [14C]-deoxy-glucose autoradiographic techniques could demonstrate that interictal discharges (without essential changes in animal behaviour) projected only as far as the first synapse and were stopped. In moderate seizures (with head and face jerking and wet dog shakes) metabolic activation occurred beyond ipsilateral dentate gyrus in Ammon's horn, the ipsilateral basolateral nucleus amygdalae, nucleus accumbens, ventral pallidum area and bilateral septum. Mild activitation of the contralateral Ammon's horn was observed also. The relative magnitude of metabolic change within the hippocampus in this seizure state primarily reflects the strength or proximity of anatomical connections to the seizure focus, *i.e.*, in this case, entorhinal cortex > dentate gyrus > CA 3 > CA 1 (see Fig. 2). Moreover, these experiments suggested that metabolism in the basolateral amygdala was activated only within a polysynaptic seizure spread from subicular fields and lateral entorhinal cortex (Petersen 1981). During the severe seizure state the metabolic pattern showed bilateral intense activation of the whole limbic cortex, and a major change in seizure phenomenology (with overt convulsive behaviour of the experimental animals) was usually observed.

Such metabolic animal studies are in agreement with results obtained by depth-recordings from human epileptics showing that preferential seizure propagation within the limbic system follows the known hodology (Wieser 1981 b).

Knowing the preferential pathways is important for the following reasons. Monitoring of the spread of seizure discharges helps to explain the accompanying ictal signs and symptoms (Wieser 1983 a) and in many instances gives additional indirect confirmatory evidence for seizure origin. In certain instances where resection of the focus is not possible, the

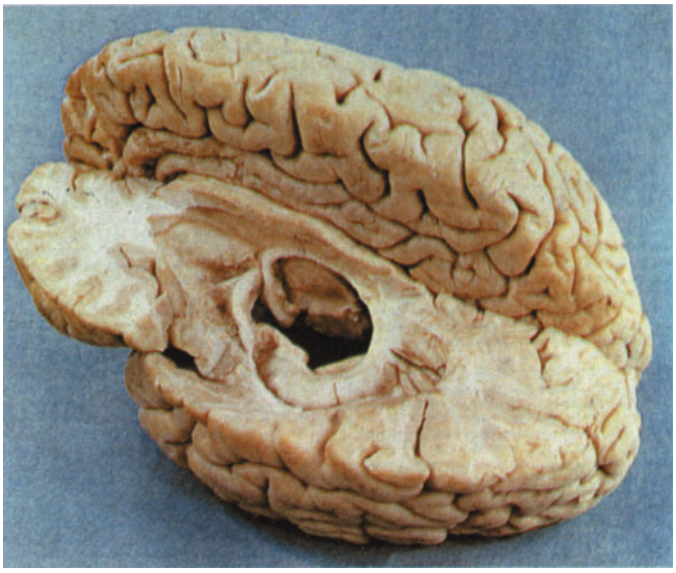


Fig. 1. A dissection of the left cerebral hemisphere from the superolateral aspect to demonstrate various structural features of the limbic system. The corpus callosum is divided sagittally in the region of its body only; the frontal, temporal and occipital lobes have been sectioned horizontally and their superior parts removed. The left lentiform nucleus, much of the caudate nucleus and dorsal thalamus have been removed, and the floor of the inferior horn of the lateral ventricle laid open. Note: 1. The horizontally sectioned head of the caudate nucleus; 2. the spiral disposition of the fornix as it curves from the mamillary body through its left column, body, crus and fimbria; 3. the curved elevation of the hippocampus projecting into the floor of the inferior horn of the ventricle, and ending anteriorly as the grooved pes hippocampi; 4. the anterior commissure entering the left hemisphere immediately anterior to the column of the fornix, and passing laterally, to diverge into small anterior and large posterior components; between the latter the deep aspect of the anterior perforated substance is visible; 5. within the curve of the fornix the medial aspect of the right thalamus crossed superiorly by the stria medullaris thalami; 6. coursing above the corpus callosum a longitudinal white stria is visible, and above this arches the right cingulate gyrus. (From Gray's Anatomy, 35th edition, pp. 931, 1973, with permission)

preferential pathways themselves may be attacked by means of stereotactic surgery. Furthermore, some of the behavioural effects (MacLean 1954, Waxman and Geschwind 1975) and mental alterations frequently observed in limbic epilepsy (Wieser 1983 b) may be due to propagated spike activity presenting some "noise" for otherwise normally functioning neuronal networks (Ward 1975, Masui *et al.* 1984). Also related to seizure spread over preferred pathways are the phenomena of "kindling" (Goddard 1983), "mirror foci" (Morrel 1969), and the "maturation" of a focus. Although the

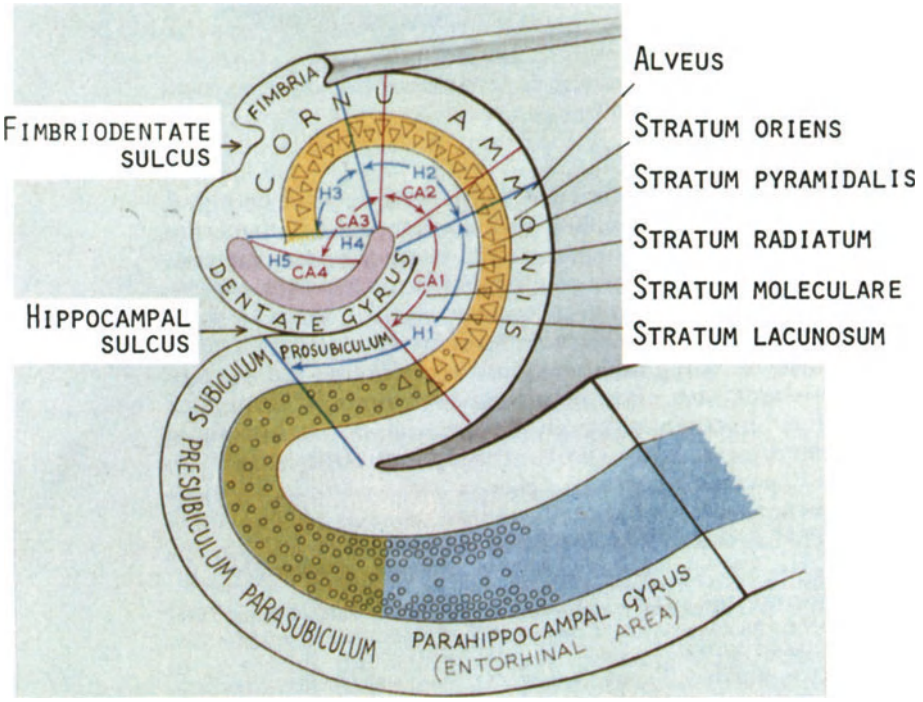


Fig. 2. An analysis of the major topographical zones and the complex terminology applied to the hippocampus and related structures seen in a coronal section of the floor of the inferior horn of the lateral ventricle in a mature human brain. The approximate limits of the various subdivisions of the subiculum are labelled. *CA 1–4* are the Cornu Ammonis fields of Lorente de Nó (1934) and *H 1–5* are the hippocampal fields of Rose (1926). (From Gray's Anatomy, 35th edition, pp. 940, 1973, with permission)

significance of kindling for human epilepsy remains uncertain, clinical observation strongly suggests that at least similar mechanisms are active in uncontrolled focal epilepsy (Wada 1981). Thus in the light of recent experimental evidence, the old clinical notion that the brain "learns" how to have a seizure is now put on a firmer foundation.

Finally, of great importance are data which show that an active epileptogenic focus continues to undergo active pathological changes (Westrum *et al.* 1964, Scheibel and Scheibel 1973). Recent experimental data, reviewed by Engel (1983 a), suggest a multifactorial concept with the excessive synaptic activation (particularly along limbic pathways) being the unifying feature of neuronal damage. Whether this localized hyperexcitation destroys neurons by enhanced release of endogenous excitotoxins such as glutamate and aspartate, abnormally increased intracellular calcium concentrations (see p. 48), focal increased vulnerability to hypoxia

(Elger and Wieser 1984), or other metabolic mechanisms (Galella *et al.* 1983), remains in dispute at present and awaits further research.

Meldrum (1983) has advanced an attractive "calcium toxicity" hypothesis for selectively vulnerable neurons. He postulates that such neurons are characterized by an abnormally large entry of Ca^{2+} during seizures. This overwhelms the capacity of the neurons to extrude or sequester Ca^{2+}, and finally leads, under certain circumstances, to a sequence of events ending in cell death.

Recurrent seizures, even if partial ones and not necessarily generalized convulsions, may be damaging to the affected brain. The logical step should be early effective treatment to prevent neuronal loss and gliosis. In the case of limbic epilepsy these are most prominent in hippocampal pyramidal cells of the end folium, or Somer's sector 3–5, which contains the subregions CA 3 and CA 1 (see Fig. 2). Subiculum and olfactory cortex are usually less severely affected. Sometimes pathological changes may also occur in amygdala and other subcortical limbic nuclei, resulting then in the well-known "mesial temporal sclerosis" (Falconer *et al.* 1964).

Thus *in summary* the surgical therapy has three objectives. It aims at (1) seizure control, (2) functional and behavioural improvement, and (3) possible prevention of kindling-like mechanisms, thereby interrupting an otherwise continuing epileptic process. Selective resective operations offer a real chance to reach these goals only if a narrowly confined epileptic focus is present. Such a focus has to be identified as accurately as possible. The focus is initially localized by the clinical pattern of the typical seizure, and the suspected site is confirmed using modern functional diagnostic means, such as EEG, single-photon emission computed tomography (SPECT) and positron emission tomography (PET) (Engel *et al.* 1982 a, c, e, 1983 a, b, Gloor *et al.* 1984), if available. A structural lesion at the site, or one structurally related to it, should be confirmed or excluded using CT scan and/or magnetic resonance imaging (MRI). As the study of human epileptogenesis depends more on techniques which reveal abnormalities of neuronal function, as opposed to structure, the diagnoses of seizure disorders continue to depend largely on electrophysiological measurements (Ojemann 1983). Because of the well-known restrictions of surface EEG, especially with respect to precise localization within the TL, special recording techniques (Lueders *et al.* 1982) and particularly stereotactically implanted depth electrodes are now used by most surgically active epilepsy centres (Bancaud *et al.* 1965, Crandall *et al.* 1983, Engel *et al.* 1981, Engel 1983 b, Fisher and Uematsu 1982, Lieb *et al.* 1976, Gloor 1984, Rossi *et al.* 1980, 1982). Although the number of anatomical sites that can be sampled is obviously limited and false localization is still possible (Gloor 1984, Ojemann 1983), this method has stood its practical test, provided that the

basic principles for applying the technique are rigorously observed. Some of them will be described in the next section.

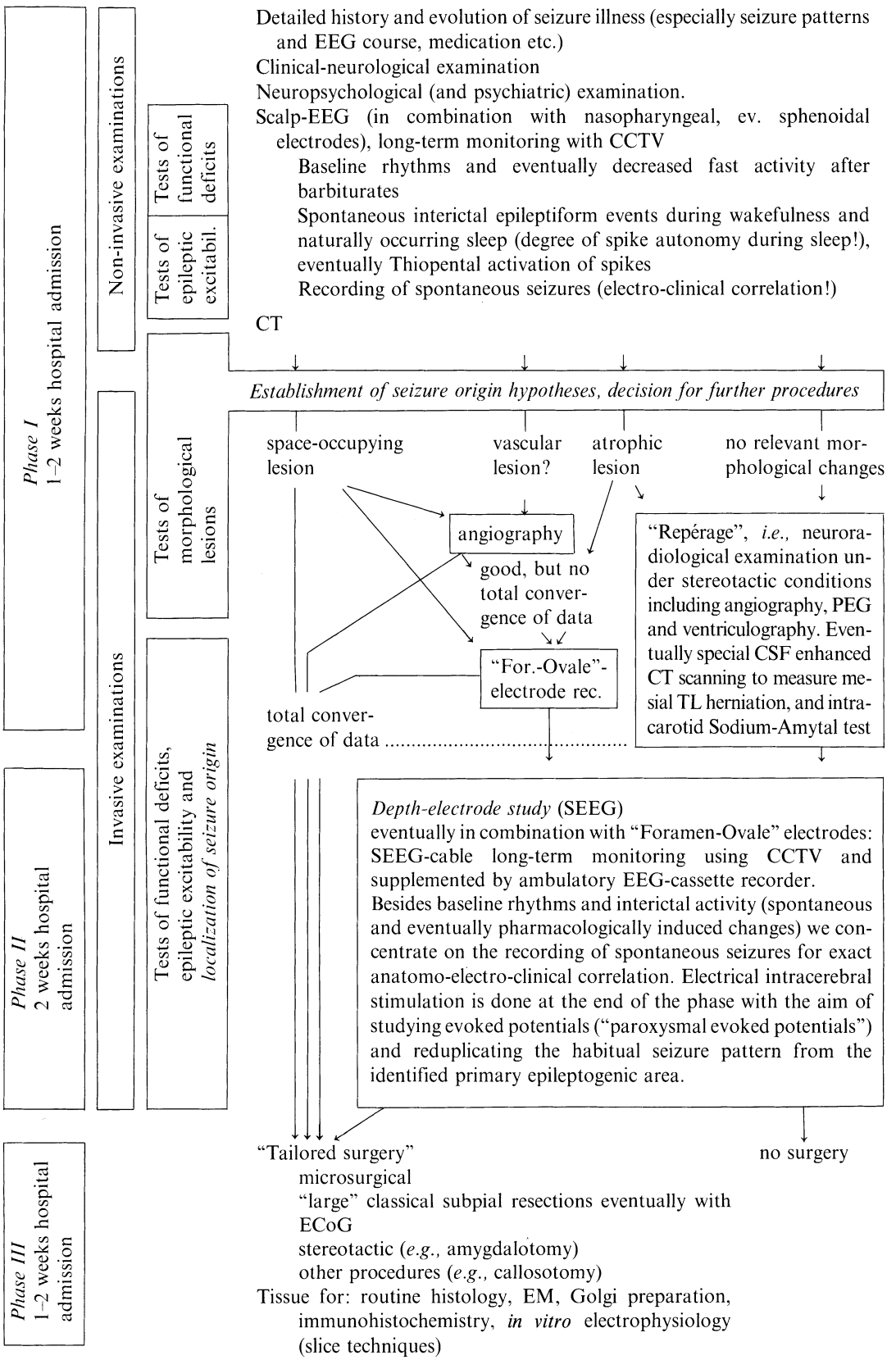
1.3. The Evaluation Protocol

The evaluation protocol used for patients of this series is shown in Table 1, and remains essentially the same as that previously published (Wieser 1981 a, 1983 a).

Requirements for admission to Phase I include a history of frequent complex partial seizures and failure of adequate medical treatment. Routine evaluations including skull films, CT scan and several EEGs, are supplemented by a set of tests which focus on the demonstration of functional deficits and include neurological, neuropsychological, psychiatric, ophthalmo- and otoneurological examinations. Interictal EEG abnormalities and the patient's habitual seizures are recorded by means of scalp and sphenoidal recordings and synchronous closed-circuit-video monitoring of the patient and the EEG. If these are unequivocally in line with evidence of gross structural abnormalities at the suspected seizure originating sites, the structural abnormality will largely determine the surgical treatment. In the case of space-occupying lesions, depth electrode evaluation is not considered necessary. In certain cases, however, we had to consider whether removal of the seizure-prone mesiobasal structures should be performed in addition to the microsurgical resection of the lesion itself. In such cases the lesion usually was located in the vicinity of the amygdala and/or hippocampus. Direct evidence was missing, that these structures themselves were affected by the lesion, although the habitual attack pattern would have suggested it. In such cases the "*Foramen ovale" (FO) electrode technique* was used to good effect. The details of this new recording technique have been published elsewhere (Wieser *et al.* 1985 b). It allows epicortical recording from the mesial aspects of the TL in AC and DC mode by placing electrodes through the foramen ovale. The technique of insertion of the electrode is similar to that used in "percutaneous trigeminal rhizotomy" (see Figs. 3 and 4). It is well tolerated and provides stable recording conditions for as long as two weeks and probably more. The quality of recordings and the localizing value is much better than with sphenoidal electrodes, especially when multiple contact probes are used.

Localization on the basis of functional deficits alone should never be considered sufficient to recommend selective amygdalohippocampectomy. It is mandatory to demonstrate the *relevant epileptogenicity* of such a functional lesion using electrophysiological techniques. The information gained from the EEG falls into three categories, namely (1) spontaneous baseline activity and its changes during naturally occurring sleep or after inducing fast activity by drugs (barbiturates), (2) spontaneous and drug

Table 1. *Presently Used Evaluation Protocol at Zurich*



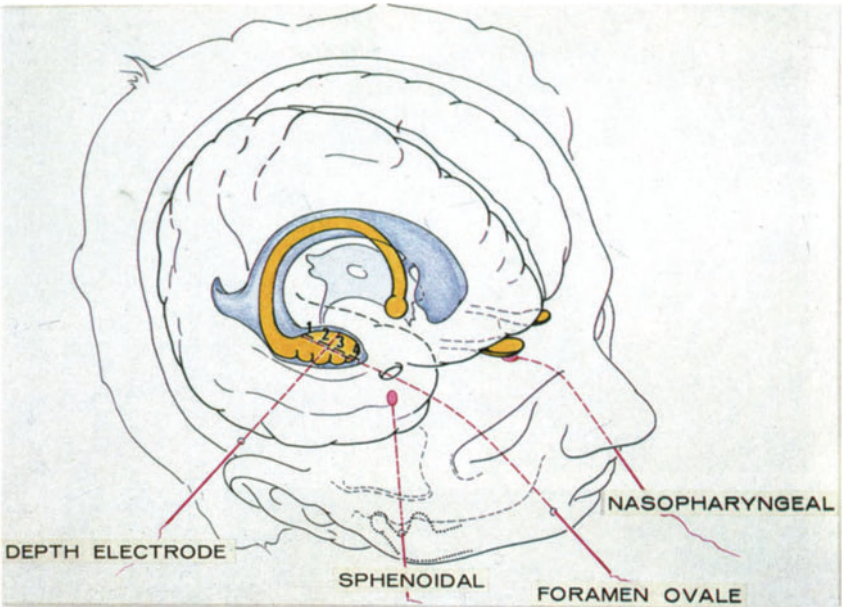
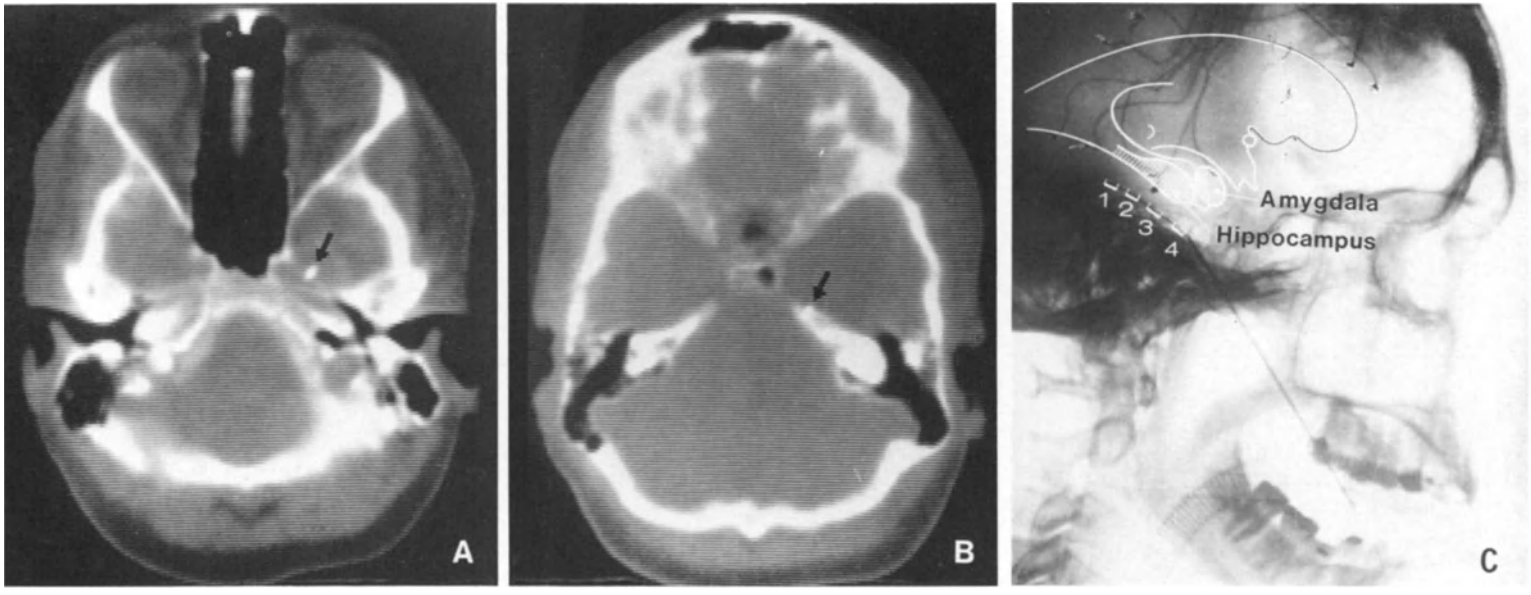


Fig. 3. Schematic drawing to illustrate techniques to improve EEG recording from the mesial aspects of temporal lobe: direct implantation of depth probes (SEEG), sphenoidal electrode technique, and placement of an electrode through the foramen ovale. The value of the non-invasive nasopharyngeal recording technique is limited

induced (thiopental activation of spikes) or drug depressed (barbiturization by intracarotid Amytal) interictal epileptic events, and (3) spontaneous ictal events. Moderate anticonvulsant reduction is sometimes necessary for practical reasons and seems to be allowed if basic rules are followed, although the risks of falsely localizing ictal onsets might increase (Engel and Crandall 1983). The localizing value of pharmacologically induced seizure activity is severely limited (Wieser *et al.* 1979) and no longer practised by us.

Long-term-EEG and Stereo-EEG monitoring is performed with the SEEG laboratory equipment as illustrated by Fig. 5. We feel that for our purpose radio telemetry (Binnie *et al.* 1981) would overcomplicate the system. We profit, however, from telemetric systems in use outside our University (especially at the Swiss Epilepsy Clinic at Zurich), which provide essential primary electroclinical data for deciding whether a patient should be considered a candidate for depth-exploration. Moreover, during the past year we have also used an ambulatory 8-channel EEG-cassette recorder (Oxford Medilog 9000) as a valuable compliment to 32-channel cable-EEG and CCTV (Stodieck and Wieser 1985 a).

Our EEG data acquisition system (Fig. 5) is simple, reliable and easily operated by experienced EEG technologists and does not depend on an engineering



Figs. 4A and B. CT scan showing the position of a "Foramen ovale" electrode (arrows)

Fig. 4C. X-ray (lateral view) of a patient with a multicontact (*1–4*) electrode placed through the foramen ovale and with stereotactically implanted depth electrodes. The position of the ventricular system and the mesiobasal-limbic structures (amygdala, hippocampus), as outlined by ventriculography, is superimposed in white. The needle, with its tip in the vicinity of the clival line, has been left to visualize its direction using the technique of percutaneous placement as described by Kirschner (1932)

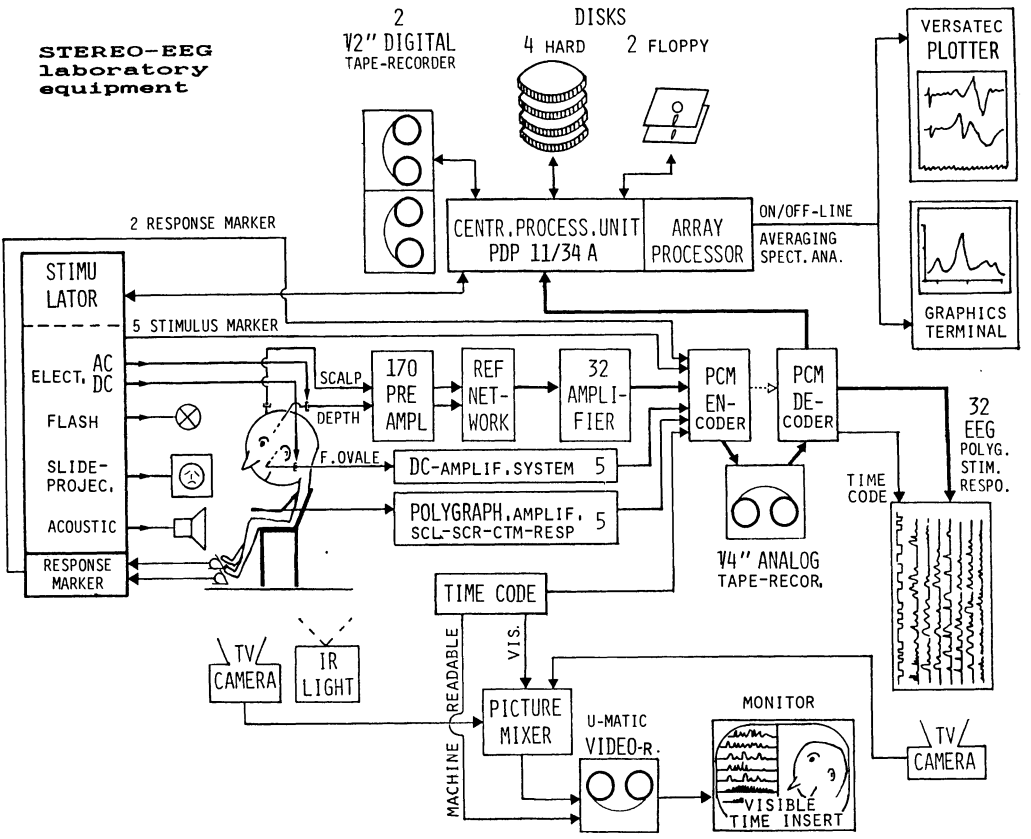


Fig. 5. Block diagram of SEEG laboratory equipment illustrating the major elements: the patient, stimulators, amplifiers, recording and display. *Abbreviations:* ELECT electrical stimulation, AC alternating current, DC direct current, SLIDE PROJ tachistoscopic visual hemifield or full-field stimulation, PREAMPL pre-amplifiers, AMPL amplifiers, POLYGRAPH = POLYG polygraphy, SCL skin conductance level (bimanual), SCR skin conductance response (bimanual), CTM cardiotachometer (heart rate), RESP respiration, RECOR = R recorder, REF referential, CENTR PROCESS UNIT central processing unit (Digital Equipment Corporation), PCM pulse coded modulation, SPECT ANA spectral analysis using Fast Fourier Transformation, IR infra-red light, STIM stimulus marker, RESPO response marker

department of a highly specialized institution. By placing the pre-amplifiers near the head of the patient our assembly greatly reduces movement artefacts, caused by the normal activity of the patient, who is however, limited to head movements within a radius of about $^3/_4$ meters. As the pre-amplifiers can easily be moved within a radius of about 3 meters, the patient is able to rise from sitting or lying position and to move around a few steps. The large number of pre-amplifiers (170) does not permit this entire unit to be worn on the head of the patient.

An output cable from the pre-amplifiers runs to a referential network permitting choice of every desired recording and grounding network within a maximum of 170

depth and surface locations including polygraphic measurements of various other parameters (EOG, ECG, respiration, etc.). At present, the output of 32 amplifiers is recorded on magnetic tape (PCM ¼″ ANALOG) which also receives the central time code. From here information is fed to a computer (PDP 11/34A), mainly for further off-line analysis, and at the same time to a 32-channel stripchart recorder, showing the selected surface and/or depth EEG together with the time code. Synchronous video monitoring of the patient and the EEG recording is stored on video tape, together with the time code, and displayed on TV monitors permitting direct control of the quality of the record. Special stimulators allow for peripheral sensory and intracerebral electrical stimulation and simultaneous recording of all other, non-stimulated electrode contacts. Infra-red light video monitoring allows for monitoring the patient in the dark and is used for all night sleep studies.

Metrizamide enhanced CSF CT scanning for identification of mesial temporal lobe herniation in candidates for selective amygdalohippocampectomy has been used over the past years*. Bolender and Wyler (1982) devised this method using high resolution CT and reported a reasonably good prediction in identifying pre-operatively the presence or absence of chronic herniation of mesial TL structures. We also have found it a valid additional method in predicting the post-operative outcome, which is better in the presence of TL herniation. We found metrizamide enhanced CSF CT scanning to be 70% accurate in diagnosing mesial TL herniation, as verified at operation and supported by histological diagnosis of mesial temporal sclerosis (Wieser *et al.* 1985 c). In patients undergoing a stereotactic neuroradiological examination prior to depth electrode implantation (Talairach *et al.* 1974, Bancaud *et al.* 1965), we instil the contrast medium during ventriculography and may then perform CT scanning at an appropriate time thereafter. After about 1–2 hours the contrast medium is distributed in the basal cisterns and no additional injection of metrizamide is necessary. So far there have been no complications using this technique.

Comprehensive neuropsychological testing is important during the presurgical and post-operative evaluation. In addition to more general tests which measure language, sensation, perception and motor skills, we utilize a number of tests particularly sensitive to TL dysfunctions (Perret 1973, Birri *et al.* 1982, Gonser 1983, Nadig 1985). Special attention was given to the results in the tests of verbal learning (paired associates) and memory (short stories) of the Wechsler Memory Scale, and of figurative (so-called "non-verbal") and spatial (visually guided maze) learning and memory (Rey's complex figure and recognition of simple geometric designs). Special batteries have been developed to measure lateralization of TL dysfunctions by comparing a patient's performance on verbal and non-verbal learning

* With the use of Magnetic Resonance scans CSF enhanced CT scanning will become obsolet because MRI scans can show the presence of mesial sclerosis with or without herniation (Wyler, unpublished data).

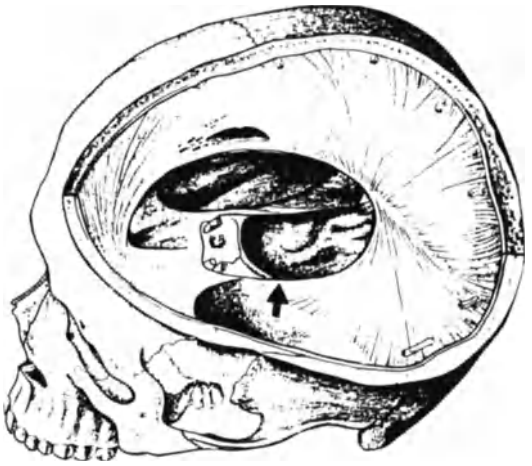


Fig. 6. The cerebral dura mater and its reflexions exposed by the removal of a part of the left half of the skull. The free edge of the left tentorium cerebelli is arrowed

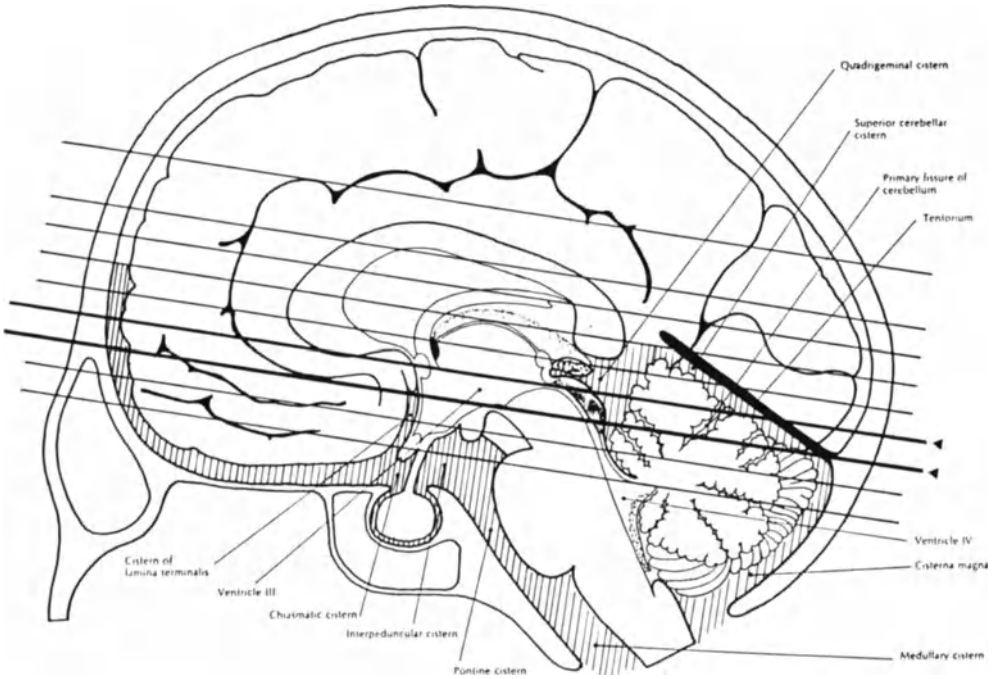


Fig. 7. Scheme illustrating serial axial CT scanning with cuts at an angle of + 4° with reference to the orbital meatal line. This procedure was found most useful for CT measurement of mesial TL herniation. Cuts with 5 mm increments are made throughout the TL and indicated by thin lines. Two + 4° cuts at the level of the cerebral peduncles are indicated by thick lines (arrows). Cisternal CSF space is hatched

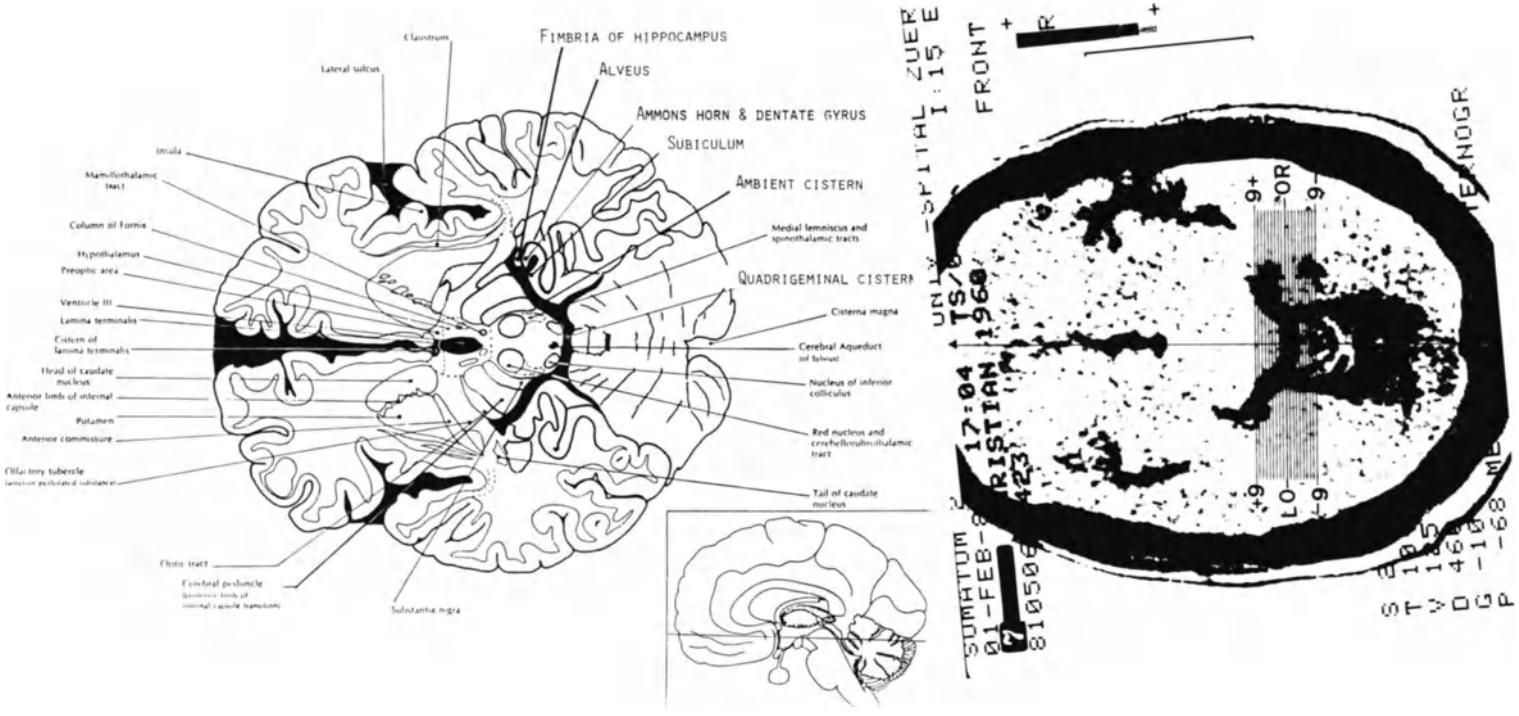


Fig. 8. CSF cistern morphology: a 5 mm cut (magnified 2.5 times photographically) at the level of the cerebral peduncles is shown with the measurement system applied. The reference line (0) is placed at the anterior edge of the quadrigeminal cistern with the vertical reference line adjusted to the midline. Measurements are made in millimeters between the vertical reference line and the mesial edge of the temporal structures (see anatomical situation at left). Beginning with the horizontal line at the reference point (0 mm) measurements are taken 9 mm frontal (+) and occipital (−). This gives 19 measurements for each side (R, L)

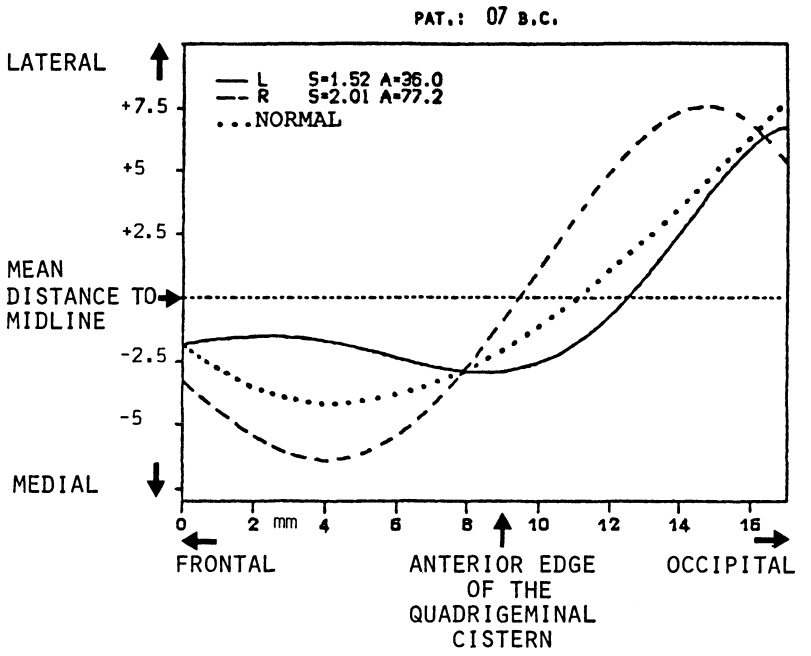


Fig. 9. Diagnostic curve of patient 07 (also shown in Fig. 8) together with a normal curve. Using a similar method to that described by Bolender and Wyler (1982), we plotted the sixth degree polynomial regression function of the measurement points to obtain the diagnostic curves. This procedure smooths the curves and allows taking their slope (*S*) at intersection with the x-axis, and the area (*A*) between the curves and the x-axis, as diagnostic parameters (courtesy of Dr. S. R. G. Stodieck)

and memory tests. They are described in outline below. It is evident that interpretation of the neuropsychological profile is dependent upon knowledge of the hemispheric organization of language. If any doubts arise on this point, especially in left-handers, dichotic listening tests or the intracarotid amytal test may resolve this question (Kimura 1983).

Description of the material and procedure used for testing learning and memory performance (Nadig *et al.* 1985).

Learning performance was tested with three series of 15 items each drawn or written in black ink on white cards 15 by 10 cm in size (see Fig. 10). The items were presented to the subjects one at a time. The items of the first series were nonsense designs (hereafter called "designs"). The second series consisted of drawings of common objects (hereafter called "drawings"). Concrete nouns (shortened to "nouns" in the following) were used in the third series.

The recall of as many items as possible of each series after a filled distraction interval of 30 minutes made up the *memory performance*. To avoid memory savings from pre- to post-operative testing, two parallel

versions A and B of the 3-item series were set up. Half the subjects of each patient group were tested pre-operatively with version A and post-operatively with version B, the other patients being tested first with version B and later with version A.

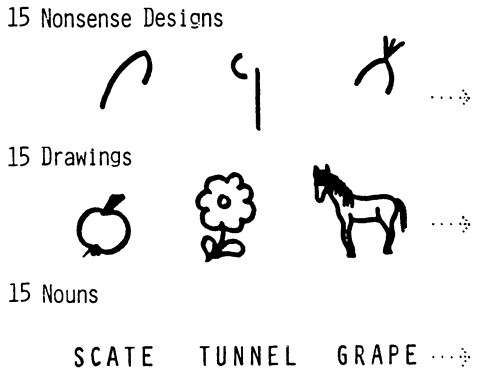


Fig. 10. Three examples of each test material for learning and memory assessment (courtesy of Dr. T. Nadig)

In the *learning* of designs, the 15 items were presented to the subject at a rate of approximately one item every 2–4 seconds. The subjects were instructed to evaluate each design as "pleasant" or "unpleasant" in order to prevent verbalization. They were asked to watch the designs carefully and to take good notice of each of them, because they would be asked later on to reproduce them on paper from memory in any order. In the subsequent presentations, only those items were presented anew which had not been reproduced in the immediately preceding trial. This procedure was repeated

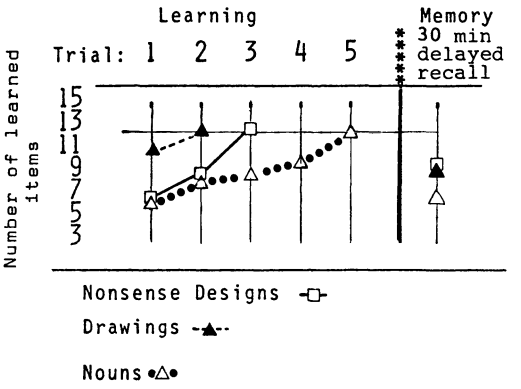


Fig. 11. Test-protocol of a patient with left temporal deficit

until the subjects were able to reproduce at least 12 out of 15 designs, but not more than 5 times. The same procedure was applied for the learning of drawings (with the difference that the drawn objects had to be named and not rated as to their being pleasant or unpleasant), and again with the nouns, which had to be read aloud by the subjects.

The distraction interval was filled for 30 minutes with the administration of psychometric tests which did not involve learning or memorizing new information.

Memory performance was then assessed by asking the subjects for the delayed recall of the three types of material, *i.e.*, designs, drawings and nouns. One important aspect of this testing procedure is that both learning and memory performances are measured with the same designs, drawings and nouns. An example of a test-protocol is shown in Fig. 11.

Both major therapeutic approaches, drugs and surgery, depend upon knowing whether the patient's problem is basically focal, multifocal or generalized. The surgical approach, however, requires *definite* and *very accurate* delineation of epileptogenic foci within the brain. As will be shown by a few examples, *depth recordings of spontaneous seizures* in a patient who is a candidate for surgical therapy very often is *the* significant step towards a rational surgical approach and considerably sharpens the criteria for recommending surgery.

Although Spencer (1981) found in her review that the reported surgical success rate is no better at centres employing depth EEG than at those which do not, this is no valid argument against depth EEG. It is evident that a more difficult population of patients, whose seizure foci are not easily localized by simple means, are referred to centres that have depth EEG. When depth and scalp EEG studies were compared in 178 patients, it was found that the use of depth EEG would have enabled 36% more patients to be selected for surgery by defining otherwise unidentifiable single epileptogenic foci. Furthermore, depth EEG could have prevented surgery for another 18% by demonstrating different or additional epileptogenic foci in patients who were thought to have a single discharging focus amenable to resection. Based on their own experience with 32 patients, Spencer *et al.* (1982) concluded that depth EEG data appear to be the most accurate of the presently available localizing techniques.

In addition, a so-called *"palliative" resection* might be sometimes performed which would not be done without depth EEG data. This was a relatively frequent finding in the series under consideration. To give a typical example: how should one proceed if depth EEG demonstrated a seizure origin near Wernicke's speech area but propagation and maintenance of the seizure discharge always seemed to depend critically on mesiobasal-limbic structures? Obviously the focus in such a case is located in an area of cortex which cannot be surgically removed without major deficits. In the case of intractable seizures refractory to adequate medical

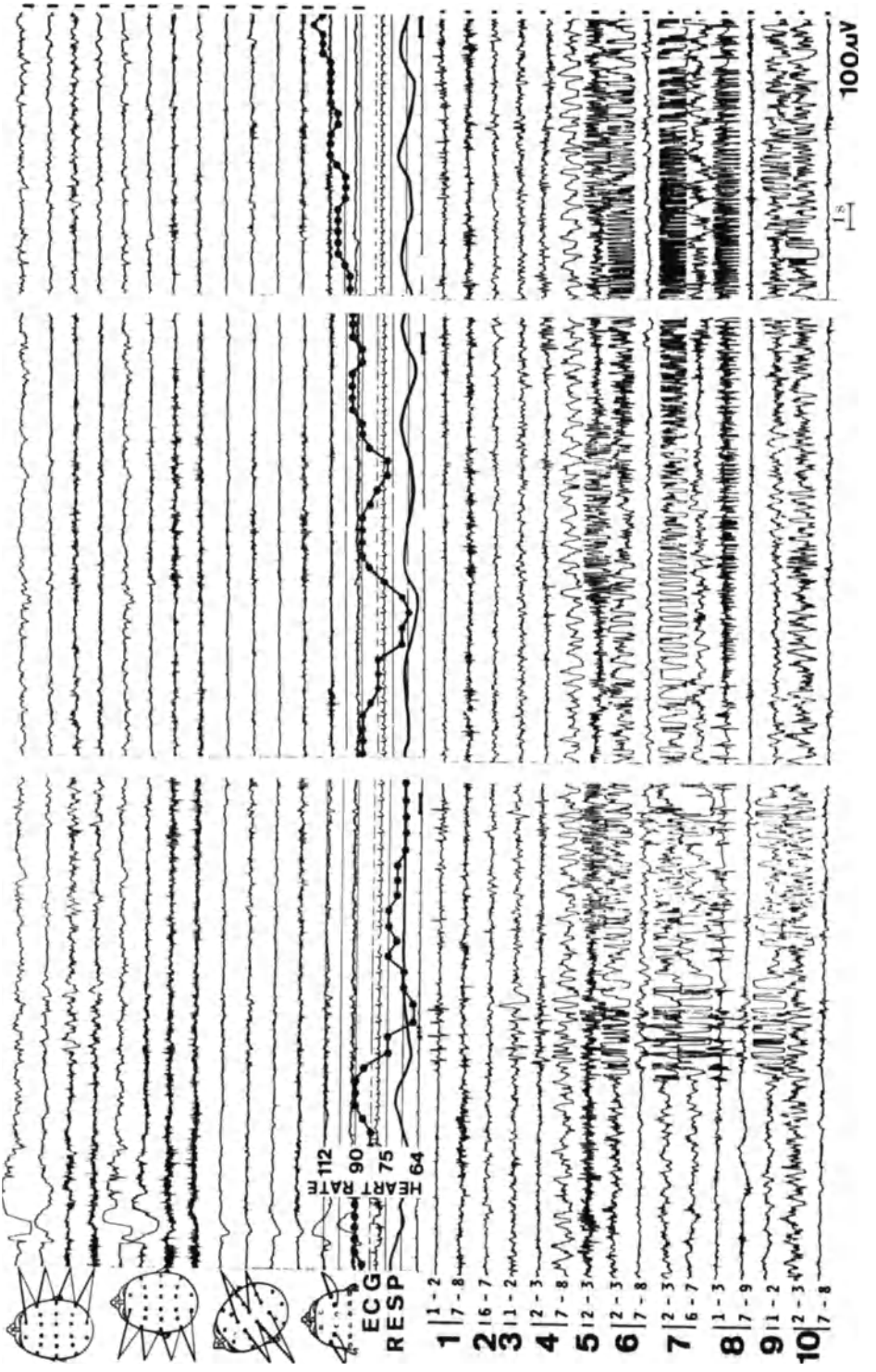

ECG
RESP
HEART RATE
112
90
75
64
1 1-2 7-8
2 6-7
3 1-2
4 2-3 7-8
5 2-3 7-8
6 2-3 7-8
7 2-3 6-7
8 1-3 7-9
9 1-2
10 2-3 7-8
ST
100μV

Fig. 12 a. Combined surface and depth EEG recording of a 30-year-old male with drug resistant complex partial seizures showing the electrical concomitants of a typical complex partial seizure with epigastric aura, marked vegetative signs, fear, automatisms and progressive loss of consciousness. Note the regional, *i.e.*, relatively widespread seizure onset. The high frequency seizure discharge, however, starts at right amygdala (8/1–3) and propagates stepwise to right anterior hippocampus (7/2–3) and then to the posterior hippocampus (6/2–3). The posterior parahippocampal gyrus (5/2–3) is also affected by these discharges. There is only moderate involvement of contralateral TL (10/2–3 = left hippocampus; 10/7–8 = left second temporal convolution). Note the changes of heart rate and respiration. Coinciding with the seizure onset the heart rate drops from about 90/min. to about 65/min., and arrest of respiration occurs. Whereas the initial widespread ictal discharges can be seen in the surface-EEG, the later mesiobasal-limbic discharges are not picked up in the conventional surface EEG. A transient and moderate flattening, however, is visible. Coding in this and subsequent figures is as follows: the large numbers correspond to the electrode, the small hyphenated numbers correspond to the contacts. For example 7/2–3 describes the signal at the contacts 2 and 3 of electrode 7. The surface EEG montage is that used at the EEG Institute of the University Hospital Zurich (see also Hess 1976). (Calibration: 1 second, 100 μV, TC 0.3, F ∞)

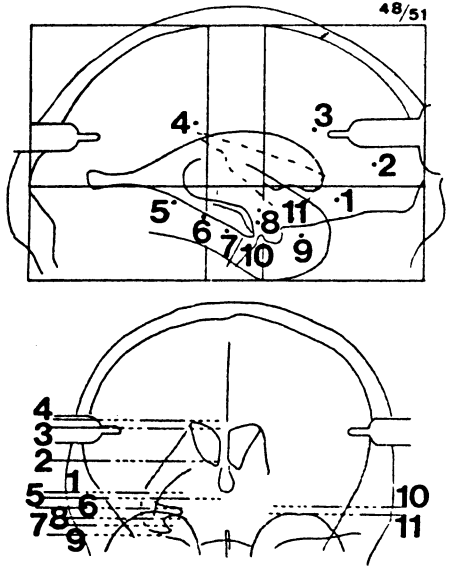


Fig. 12 b. Position of depth electrodes in the individual brain map with lateral and antero-posterior views. The presently used stainless steel, hollow-core, depth probes (Comte *et al.* 1983) consist of ten contacts arranged in two groups of 5 contacts. The diameter of the electrodes is 0.9 mm. The length of the contacts and their intercontact distance is 2 mm. The distance between contact 5 and 6 varies according to individual conditions. The contacts are numbered from medial to lateral with 1 to 10.

therapy and representing a severe handicap, we were tempted to offer the limited chance of possible amelioration and not that of a cure, which is rather unlikely with such a constellation. If diminution of the number of pacemaker neurons is possible, one might expect that such an operation would be effective in controlling overt clinical seizures, although the aura and interictal EEG spiking usually persist. As will be discussed later, the overall results of our "palliative" operations are not as good as in the causally operated patients, but good enough to seriously consider such "palliative" intervention. Provided that no relevant deficits emerge from the resection, such a policy can help a considerable proportion of patients who are otherwise judged as surgically inaccessible. It must be emphasized, however, that without proper identification of the secondary epileptogenesis of accessible mesiobasal structures such a "palliative" approach cannot be recommended.

The valuable information obtained by proper depth-EEG studies, especially in identifying mesiobasal TL foci, has been the matter of many publications (Wieser 1983 a, b, Wieser *et al.* 1985 a, b) and is illustrated by Figs. 12–14, 16, 18, 21, and 23. The seizure discharges illustrated show the spectrum of the causally operated non-lesional patients in this series. The reported cases include those of *strictly localized,* frequently occurring hippocampal discharges (Fig. 14) with "only" behavioural abnormalities. Hippocampal status epilepticus with cognitive deficits and associated with a monosymptomatic gustatory aura is illustrated with Figs. 16 and 17. More wide-spread seizure discharges are shown in Fig. 12, demonstrating a *regional seizure onset* with primary amygdalar, then hippocampal high frequency discharges and marked autonomic changes together with an epigastric aura. Fig. 13 shows a primary right hippocampal seizure onset with *stepwise propagation* to homolateral amygdala and frontal cortex and late contralateral hippocampal and amygdalar seizure spread.

Whereas the examples with full-blown and widespread seizure discharges (see also Fig. 22) represent typical complex partial seizures with the usual symptomatology, in the following patient with narrowly confined but frequently occurring hippocampal seizure discharges (Fig. 14), a marked behavioural and personality change including irritability, aggression, and rejection of authority was observed. Unusual "stickiness" and "circumstantiality" also were noted during these frequently occurring high-frequency discharges (Table 2) lasting several days. A short description of this patient follows.

Case Report (Pat. N., SEEG no. 100)

This 16-year-old right-handed girl had no significant medical history until aged 9. She was the second of 3 daughters of an upper middle class family; both parents had a university level education. Her delivery was normal and there was no history

of febrile convulsions. Her parents felt her to be their brightest child and during the first 3 years of school she was always the best in her class. At the age of 9 the first attacks occurred. They were initially absence-like, but within 2 years "classic psychomotor" seizures, starting with an olfactory aura combined with a sense of diminished vision and hearing and with fear, also frequently occurred. Several neurological examinations, EEGs and cranial CT scan, were within normal limits. A wide variety of anticonvulsant drugs was tried, all without success. At age 11, for the first time, psychodynamic factors were thought to be largely responsible for the clinical picture, and psychotherapy as well as family therapy was initiated, again without apparent success.

The years between ages 11 and 16 were marked largely by a change in behaviour and a social decline. The girl had concentration difficulties, lost her friends, ran away from home several times and started shoplifting. Her school performance deteriorated to the point that she was forced to leave school at age 15. She had spent over a year as an in-patient in psychiatric hospitals for adolescents. During these years a change in behaviour was noted by her parents, psychologists and various members of medical institutions. She was noted to be episodically aggressive, to reject authority, and to neglect hygiene. She was described as unusually "sticky", and as developing an abnormal concern for other patients' problems, trying to help them and care for them in an exaggerated way. She was felt to be very "circumstantial" and hypercorrect. On the other hand several episodes of sexual disinhibition occurred. On neuropsychological examination, slowness, difficulty in concentrating and impaired verbal performance were noted. EEGs have either been normal or have shown a left temporal focus and signs of a general hyperexcitability. The frequency of her absence-like and complex partial seizures had increased since age 11. One or two seizures per month, up to daily fits, were reported. Mobile long-term EEG monitoring at age 15, however, revealed that the seizure frequency was much higher. During one day, 29 complex partial seizures were observed. These seizures consisted of short "arrest" reactions with staring, occasionally associated with motor automatisms and head deviation. The patient was amnesic for many of these episodes, but almost always remembered initial fear and a sense of strangely diminished vision and hearing. While hospitalized at this time she had an "atypical non-convulsive status" of 30-minutes duration which was interrupted by injection of clonazepam (Rivotril®). The patient was admitted at age 16 for depth electrode recording. Neurological examination was normal except for an unusual amount of synkinetic movements and bilaterally absent ankle jerks. She was orientated in time and space, but slow and fearful. She had concentration difficulties, showed an impaired word-list generation, impaired verbal memory and occasional word-finding difficulties. The entire neuroradiological examination, including CT and bilateral carotid angiography, was normal. Several surface EEGs showed wide-spread "paroxysmal dysrhythmic" abnormalities and occasionally sharp-waves over the left anterior or midtemporal region.

Stereo EEG Findings

During 18.6 hours analysis time within 5 days, 91 left mesiobasal-limbic epileptic discharges were recorded (Fig. 14). Taking into account the duration of the discharges, 11% of the analysis time was covered by tonic or tonic-clonic epileptic

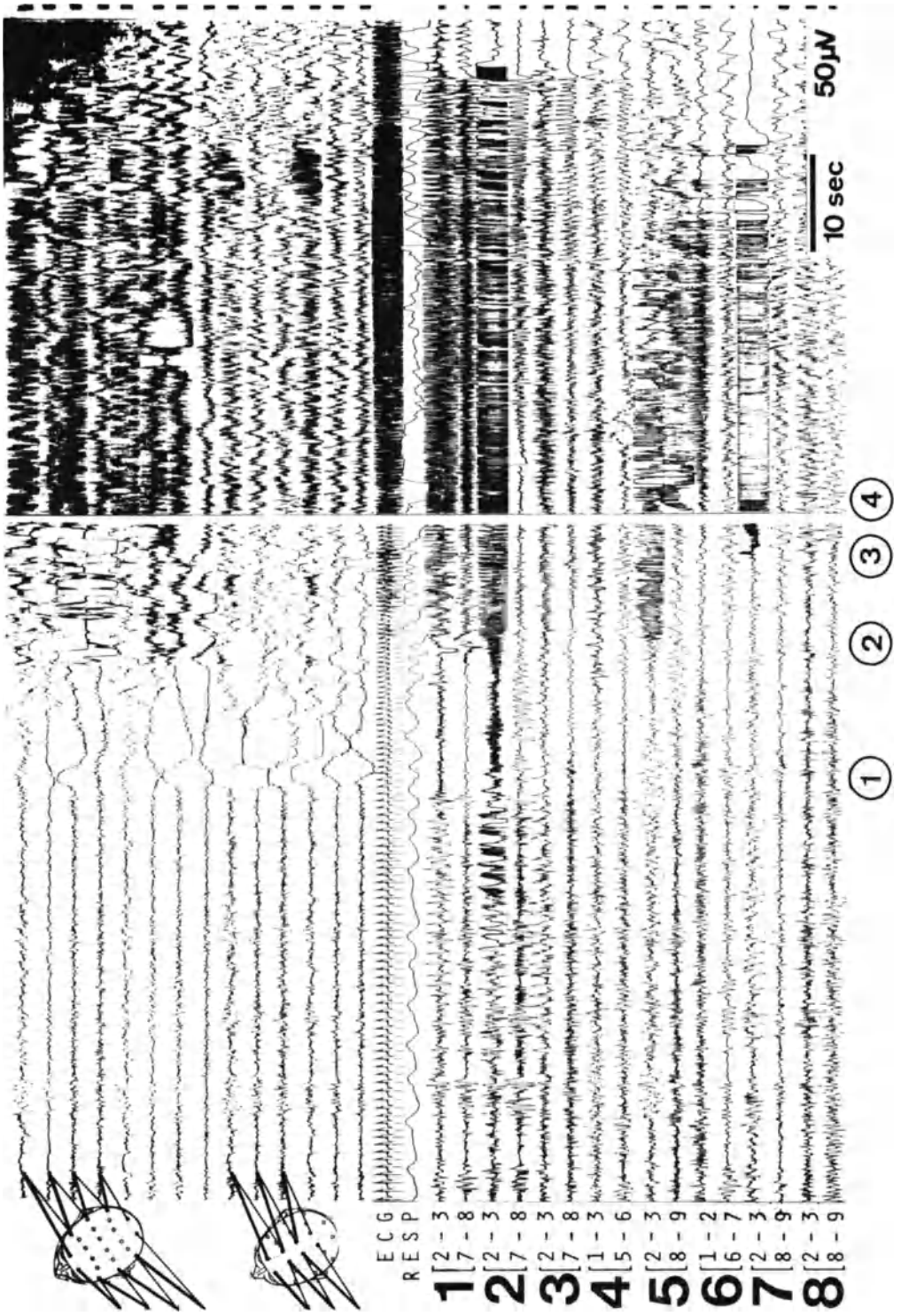

ECG
RESP
1 [2 – 3 / 7 – 8]
2 [2 – 3 / 7 – 8]
3 [2 – 3 / 7 – 8]
4 [1 – 3 / 5 – 6]
5 [2 – 3 / 8 – 9]
6 [1 – 2 / 6 – 7]
7 [2 – 3 / 8 – 9]
8 [2 – 3 / 8 – 9]
① ② ③ ④
10 sec
50µV

Fig. 13 a. Combined surface and depth EEG recordings showing a complex partial seizure of a 31-year-old male. This seizure starts in right mesiobasal-limbic structures, *i.e.*, right hippocampus (2/2–3) and right amygdala (1/2–3) (see individual brain map, Fig. 13 b), but later on propagates to homolateral anterior cingulate gyrus (5/2–3 = Brodmann's area 24), an important link in the Papez circuit (see MacLean 1954). About 10 seconds later the seizure discharges propagate to contralateral hippocampus (7/2–3 = left hippocampus) and another 10 seconds later to left amygdala (6/1–2). The concomitants of this seizure consisted of *1* arrest and distorted vision, *2* fear, fumbling and pallor, *3* loss of consciousness, *i.e.*, unresponsiveness, and *4* head turning to the left as well as complex postural changes. (Calibration 10 seconds, 50 μV, TC 0.3, F 70)

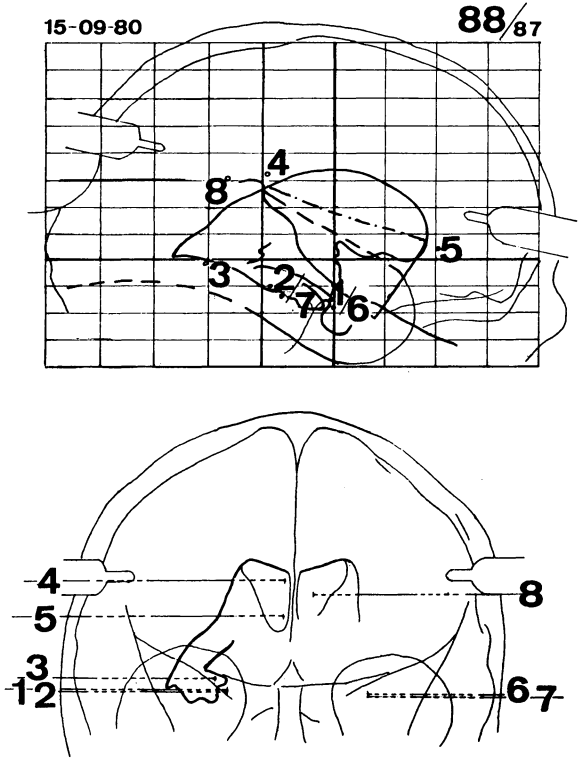


Fig. 13 b. Individual brain map with position of depth electrodes

discharges of the hippocampal formation alone or in combination with the homolateral amygdala (Table 2). Only 2 of these 91 discharges propagated to the homolateral neocortical temporal and frontal areas (the patient's "milder" but more frequent habitual attack pattern associated with an aura and head deviation), or later on to the contralateral temporal lobe (the patient's more severe habitual attack pattern, being associated with marked impairment of consciousness and prolonged automatisms and amnesia). Likewise the interictal hippocampal spikes spread in a typical manner to the homolateral amygdala and especially to the posterior cingulate cortex, indicating the preferential propagation pathways of this mesiobasal-limbic seizure type.

Immediately after left selective amygdalohippocampectomy, the patient's behaviour improved markedly and during the 3 years follow-up she continued to improve steadily in terms of both intellectual capacities and personality traits. Post-operatively she has been seizure-free, and anticonvulsant drugs have been considerably reduced.

Such patients with *hippocampal epileptic status activity* represent an ideal though rare model to study the possible function of this structure. It should, however, be kept in mind that the discharging focus, even when very restricted, represents only one aspect of the problem. As the following study of a patient aims to show, the concomitant dysfacilitation of the surrounding brain is most likely equally important for explaining the observed clinical signs and symptoms.

There is at least one valid observation which suggests that the existence of a spike focus, presenting some "noise" for other brain areas and giving rise to surrounding dysfacilitation, might be the primary pathogenetic mechanism for the frequently claimed cognitive impairment of TL seizure patients, especially in terms of memory decline and impaired learning. This is the fact, that resection of the temporal spike focus, either by standard *en bloc* removal of the anterior TL or by our technique, is commonly followed by an improvement of these functions, and particularly that of behaviour (Falconer 1973, Walker and Blumer 1975). However, in comparison to possible structural pre-operative damage, more tissue is lost at surgery than was effectively the case before the operation. Thus the "deficit theory" alone simply does not stand up to examination and cannot sufficently explain the behavioural concomitants (Geschwind 1983).

Tachistoscopic tasks (see Fig. 15) were performed in a 26-year-old female, M., with left hippocampal status epilepticus (SEEG no. 102). During SEEG evaluation this patient re-entered an "aura status" with gustatory sensations accompanied by epileptic discharges in the left hippocampus. These discharges were restricted to the hippocampus and could not be picked up by the surface EEG.

During depth electrode recording of these discharges the patient was extensively tested with two hemifield tachistoscopic tasks: a lexical decision

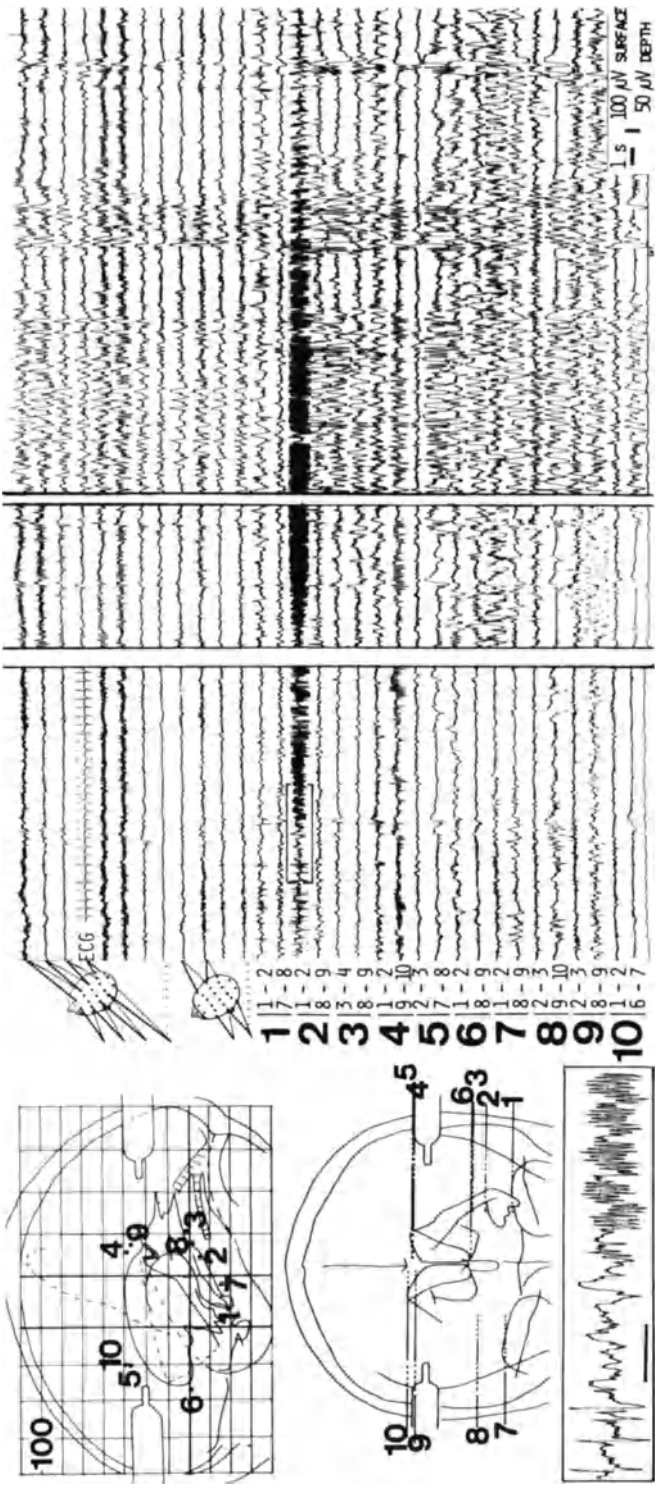


Fig. 14. Patient N. (SEEG no. 100). Three sections of combined surface and depth recordings during frequently recurring, narrowly confined left hippocampal (2/1–2) epileptic discharges. To show the frequency a portion of the left section is enlarged below the individual brain map

Table 2

Patient N., 1966 SEEG 100	Analysis time (minutes)	Discharges		Time of discharges in % of analysis time	Average discharge interval (minutes)
		No	Duration (minutes)		
14-06-82	150	20	31	21%	8
15-06-82	330	28	41	13%	12
16-06-82	302	19	16	5%	15
17-06-82	281	18	24	8%	16
18-06-82	52	6	9	17%	9
$\sum$ (5 days)	1,115 (18.6 hours)	91	121 (2 hours)	11%	12

task, typically showing a superior performance with right visual field (RVF = left hemispere) stimulus presentation, and a facial matching task, typically showing a left visual field (LVF = right hemisphere) advantage. Tachistoscopic recording was directly coupled with EEG and SEEG registration, *i.e.*, in channel 1 the stimulus onset was registered and in channels 2 and 3 the response latencies (button presses) of the right hand and the left hand (see Fig. 15). This set-up allowed for direct computation of the tachistoscopic performance in relation to the epileptic activity. Five

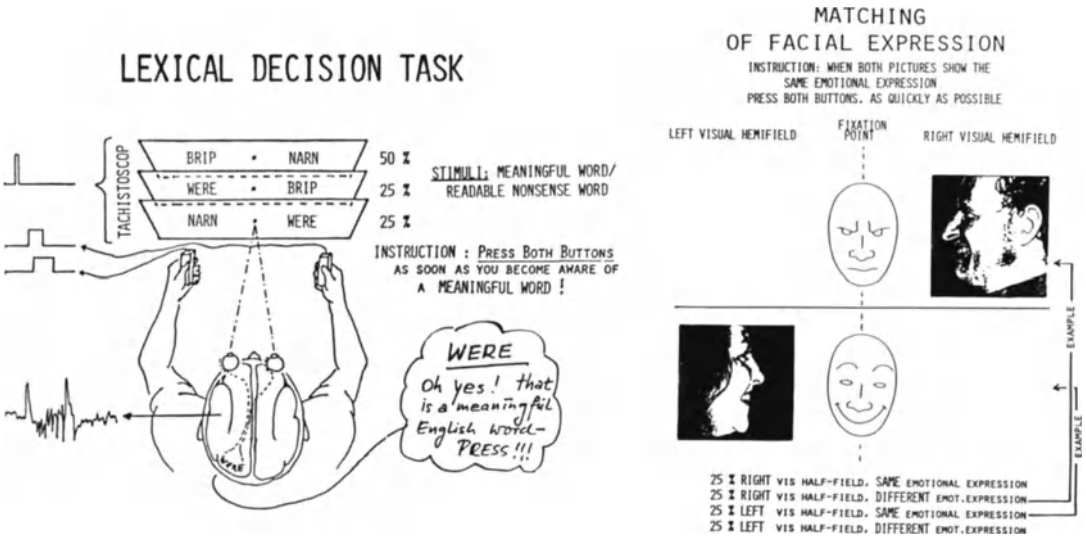


Fig. 15. Scheme illustrating the tachistoscopic test situation during hippocampal epileptic status activity of patient M. (SEEG no. 102) as described in the text

hippocampal EEG patterns (Fig. 16) could be differentiated in this patient: flat activity without epileptic potentials, frequently initiating or following tonic discharges (= 1); slow clonic discharges (= 2); fast clonic discharges (= 3); tonic discharges (= 4); and tonic-clonic discharges (= 5).

In the double simultaneous stimulation go/no-go *lexical decision task* the patient was presented with meaningful high frequency filler words and with pronounceable nonsense words. The stimuli were presented horizontally to the left and right of the fixation point (*i.e.*, presented to the right and left hemispheres). The stimulus set consisted of 48 cards, of which 24 had one meaningful stimulus word and one nonsense word with balanced presentation to the LVF and the RVF (see Fig. 15). The other 24 cards consisted of pairs of nonsense words. Stimulus exposure time was 100 ms. The patient was instructed to press the response buttons as quickly and synchronously as possible when she read a meaningful word. There was one trial run and 17 experimental runs totaling 816 stimulus exposures.

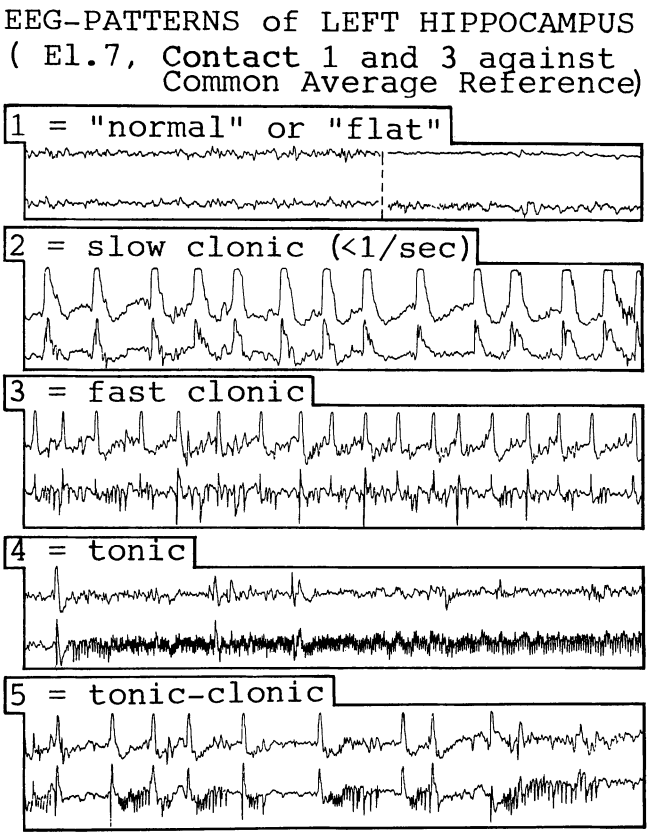


Fig. 16. Patient M. (SEEG no. 102). Illustration of the different electrical patterns of left hippocampus. Tachistoscopic stimulus presentation was during one of these patterns. Patterns 2 to 5 are epileptic discharges of different quality. Ordering of pattern is purely descriptive and does not imply any meaning. Frequently, however, "flat" activity (pattern 1 at the right) was preceding or following pattern 4. In retrospect, and on the basis of our results we would have done better to look at "flat" activity separately and not to lump it together with "normal" activity (pattern 1, left)

In the go/no-go *facial match task* the patient had to press the response buttons when presented with two identical facial expressions. Again, the set consisted of 48 cards, 24 with target stimuli and 24 with non-target stimuli (see Fig. 15). Stimulus exposure time was 150 ms. There was one trial run and 17 experimental runs, altogether 816 stimulations.

For details regarding tasks and procedure see Landis *et al.* (1979, 1981), Regard and Landis (1985), and Wieser *et al.* (1985 a).

The following variables were computed for each task: the percent of correct responses, the response latencies for each hand and the mean of both hands, the difference between both hands and the mean press durations of both hands. The results are graphically summarized in Fig. 17.

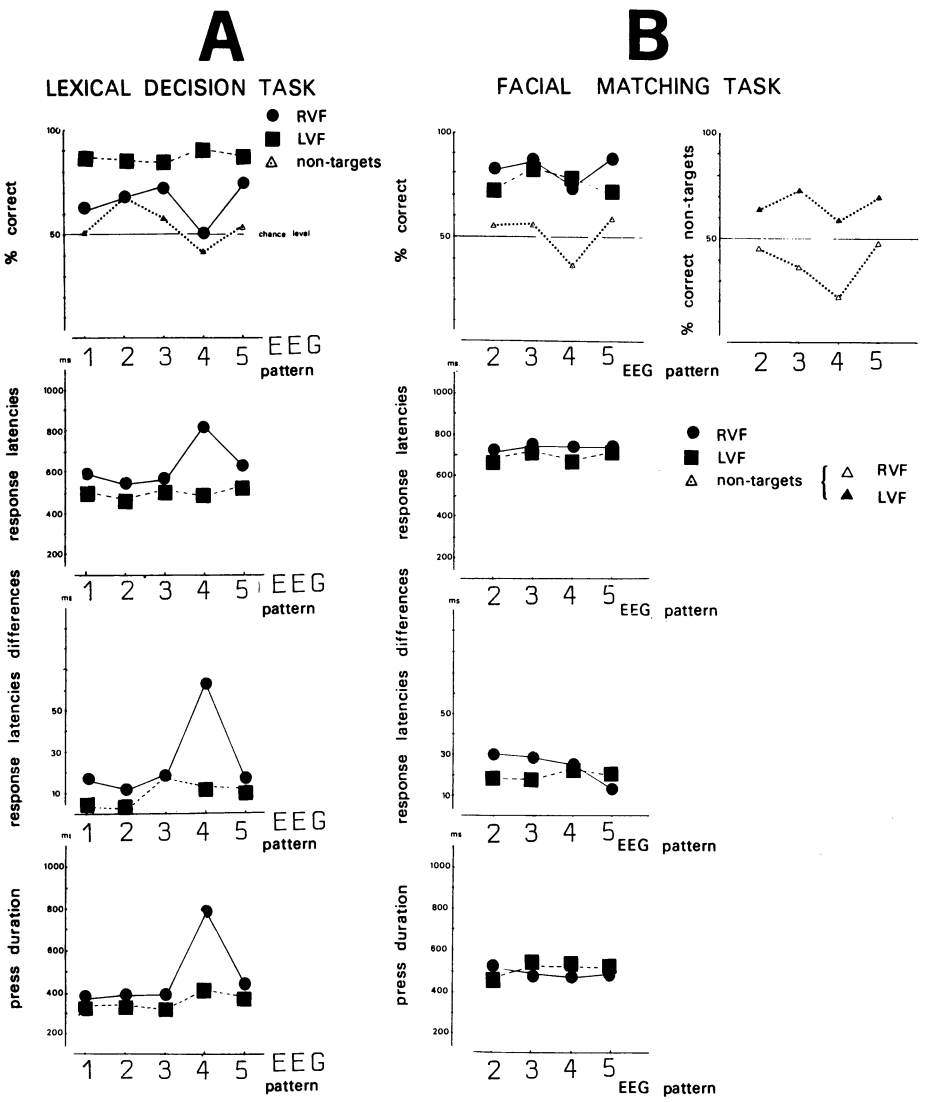


Fig. 17. Graphical synopsis of results obtained in patient M. (SEEG no. 102) using two tachistoscopic tasks. See text

Lexical decision task. The number of correct responses per visual field for all 5 EEG patterns is illustrated in Fig. 17a. Chi^2 tests between both visual fields (VF) revealed significant differences for hippocampal EEG pattern 1 (4.19, $p < 0.05$) and pattern 4 (11.43, $p < 0.05$). There were no overall effects for each VF and the non-targets, but single comparisons within the 5 EEG patterns revealed significant lower performance to RVF stimulations at pattern 4 (compared to 3 = 4.3, $p < 0.05$, to 5 = 4.65, $p < 0.05$). The percent of correct responses was also reduced for non-targets at pattern 4 (compared to 2 = 6.69, $p < 0.05$). The response latencies and press duration times of the correct responses also are shown according

to VF and hippocampal EEG pattern. A poorer overall performance was found to RVF (left hemisphere) than to LVF (right hemisphere) stimulation, with a striking decrease in performance with EEG pattern 4. Statistical analyses were conducted with a MANOVA design (2 visual fields by 5 EEG patterns), adjusted for unequal cell occupancies. For single comparisons, the Duncan multiple range test was used ($p < 0.05$). There was a significant VF effect for the response latencies of the right hand ($F = 4.1$; 15.555; $p < 0.001$). Single comparisons were significant for pattern 4 (RVF) compared to patterns 2 and 3 (critical difference = 135.3). For the left hand, also, a significant effect for VF was found ($F = 4.1$; 16.538; $p < 0.001$) as well as a significant increase in response latency at pattern 4 to RVF stimulation compared with all other four patterns (critical difference = 139.3). Regarding the response latency differences between both hands, there was a significant main effect for EEG ($F = 4.1$; 2.573; $p < 0.05$) and a strong trend for VF ($F = 4.1$; 3.779; $p = 0.053$). Again, single comparisons revealed a slower performance to RVF stimulations for pattern 4 (critical difference = 20.5). Press duration time also showed a significant main effect for EEG ($F = 4.1$; 4.157; $p < 0.005$) and for VF ($F = 4.1$; $p < 0.001$) and a significant EEG × VF interaction ($F = 4.1$; 2.599; $p < 0.05$). Performance to RVF stimulation of pattern 4 was again significantly poorer compared with the other patterns (critical difference = 151.3).

Facial matching task. Fig. 17 b illustrates the percent of correct responses for both visual fields, as well as for the non-targets, for four EEG patterns. EEG pattern 1 was excluded from the analysis owing to too few measurements. Chi^2 tests within both VF and between the LVF and the RVF revealed no significant performance differences. However, if we look at response correctness for the non-targets separated for each VF (Fig. 17 b, top at right), the RVF performance was significantly poorer than the LVF performance (11.16, $p < 0.05$), and pattern 4 was significantly different from pattern 2 (8.47, $p < 0.005$) and from pattern 5 (9.66, $p < 0.005$). The performance was also significantly different from LVF and RVF targets at pattern 3 (13.13, $p < 0.001$), pattern 4 (16.90, $p < 0.001$) and pattern 5 (4.10, $p < 0.05$). Fig. 17 b also illustrates the response latencies and press duration times. No significant main effects or interaction were found for these variables.

Conclusions of the tachistoscopic experiments. In the lexical decision task, during left hippocampal epileptic discharges, this patient's performance was better for LVF (right hemisphere) stimulations than for RVF (left hemisphere) stimulations. Her performance decreased significantly only with EEG pattern 4, *i.e.*, with tonic discharges that originated in the left hippocampus. At the same time, the number of correct responses increased for LVF (right hemisphere) stimulations, though not significantly. From these results one must conclude that only left hemispheric cognitive activity, as measured by the lexical decision task, decreased during tonic seizure activity in that hippocampus. The performance of the right hemisphere was not impaired (LVF stimulatons). This conclusion is well supported by the fact that her performance in the facial task remained intact for all EEG patterns. Obviously, this normally right hemispheric task remains un-

touched by left hemispheric seizure activity except for the significantly poorer response accuracy for RVF non-targets.

Thus the results of these tachistoscopic experiments clearly reflect the poor performance of the epileptically discharging left hemisphere and this in a clear-cut relation to the quality of the EEG pattern of the left hippocampus. As measurements of response latencies and press durations in the lateralized stimuli of the lexical decision task by definition refer only to the correctly identified stimuli, the prolonged response latencies for stimuli addressing the left hemisphere, especially at the time of tonic discharges of the left hippocampus (pattern 4), can be interpreted in terms of prolonged problem solving time alone and/or prolonged motor action. The fact that press durations are also prolonged when stimuli address the left hemisphere during tonic discharges is a strong argument that the motor output system also is impaired. The observation that the right hemisphere identifies stimuli best at EEG pattern 4, as well as the fact that *differences of response latencies between both hands* are significantly prolonged for stimuli addressing the left hemisphere during tonic discharges of the left hippocampus, point to some form of block of left hemispheric functions during left tonic hippocampal discharges. In addition, the differences in response latencies between both hands in the lexical task might be an argument in favour of an interhemispheric block. Only when the stimuli address the tonically discharging left hemisphere, the normally delayed left hand (directed by the right hemisphere) shows an additional delay compared to the right hand. This probably means that the flow of information from the left hemisphere to the motor centres of the right hemisphere is more impaired than it is to the motor centres of the left hemisphere. In the facial matching task there is no EEG pattern-dependent asynchrony either for the onset or for the end of the button presses. The finding that the performance for non-target stimuli (different facial expressions) is bad, and especially bad with the facial match stimulations to the RVF (the epileptically discharging left hemisphere) during pattern 4, leads us to question whether recognition of different emotional expressions in this facial match (asking no button presses for a correct response) is a function predominantly served by the left hemisphere, whereas recognition of identical emotional expressions (asking for button to be pressed for a correct response) is a better lateralized right hemispheric function. Since in previous control experiments with this test (Landis *et al.* 1979, Landis *et al.* 1981) this question was not directly analyzed, it remains open for further study. Recently Gazzaniga and Smylie (1983) have provided data that suggest that the right hemisphere superiority is not specific to faces and is also not caused by specialized differences in sensory processes, but rather is related to differences in each hemisphere's ability to encode stimuli that cannot be adequately differentiated with a verbal description.

In summary, several findings of these tachistoscopic studies, such as the improved performance of the right hemisphere and the dissociation of the motor responses between left and right hand during tonic discharges of the left hippocampus in the lexical task, point to a form of functional block of the interhemispheric cross-talk due to strong inhibitory forces coming into action during tonic discharges. This inhibition might be an indication of a protective mechanism, which prevents the discharging hemisphere from excessively bombarding the opposite one. Such an interpretation would help to explain the lack of seizure spread to the opposite hemisphere in this case and would reflect a kind of temporary "functional split-brain" phenomenon of epileptic nature.

The findings of these two patients with a narrowly confined unilateral mesiobasal-limbic status epilepticus address a rare, but highly interesting problem, namely *complex partial status epilepticus*. The clinical phenomena accompanying the latter may consist of long-lasting mental confusion (such as twilight states) or altered mental state (such as hallucinations and recollections), automatic behaviour [such as fugues (Gastaut *et al.* 1956)] and disturbances of emotion, sometimes with marked anxiety and fear, together with motor phenomena (Ballenger *et al.* 1983, Williamson *et al.* 1985). As a rule, the observed phenomena are polymorphic and show a marked dynamic course (Wieser 1980). Often the impression of a cyclicity occurs (Treiman and Delgado-Escueta 1983), especially in patients with the recurrent form. Continous seizures, however, usually also show fluctuating responsiveness.

Ictal Signs and Symptoms of Mesiobasal-Limbic Seizures

Usually epileptic discharges in the TL are limited in time, *i.e.*, they last a few minutes, and are accompanied by psychosensorial and psychoaffective phenomena occurring with or without automatisms. Although a single ictal sign or symptom remains of doubtful diagnostic value, from the sequence of the symptoms more reliable conclusions can be drawn regarding the seizure originating site. We have addressed this problem elsewhere in great detail (Wieser 1983 a, 1986).

The typical hippocampal seizure onset (see Fig. 18) may be accompanied by an arrest (Delgado-Escueta *et al.* 1979, 1982, Wieser 1983 a). If seizure discharges remain unilateral, no other symptoms are necessarily seen. A warning of an imminent seizure is, however, not uncommon. During mesiobasal-limbic discharges, recollections (déjà or jamais experiences), dreamy states, delusions, hallucinations, ecstasy and/or fear may occur (Wieser 1982). Strong fear (Wieser 1983 b) as well as strong vegetative signs (Stodieck and Wieser 1985 b) point to an amygdalar seizure origin (see Fig. 23) or at least to ictal involvement of the amygdala (see Fig. 12). In such a case propagation of the epileptic events to the hypothalamus can be seen

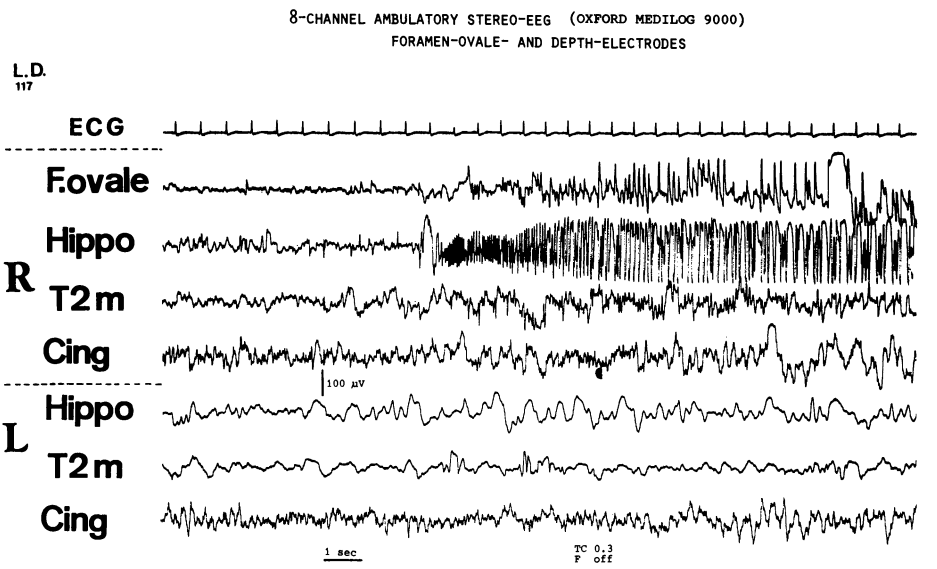


Fig. 18 a. Right hippocampal seizure onset (= R Hippo) with moderate propagation to homolateral neocortical temporal lateral cortex (RT_2 m = right second temporal convolution, middle portion) and homolateral parietal cingulate gyrus (Cing). An electrode inserted through the right foramen ovale (F. ovale) and recording from the medial aspect of uncus hippocampi also picks up epileptiform activity. There is no propagation to the contralateral hemisphere. Clinically this unilateral and well-localized seizure started with an arrest reaction

Fig. 18 b. Picture of this patient (SEEG no. 117) taken during recording from selected intracerebral depth electrodes and the "foramen ovale" electrode using an 8-channel ambulatory cassette recorder (Oxford Medilog 9000)

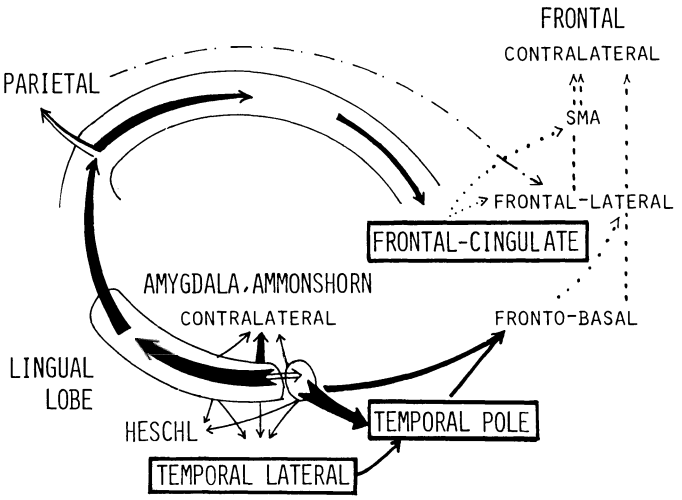


Fig. 19. Main characteristics of unilateral temporobasal-limbic seizure type. The symptoms are listed in decreasing order of their correlation with this seizure type and consist of: (1) Warning, progressive clouding of consciousness. (2) Arrest. (3) Viscerosensitive symptoms, such as epigastric aura, constriction, nausea, cephalgic sensations. (4) Visceromotor, such as pupillary change, flush, pallor. (5) Automatisms, mainly of oro-alimentary type. (6) Psychic phenomena, such as recollections (déjà experiences), dreamy states, delusions and hallucinations. (7) Change in emotional sphere such as fear, sadness. (8) Motor phenomena such as unilateral face twitching and postural changes

(see Fig. 21). Recently, an intense interest has focused on the nature of the representation of emotion in the cerebral hemispheres. Studying the spontaneous facial expressions occurring at onset of focal seizure activity, Strauss *et al.* (1983) did not, however, reveal a consistent relation between side of seizure onset and type of facial expression.

The most frequently experienced aura associated with amygdalar seizure onset is the epigastric one, usually associated with nausea. Often the patients complain of a warm pressing sensation at the stomach which rises to the chest or heart and may reach the head ("cephalgic aura"). Oro-alimentary automatisms (licking, lip-smacking, swallowing) likewise point to amygdalar seizure discharges and especially to bilateral seizure activity involving both amygdaloid bodies (Bancaud *et al.* 1965).

Olfacto-gustatory auras seem to be more frequently associated with tumours than other symptoms. Ipsi- as well as contraversive head-turning may occur during the course of seizure spread and is frequently associated with frontal seizure propagation (see Fig. 13). As the first ictal sign of an

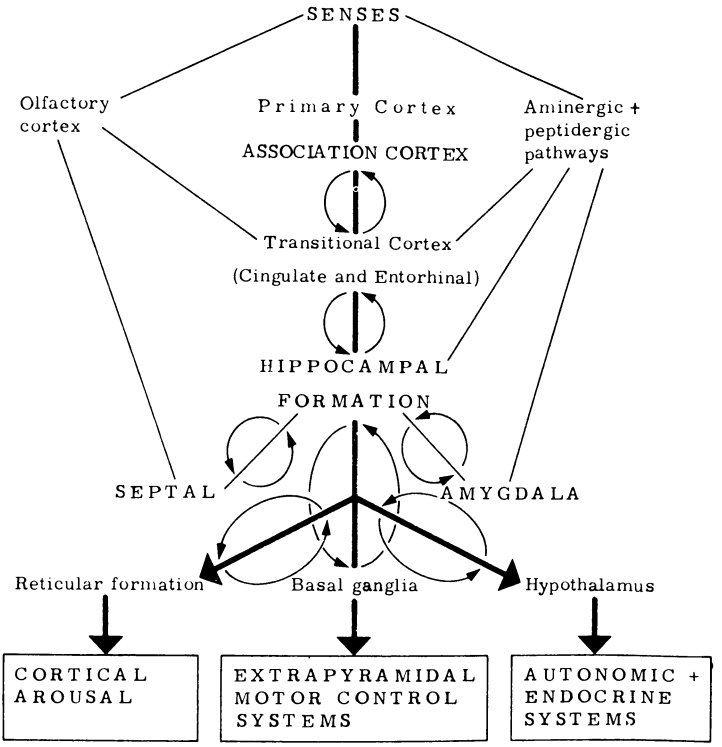


Fig. 20. Schematic diagram of the most important connections of the limbic system. Hippocampus—area septalis—amygdala are the fundamental structures reciprocally linked to each other. They receive afferents from olfactory and other sensory areas via associative, neocortical areas. Transitional cortex consisting of the cingulate gyrus and area entorhinalis serves as a bridge for the reciprocal relationship between neocortex and hippocampus and amygdala, respectively. The common efferent projections are indicated by three targets—reticular formation, basal ganglia, hypothalamus—and are linked to the limbic system by multiple feedback loops (omitted in the diagram) (from: Akert 1980, with permission)

epileptic seizure, however, head-turning has no lateralizing or localizing significance (Robillard *et al.* 1983, Ochs *et al.* 1984). Ipsilateral face twitching may occur simultaneously with amygdalar discharges and was recently observed by us during electrical stimulation of the amygdala leading to a local after-discharge.

A scheme of this mesiobasal-limbic seizure type is shown in Fig. 19 and summarizes the accompanying ictal signs and symptoms according to their correlative rank order.

The prototype of mesiobasal complex partial seizures as recognized by conventional surface EEG recordings is illustrated in Fig. 22.

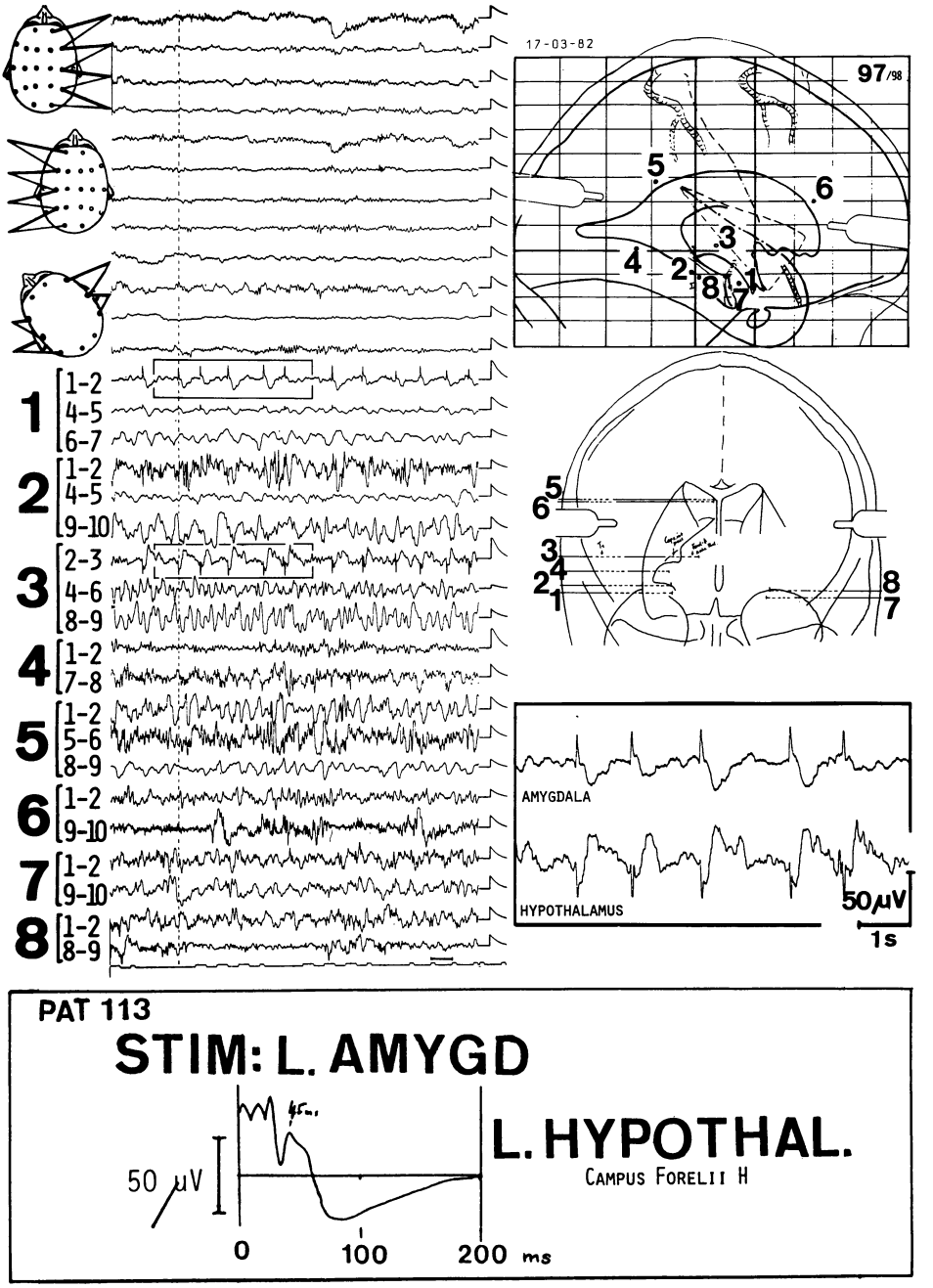


Fig. 21. Top section: combined surface and depth recordings showing repetitive sharp-slow-waves of about 0.5 to 1 cps in the right amygdala (1/1–2) and in the homolateral hypothalamus (3/2–3). The target point of electrode 3 was calculated to be the Forel-H field. Details are enlarged below the individual brain map to emphasize the close time relation of these epileptiform potentials. Bottom section: in another patient (SEEG no. 113) evoked potentials were recorded in the left hypothalamus (Forel-H field) after repetitive electrical single pulse stimulation of the homolateral amygdala. Averaged response (n = 16)

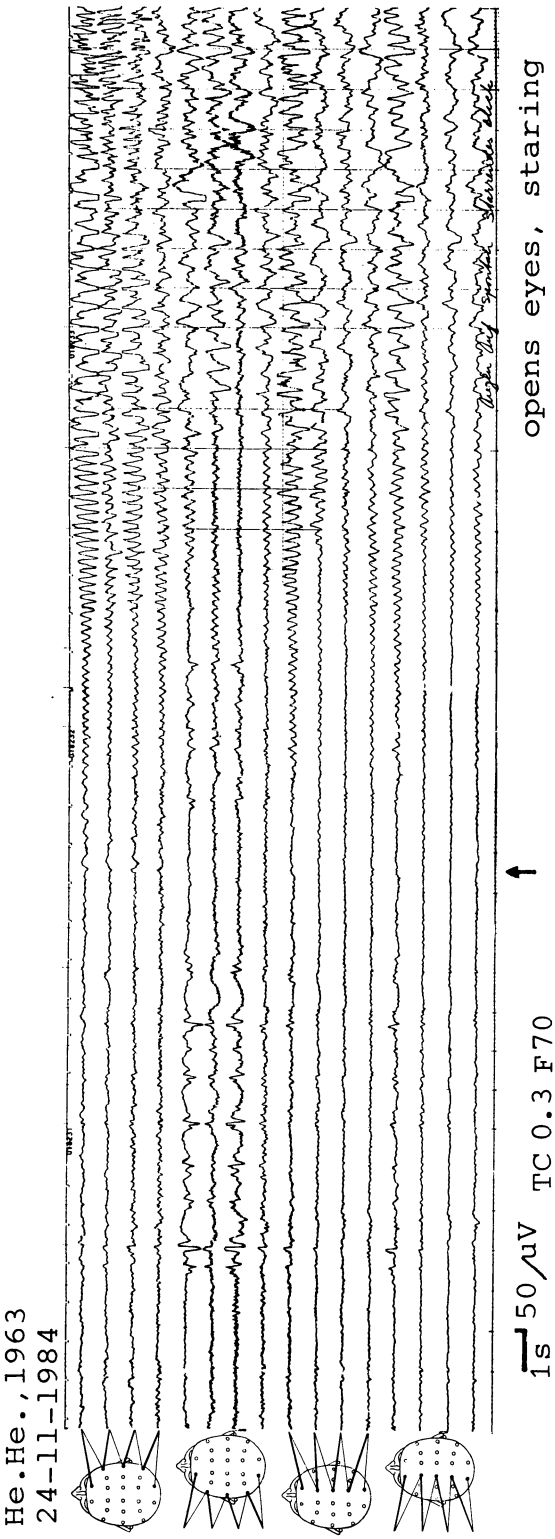


Fig. 22. Prototype of a surface recorded complex partial seizure. Together with an arrest reaction (arrow) the EEG shows right frontotemporal rhythmic activity with strong propagation to frontal derivations of both hemispheres and to contralateral temporal region. Note that pre-ictally left frontotemporal repetitive discharges precede this seizure. This patient had a calcified venous angioma right temporal. The interictal EEG showed bilateral epileptogenic anterior TL foci, predominant at left and independent from each other. The EEG at seizure onset, however, unequivocally pointed to a right TL origin of the seizures, as illustrated here

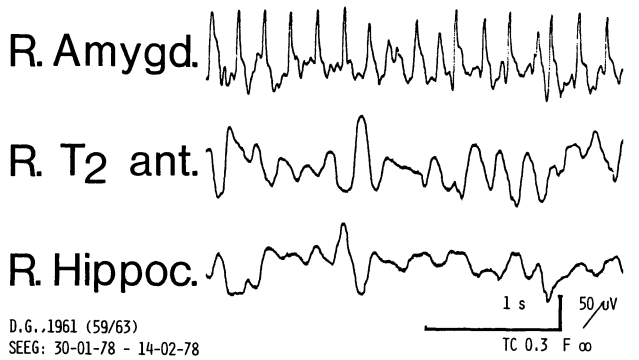


Fig. 23. Right amygdalar 5 cps epileptiform discharges (channel 1) without propagation to homolateral hippocampus (channel 3). RT_2 ant. = anterior part of second temporal convolution. Clinical concomitants: strong fear and "strange" sexual feeling

2. Results

This selective amygdalohippocampectomy series consists of 103 patients. Fig. 24 shows CT scans after selective amygdalohippocampectomy.

Fig. 25 gives a synopsis of the results of this series. *Patients are grouped* according to the presence or absence of benign or malignant tumours. As SEEG evaluated patients without gross structural lesions are of greatest interest, they are treated as a separate subgroup, thus leaving a further "mixed" subgroup with predominantly vascular lesions ("non-tumoural/no SEEG").

This grouping is used throughout, although it should be kept in mind that a certain overlap exists. For example, in one patient of the "non-tumoural SEEG" group an astrocytoma was found, and two patients with known or highly suspected oligosymptomatic tuberous sclerosis had to be evaluated by SEEG.

The information of Fig. 25 is subsequently presented in Tables 3 to 15 and Fig. 27. Table 3 gives the numbers of patients with special features (marked by different symbols and colours in Fig. 25) which might influence the outcome data, as well as the numbers of patients falling into a given histological classification.

As can be seen from Table 4 *more males than females* have been operated upon. Only the "non-tumoural/no SEEG" group behaves differently. In all groups the operated side is equally distributed. However the groups "non-tumoural/SEEG" and "benign tumour" show a right, and the "non-tumoural/no SEEG" and "malignant tumour" groups exhibit a left preponderance.

The *mean age at operation* was 30 years. The "non-tumoural/no SEEG" patients came to operation at a younger age, whereas the "malignant tumour" group presented at 41.5 years.

The *mean age at seizure onset* was 20 years. For the "non-tumoural SEEG" group it was 9.2 years; however, for the "malignant tumour" group the mean age was 38.5 years.

The *mean pre-operative duration of illness* with recurrent seizures was 10 years. In the "non-tumoural SEEG" group it amounts to 19 years, whereas in the "malignant tumour" patients it is only 3 years. Note that pre-

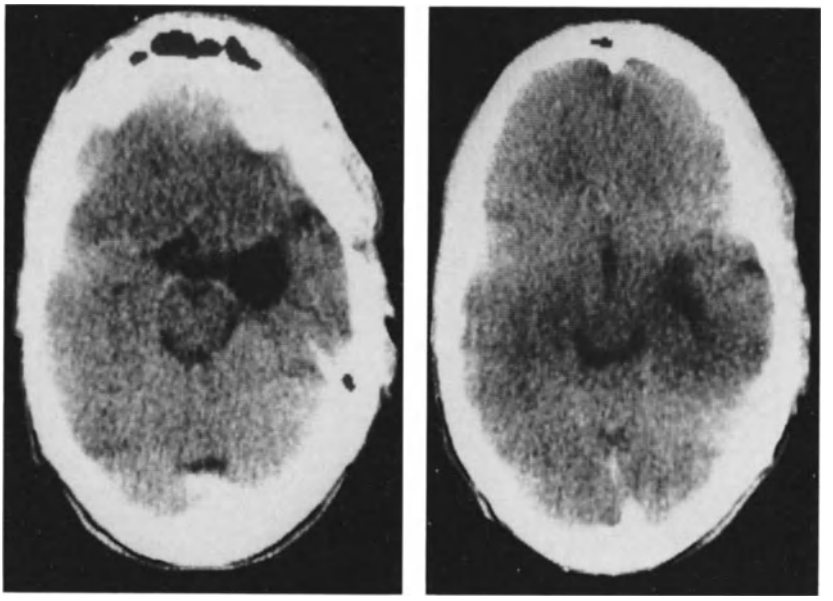


Fig. 24. CT scans after selective amygdalohippocampectomy

operative seizures could date back 20 years in a case with a benign lesion and even 12 years in a case with a histologically malignant tumour.

The *follow-up* is shown in Table 8. Ranging from 12 to 118 months, it was longer (mean 3½ years) in "benign tumour" and "non-tumoural SEEG" groups than in the other groups.

The *general clinical outcome,* as rated by the patient and the relatives as well as by neurologists, neurosurgeons and neuropsychologists, was graded into four classes. This is probably at least equal in importance to the seizure outcome itself. *Complications related to diagnosis and/or surgery* were fully integrated into this assessment.

As shown in Table 3, ten patients of this series have died. Two of them are within the "non-tumoural SEEG" group and had been inoculated with Creutzfeldt-Jakob disease. The circumstances of this extraordinary complication have been reported elsewhere (Bernoulli *et al.* 1977). The other 8

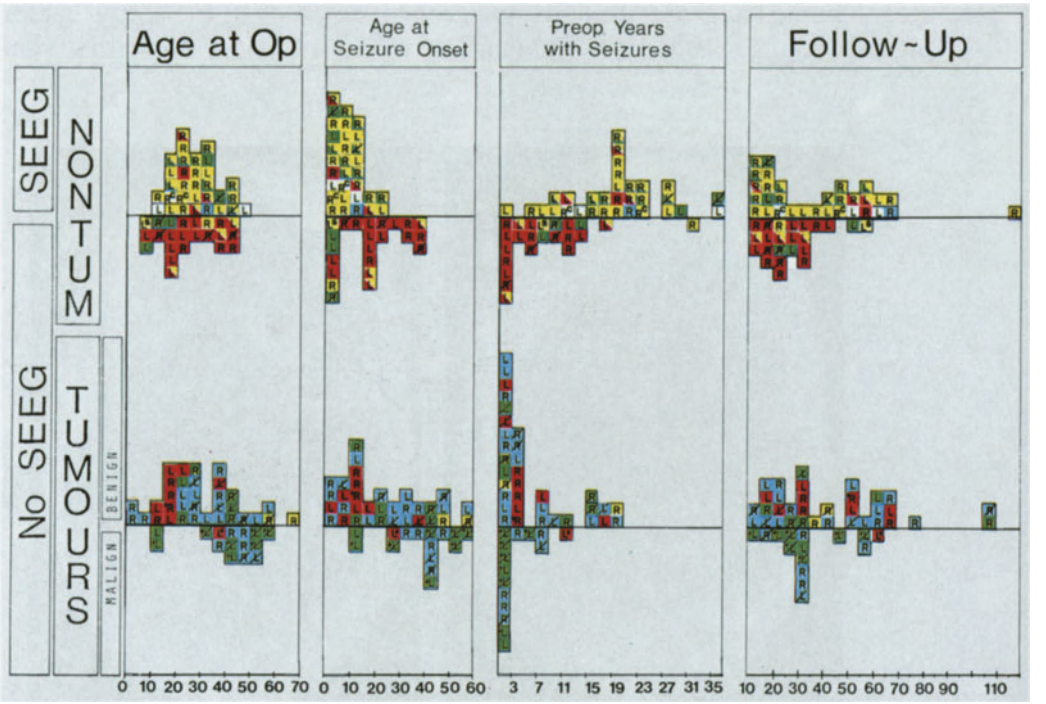
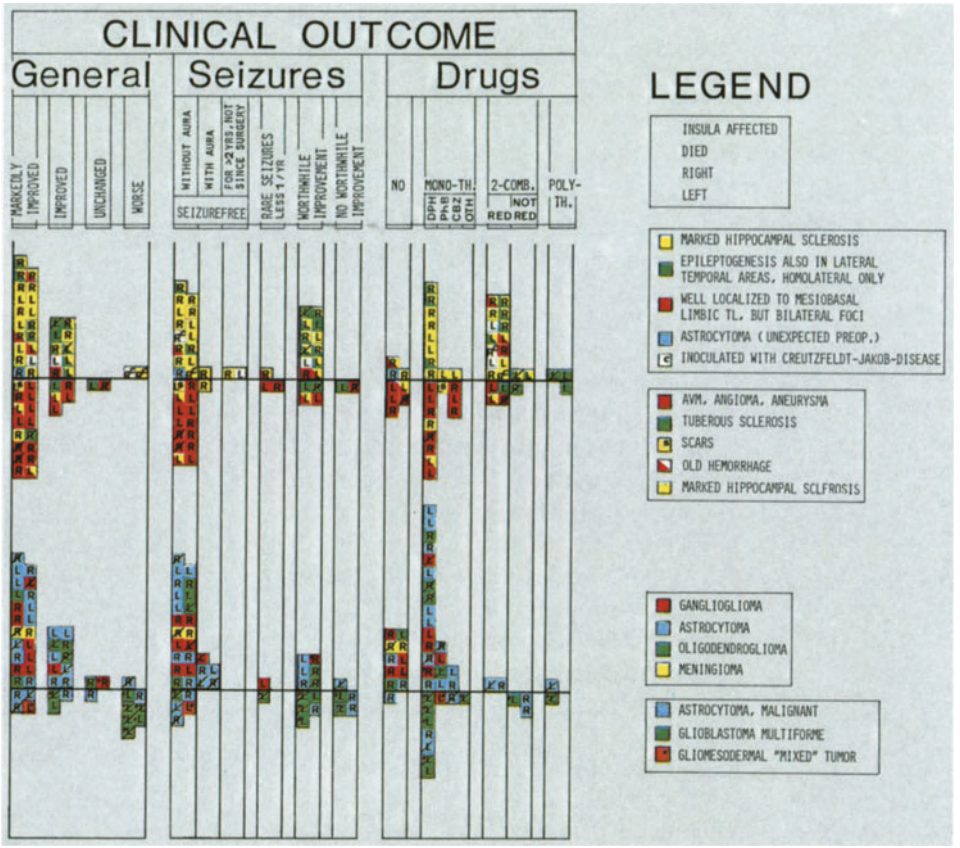


Fig. 25. Synopsis of the results of the selective amygdalohippocampectomy series encoded by one square. Colour code is given in the legend at right and refers only to top) were used

patients died as a consequence of having recurrent malignant tumour (7 patients) or of unknown reason (1 patient).

The best clinical outcome was achieved in the "non-tumoural/no SEEG" group with a mainly vascular etiology, followed by "benign tumour" patients. The outcome of the "non-tumoural SEEG" group, however, is very similar. Obviously "malignant tumours" score the worst, but to date 4 patients of this group (n = 15) are doing well.

The *seizure outcome* is shown in Table 10. Sixty-four (62%) of the 103 patients are seizure-free and only 7% have no worthwhile improvement. Rare seizures persist in 5% and the remaining 26% have a worthwhile improvement. Comparing the groups, the "benign tumour" group scores best, followed by "non-tumoural/no SEEG" and "non-tumoural SEEG". It is noteworthy that the seizure outcome of the two non-tumoural subgroups differs, in that within the SEEG group none of the 31 patients was a



(103 patients). Patients are classified in four groups (see text). Each patient is one group as indicated, whereas the same (non-coloured) symbols (legend block at throughout

complete failure (as opposed to 9% of patients of the "non-tumoural/no SEEG" group) and 58% of these "non-tumoural SEEG" patients are within the category "seizure-free". In accordance with the recommendations of the International Temporal Lobe Club (communication J. Engel, Jr., December 1981), patients with persisting auras and those who had some seizures but who became seizure-free for 2 or more years, are separately listed within the category "seizure-free".

Epileptological outcome data are incomplete without giving the data on the *actual drug regimen*. Table 11 shows that only 11% of all patients actually have a more or less unchanged anticonvulsant drug therapy. In 88% of the patients the anticonvulsants are reduced compared to the pre-operative level. Nineteen percent of these, however, are still taking 2 drugs. It is our policy to continue drug treatment post-operatively for 2–3 years, even if complete seizure control has resulted from operation. Eighteen

Table 3. *Subgrouping of Patients, Histological Findings and Other Characteristics*

Total n = 103			Insula affected	23
			Died	10
			Right	51
			Left	52
SEEG n = 31	**Non-tumoural** n = 54		Marked hippocampal sclerosis	24
			Epileptogenesis also in lateral temporal areas, homolateral only	11
			Well-localized to mesiobasal-limbic TL, but bilateral foci	4
			Astrocytoma (unexpected pre-operatively)	1
			Inoculated with Creutzfeldt-Jakob disease	2
		n = 23	AVM (13), venous angioma (1), aneurysma (1)	15
			Tuberous sclerosis	3
			Scars (1), old haemorrhage (3) + marked hippocampal sclerosis	5
No SEEG n = 72	**Tumours** n = 49	Benign n = 34	Ganglioglioma	9
			Astrocytoma	17
			Oligodendroglioma	6
			Meningioma	2
		Malignant n = 15	Astrocytoma, malignant	6
			Infiltrative oligodendroglioma + glioblastoma multiforme	8
			Gliomesodermal "mixed" tumour	1

percent of the previously drug-resistant seizure patients are already completely off drugs and remain seizure-free.

We tried to determine whether or not *lateralization* (Table 12) and *affection of the insula* (Table 13) influenced the seizure outcome. As can be seen from Fig. 25 and Table 3, in 23 patients the insula was affected by the lesion and/or by the epileptogenic process. Furthermore the presence or absence of marked *hippocampal sclerosis* (Table 14) and the outcome of "*palliative*" (see p. 59) *versus "causal"* amygdalohippocampectomies in the "non-tumoural SEEG" group were compared (Table 15). Fig. 27 finally attempts to analyze whether the *age of seizure onset* or the *pre-operative duration of the seizure illness* or *both* have an influence on the outcome data.

Table 4. *Sex Ratio and Operated Side*

		Number	Male	Female	Right	Left
Non-tumoural	SEEG	31 30%	19 61%	12 39%	18 58%	13 42%
	No SEEG	23 22%	10 43%	13 57%	10 43%	13 57%
Tumours	Benign	34 33%	22 65%	12 35%	18 53%	16 47%
	Malignant	15 14%	11 73%	4 27%	5 33%	10 66%
Total		**103** 100%	62 **60%**	41 **40%**	51 **50%**	52 **50%**

Table 5. *Age at Operation (Years)*

		Mean	SD	Minimum	Maximum
Non-tumoural	SEEG	28.2	8.7	15	46
	No SEEG	25.0	10.9	8	43
Tumours	Benign	30.1	15.8	1	67
	Malignant	41.5	12.4	13	57
Total		**30.0**	13.4	1	67

The overall data of Table 12, testing the possible influence of the *side of operation,* show that patients with right amygdalohippocampectomy do better than those with left. This finding probably has two explanations. First, malignant tumours exhibit a left preponderance; and second, left-sided operations more often include so-called "palliative" interventions. As described on p. 59 and 62, some patients with a primarily neocortical left

Table 6. *Age at Seizure Onset (Years)*

Mean		Mean	SD	Minimum	Maximum
Non-tumoural	SEEG	9.2	6.3	0.5	25
	No SEEG	16.9	13.0	0.5	40
Tumours	Benign	23.9	16.5	0.3	59
	Malignant	38.5	13.0	12.5	56
Total		**20.0**	16.0	0.3	59

Table 7. *Pre-Operative Years with Seizures*

		Mean	SD	Minimum	Maximum
Non-tumoural	SEEG	19.0	7.8	2	35
	No SEEG	8.1	7.3	0.1	31
Tumours	Benign	6.2	6.4	0.2	20
	Malignant	3.0	3.5	0.1	12
Total		**10.0**	9.1	0.1	35

temporal seizure origin near Wernicke's area underwent a "palliative" selective amygdalohippocampectomy. Results are not as good in this palliative group as in the causal group (see also Table 15). This is most important in the "non-tumoural SEEG" group, where right amygdalohippocampectomies resulted in 74% of the 19 patients being seizure-free without auras (1 a), whereas only 26% of the patients with left amygdalohippocampectomy could be classified within this category. The "non-tumoural/no SEEG" group does not show any significant lateralization. In the "benign tumour" group, patients had a slightly better outcome when operated on the right as compared to the left side.

Table 8. *Post-Operative Follow-Up (Months)*

		Mean	SD	Minimum	Maximum
Non-tumoural	SEEG	40.3	23.5	12	118
	No SEEG	28.6	11.5	14	57
Tumours	Benign	44.9	23.7	13	107
	Malignant	36.7	14.8	15	64
Total		**38.7**	21.2	12	118

Table 9. *General Clinical Outcome (Number of Patients)*

		Markedly Improved	Improved	Unchanged	Worse
Non-tumoural	SEEG	19 61%	10 32%	0 0%	2 6%
	No SEEG	16 69%	5 22%	2 9%	0
Tumours	Benign	21 62%	10 29%	2 6%	1 3%
	Malignant	4 27%	3 20%	1 7%	7 47%
Total		60 **58%**	28 **27%**	5 **5%**	10 **10%**

As expected, *involvement of the insula* by the lesion and/or the epileptogenic process resulted in a reduced success rate. If the insula was not affected, 70% of these 80 patients fell into the categories "seizure-free" and "rare seizures", as compared to only 56% of the 23 patients with insula being affected.

Table 10. *Seizure Outcome (Number of Patients)*

		Seizure-free					
		without aura	with aura for ⩾ 2 years	Rare Seizures = less 1/year	Worthwhile Improvement	No Worthwhile Improvement
Non-tumoural	SEEG	15	1 2 58%	1 3%	12 39%	0
	No SEEG	14	1 0 65%	2 9%	4 17%	2 9%
Tumours	Benign	21	5 0 76%	1 3%	6 18%	1 3%
	Malignant	5	0 0 33%	1 7%	5 33%	4 27%
Total		55	7 2 64 **62%**	5 **5%**	27 **26%**	7 **7%**

Table 11. *Actual Anticonvulsant Drug-Therapy*

		Without drugs	Mono-therapy, reduced	2-drug combination, reduced	2-drug combination, not reduced	Poly-therapy, not reduced
Non-tumoural	SEEG	3 10%	10 32%	14 45%	2 6%	2 6%
	No SEEG	5 22%	12 52%	4 17%	1 4%	1 4%
Tumours	Benign	10 29%	21 62%	2 6%	0	1 3%
	Malignant	1 7%	10 67%	0	3 20%	1 7%
Total		19 **18%**	53 **51%**	20 **19%**	6 **6%**	5 **5%**

Table 12. *Seizure Outcome: Right vs. Left Amygdalohippocampectomy*

	Total	Seizure-free (1) and Rare Seizures (2)					Improved (3) and Not Improved (4)				
		SEEG	No SEEG	TU b	TU m	Total	SEEG	No SEEG	TU b	TU m	Total
Right	51 **50%**	14 74%	8 47%	15 56%	2 33%	39 **38%**	4 33%	2 33%	3 43%	3 33%	12 **12%**
Left	52 **50%**	5 26%	9 53%	12 44%	4 67%	30 **29%**	8 67%	4 67%	4 57%	6 67%	22 **21%**
Total	103 **100%**	19 100%	17	27	6	69 **67%**	12 100%	6	7	9	34 **33%**

Table 13. *Seizure Outcome: Insula Affected vs. Not Affected*

	Total	Seizure-free (1) and Rare Seizures (2)					Improved (3) and Not Improved (4)				
		SEEG	No SEEG	TU b	TU m	Total	SEEG	No SEEG	TU b	TU m	Total
Affected	23 **22%**	0	2 12%	7 26%	4 67%	13 **13%**	2 17%	2 33%	3 43%	3 33%	10 **10%**
Not affected	80 **78%**	19 100%	15 88%	20 74%	2 33%	56 **54%**	10 83%	4 67%	4 57%	6 67%	24 **23%**
Total	103 **100%**	19 100%	17	27	6	69 **67%**	12 100%	6	7	9	34 **33%**

In the "non-tumoural SEEG" group, the 24 patients with *marked hippocampal sclerosis* had a much better outcome than those 7 patients without such a histological finding.

That the removal of pathological tissue favours a better prognosis than the removal of a histologically normal tissue is well-known (Falconer 1971, Lieb *et al.* 1981 a, Wyler and Bolender 1983).

Correlating the surface and deep EEG pattern with neuropathological findings and with the surgical outcome, it was concluded that ictal and interictal EEG recordings contain valuable non-redundant information for predicting the presence and type of underlying pathology (Lieb *et al.* 1981 a) and the surgical outcome (Lieb *et al.* 1981 b). The degree of relative hypometabolism, as measured by positron emission tomography with ^{18}F-fluorodeoxyglucose, also correlates well with the severity of the pathological lesion, particularly with mesiotemporal or hippocampal sclerosis; but the size of the hypometabolic zone is generally much larger than the area of pathological involvement as shown by the histological examination of the resected specimen (Engel *et al.* 1982 b).

Fig. 26 gives an example of a hippocampal sclerosis as found in patient no. 18 of these series.

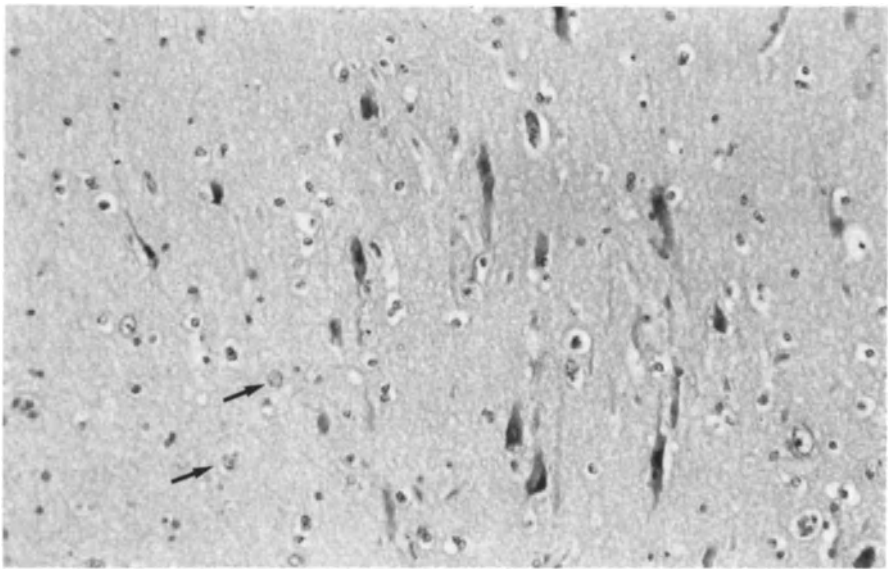


Fig. 26. Photomicrograph of CA2 region of human hippocampus (case no. 23 of this series). At time of left amygdalohippocampectomy this 9-year-old boy had frequently recurring complex partial seizures. He started to have seizures at early childhood (age 1 year). As sphenoidal recordings could provide sufficient information, no depth electrode studies were done. Following operation the patient is seizure-free. Note moderate Ammon's horn sclerosis with neuronal cell loss in the pyramidal layer accompanied by gliosis (arrows). ($\times$ 130)

Table 14. *Seizure Outcome: With Hippocampal Sclerosis vs. Without Hippocampal Sclerosis*

		Seizure-free and Rare Seizures		Improved and Not Improved	
Hippocampal Sclerosis		16	**52%**	**26%**	8
Without Hippocampal Sclerosis		3	**10%**	**13%**	4
Total	**100%**	19	61%	39%	12

"Palliative" amygdalohippocampectomies were less effective than "causal" ones. Out of the 15 palliatively operated patients, 5 fall into the categories "seizure-free" and "rare seizures".

Table 15. *Seizure Outcome: "Palliative" vs. "Causal" Operations*

		Seizure-free and Rare Seizures		Improved and Not Improved	
Palliative (ipsilateral temp. neocortex + bilateral-limbic)		5	**16%**	**32%**	10
Causal		14	**45%**	**6%**	2
Total	**100%**	19	61%	39%	12

Because of the uneven distribution and the different underlying causes, a detailed analysis of the *influence of the age at seizure onset* on the seizure outcome (Fig. 27, left), as well as of the influence of the *pre-operative duration of seizure illness* (Fig. 27, right), is difficult. In all groups, the outcome is better if the seizure onset was in later childhood and puberty as compared to seizure onset within the first 5 years of life or at a later age.

Patients having their seizure onset before age 20 show the following ratio of outcome distribution: [seizure-free and rare seizures] : [worthwhile improvement and no improvement at all] = 2.21 : 1. For patients having their onset of seizures later than age 20, this ratio only amounts to 1.78 : 1.

Table 16. *Seizure Outcome Following Various Types of Operations*

		No. of patients		Seizure-free		Rare Seizures		Worthwhile I.		No worthwhile I.	
Amygdalohippocampectomy	Non tum. SEEG Causal[1]	31	16	58%	88% 14	3%	0	39%	2		0
	Non tum. SEEG Palliative		15		27% 4		1		10		
	Non tum. No SEEG[2]	23		65%	15	9%	2	17%	4	9%	2
	Tum. TU benign	34		76%	26	3%	1	18%	6	3%	1
	Tum. TU malignant	15		33%	5	7%	1	33%	5	27%	4
Stereotact. Op.[3]	Hippocampus	5	1	40%	0		0	20%	1	40%	0
	Amygdala		4		2				0		2
Ant. 2/3 TL Resection	SEEG[4]	29		59%	17		0	31%	9	10%	3
	ECoG[5]	19		42%	8	11%	2	16%	3	31%	6
Extra-temporal Operations (SEEG)	Frontal	31	13	39%	3	3%	1	42%	6	16%	3
	Central		7		3		0		4		0
	Parietal		4		2		0		1		1
	Occipital		2		2		0		0		0
	Hemispherectomy		3		2		0		1		0
	Thalamus		2		0		0		1		1
Total[6]		187		55%	103	4%	8	28%	53	12%	23

A *comparison* of the seizure outcome of the *amygdalohippocampectomy-series with the results of TL surgery* using the classical anterior two-third resection or stereotactic approaches is given in Table 16 together with the results of extratemporal epilepsy surgery done in Zurich.

As can be seen from Table 16, the seizure outcome of the selective amygdalohippocampectomy series operated on the basis of SEEG is slightly better than in the patient group undergoing an anterior $^2/_3$ TL resection after SEEG exploration.

[1] One patient had unexpected astrocytoma.

[2] In this group the 3 patients with tuberous sclerosis had SEEG, others were pre-operatively investigated by "Foramen-Ovale" or sphenoidal electrodes.

[3] Two further patients with combined amygdalar and hippocampal lesioning, who did not benefit from stereotactic operations, underwent an anterior $^2/_3$ TL resection. Not included here.

[4] Excluded are all patients with tumours or other lesions where surgical treatment was primarily dictated by the pathological process and not by the accompanying seizures.

[5] Early series published by Krayenbühl *et al.* (1954).

[6] A total of 217 operated patients, within different epilepsy series and operated in Zurich, are followed now by the author (included is one patient with unsuccessful cerebellar stimulation).

Note: Out of 123 patients who underwent SEEG (SEEG series II/ZH), 86 patients were operated on (= 70%).

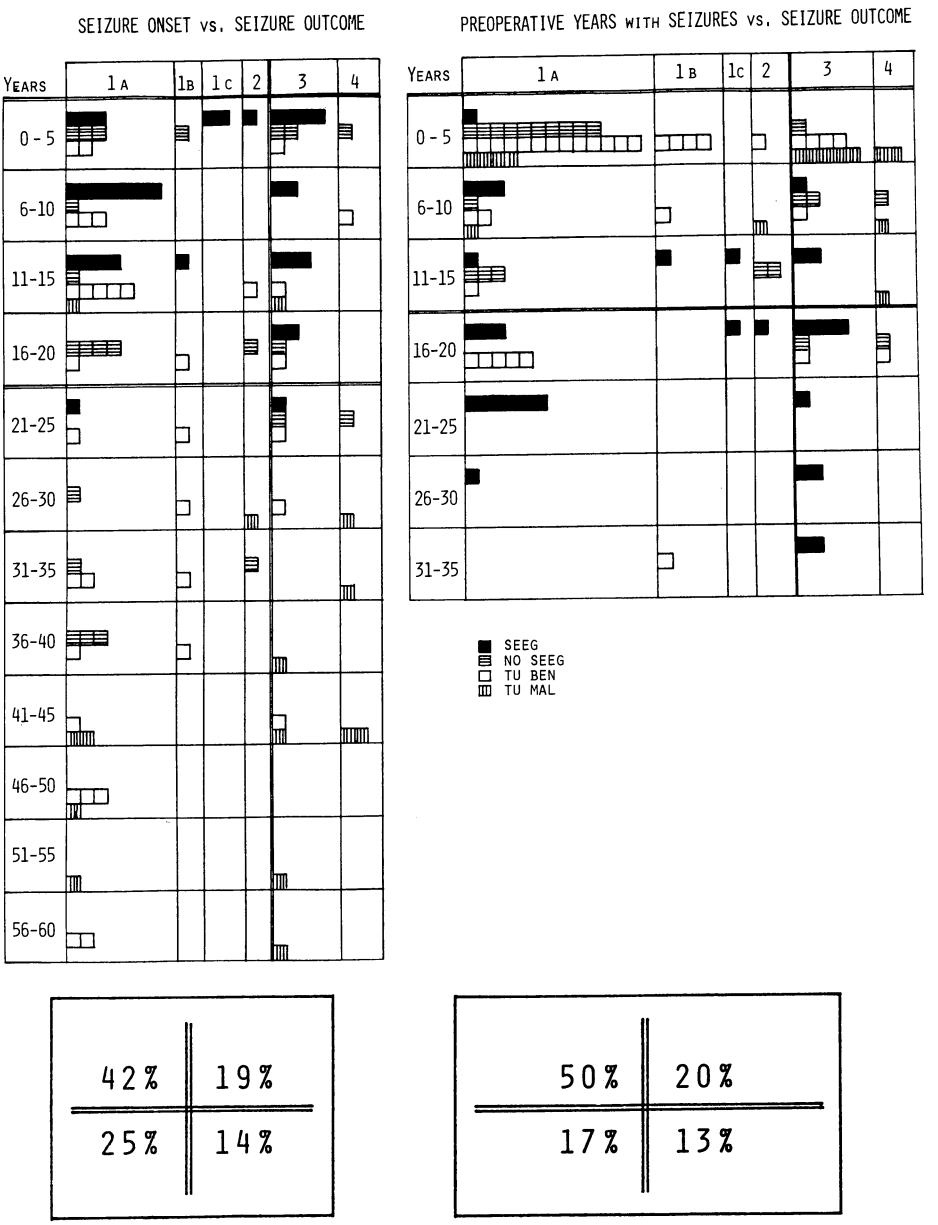


Fig. 27. The influence of "age at seizure onset" (at left) and "pre-operative years with seizures" (at right) on the surgical outcome is shown differentiating the four groups. In the upper part, each patient is represented by one square in the appropriate column. Below, the corresponding percentages of patients with seizure onset 0–20 years, and 21–60 years (at left) and pre-operative years with recurrent seizures [1–15 years and 16–38 years (at right)] are given lumping together the categories 1 and 2 ("seizure-free" and "rare seizures") and opposing them to 3 and 4 ("worthwhile improvement" and "no worthwhile improvement")

These figures, however, must be viewed in conjunction with the different etiological factors, otherwise they are misleading.

More informative are the following ratios (if one considers the number of *pre-operative years with seizures*). For patients having pre-operative seizures for less than 15 years, the ratio [seizure-free and rare seizures]:[worthwhile improvement and no improvement] is 2.25:1, whereas for patients with recurrent seizures for longer than 15 years, this post-operative outcome ratio is only 1.31:1 (Fig. 27, right).

As mentioned, our studies of the resected tissue with modern immunohistochemistry are at a premature stage and do not provide any relevant conclusions to date. In the meantime, however, a quantitative study was started which will concentrate on measurement of GAD (glutamic acid decarboxylase, the biosynthetic enzyme for GABA) positive neurons (Fig. 29), as well as on other transmitters and neuromodulators (Fig. 28).

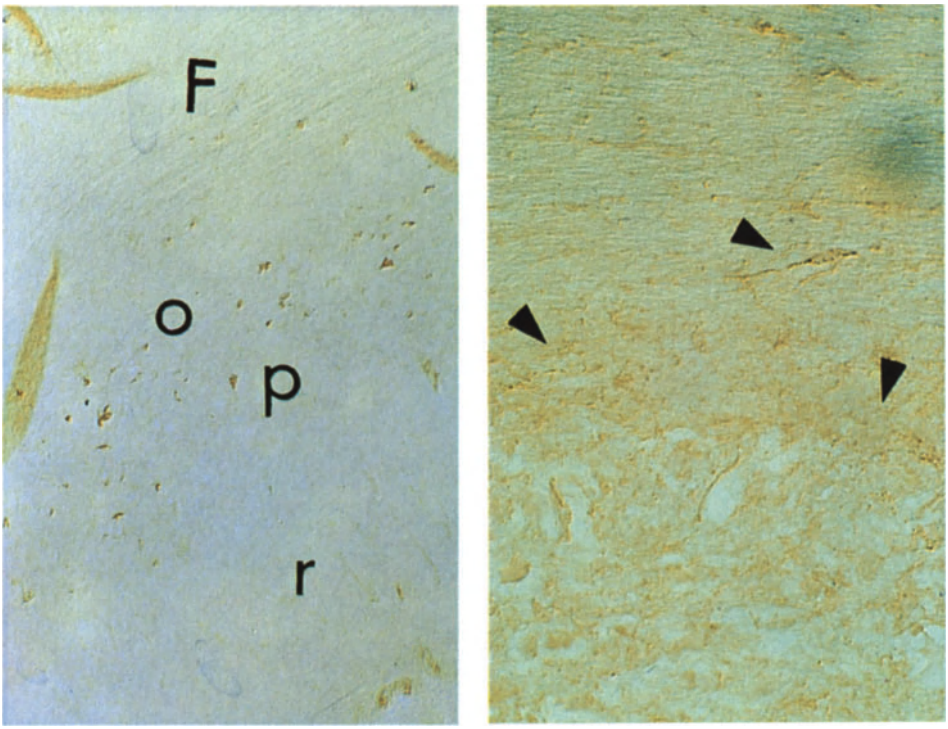


Fig. 28. Left: human hippocampus CA1: somatostatin immunoreactivity in stratum oriens. *F* fimbria; *o* stratum oriens; *p* stratum pyramidalis; *r* stratum radiatum. Right: human hippocampus, fimbria and CA1: substance P immunoreactivity in fimbria and CA1 (arrowed). [Courtesy of Dr. G. W. Roberts, Clinical Research Centre, Division of Psychiatry, Watford Road, Harrow, England. (For further details see Roberts *et al.* 1982a, b, 1983, 1984)]

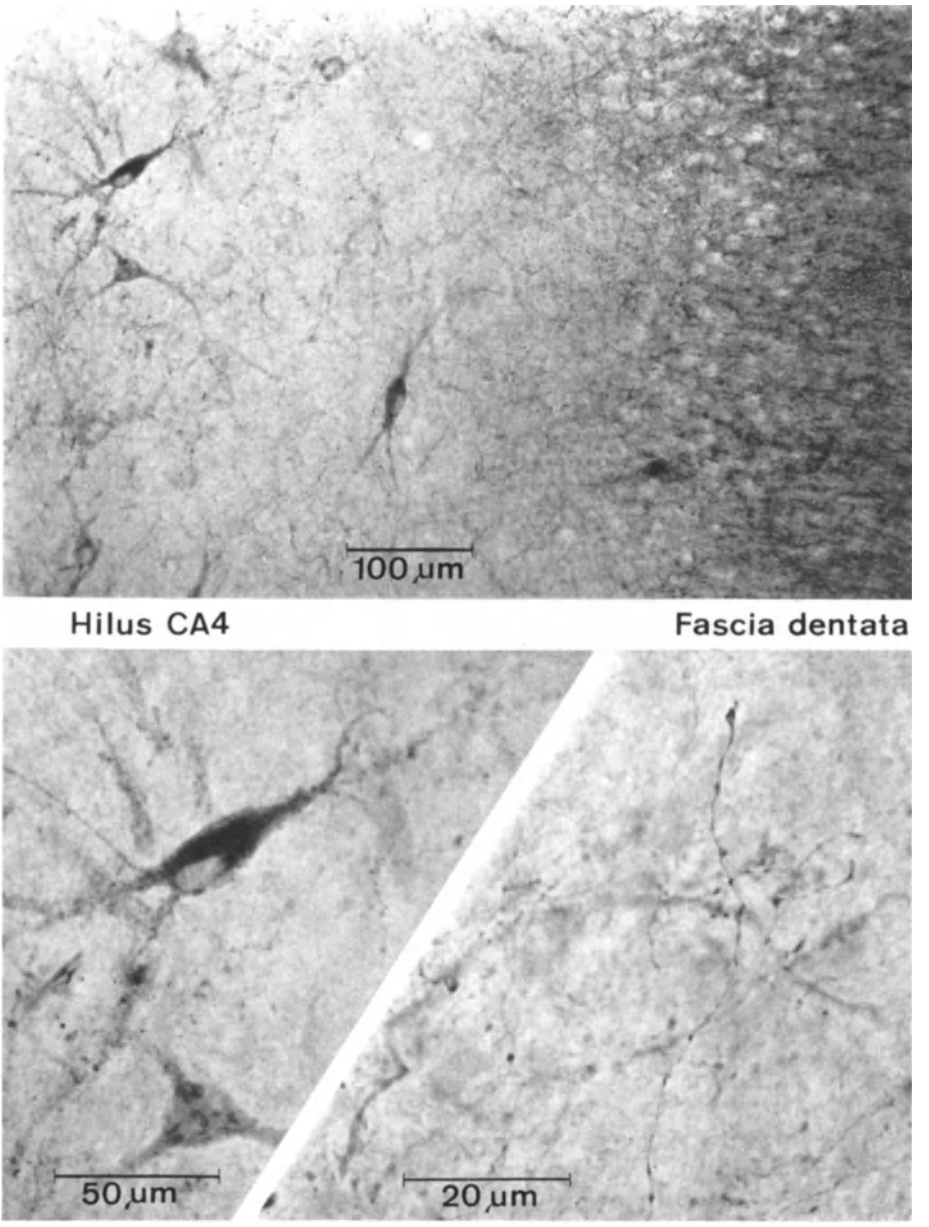


Fig. 29. Human hippocampus CA4-Fascia dentata (case no. 75 of this series). GAD positive neurons (one of them enlarged at bottom left) and axons with boutons (enlarged at bottom right). (Courtesy of Dr. E. Braak, Zentrum der Morphologie, University Frankfurt, F.R. Germany. The GAD antibody was provided by Dr. W. Oertel, Neurological University Clinic, Munich, F.R. Germany)

2.1. Neuropsychological Data

Post-operative neuropsychological assessment of patients in the selective amygdalohippocampectomy series showed that results were better (*i.e.*, fewer deficits) than in those patients who underwent a classical anterior $^2/_3$ TL resection (Birri *et al.* 1982, Gonser 1983, Gonser *et al.*, in press).

Since 1981, Toni Nadig from our Neuropsychology Department has studied systematically all our drug-resistant epilepsy patients with TL seizures referred for pre-surgical evaluation with a standardized neuropsychological protocol. This test-battery is described on p. 57 and has been developed to assess learning, memory and lateralization. The validity of these tests was confirmed comparing different patient-groups with cortical damage at various sites and controls (Nadig 1985). A summary of the performances of the selectively amygdalohippocampectomized patients follows in Figs. 30–32.

Fig. 30 a shows the pre-operative performance of *all tested patients with TL epilepsy,* whereas Fig. 30 b shows the post-operative performance of a *different population after TL surgery.* It is important to note that only 17 patients of Figs. 30 a and b are identical, *i.e.,* only these 17 patients were tested before and after amygdalohippocampectomy with the same test protocol at an appropriate time. Thus, *only on these 17 patients is a direct pre- and post-operative comparison* possible. These results are presented in Fig. 31, emphasizing the adherence of a patient to a given subgroup with respect to absence or presence of a tumour and evaluation with or without depth-EEG studies. Fig. 32 emphasizes the individual pre-/post-operative changes of performances.

As can be derived from Fig. 30 a showing the *pre-operative learning curves and the memory,* as assessed from the delayed recall after 30 minutes, patients with left temporal foci show an impaired verbal learning. Out of 16 patients only 1 patient reached the learning criterion with 2 trials, 4 needed 5 trials and 11 did not reach it within 5 trials. Similar results were reported by Masui *et al.* (1984).

These results are much worse than in the nonsense design, where 10 patients with left TL foci ($^{10}/_{16}$) reached, and 6 ($^6/_{16}$) did not reach, the

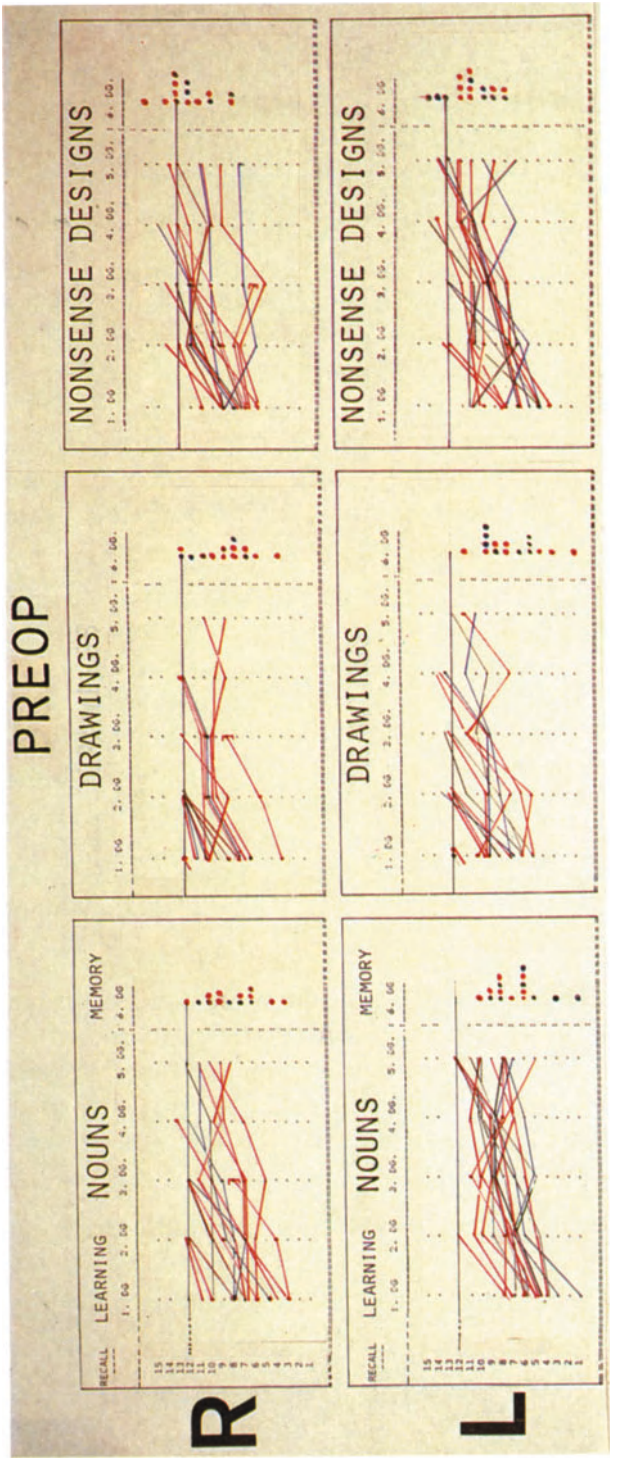


Fig. 30 a. Pre-operative learning curves and memory assessment for 31 patients (15 with right (*R*) and 16 with left (*L*) TL foci)

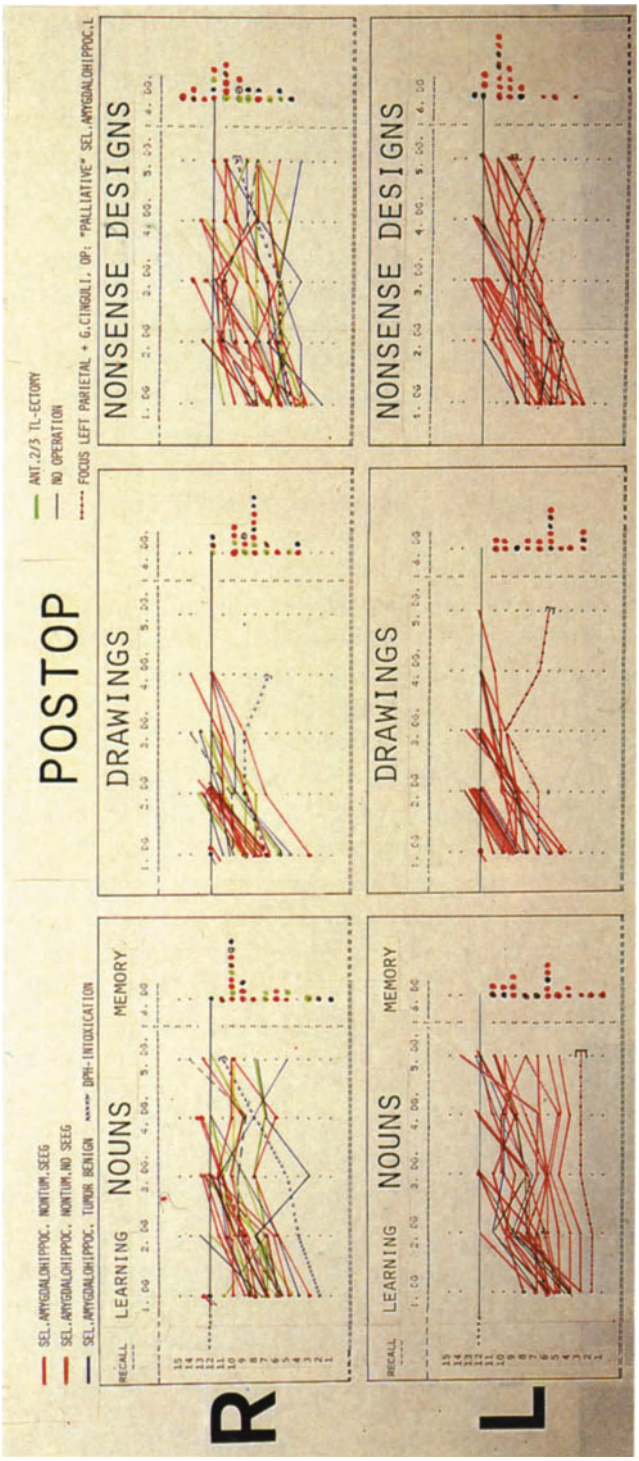


Fig. 30 b. Post-operative learning curves and memory assessment for 46 patients (19 after right selective amygdalohippocampectomy, 6 after right anterior $^2/_3$ TL resection, and 21 after left selective amygdalohippocampectomy). Note that only 17 patients in Fig. 30 a and b are identical. Colour code is given at the top of Fig. 30 b (grey in Fig. 30 b means stereotactic interventions only)

criterion. Patients with right temporal foci, however, do not clearly show a lateralized effect in the learning performances.

The *post-operative results* of a different population are presented in Fig. 30 b. Patients with left TL surgery perform worse than patients with right TL surgery in the *verbal tasks* (nouns). Exactly the opposite is true for the *nonsense design* (right hemispheric learning task), where patients with right TL surgery show worse results than those with left TL surgery. Excluding the 6 cases with anterior $^2/_3$ TL resection, out of the 19 patients with right selective amygdalohippocampectomy 14 reached the learning criterion with nouns and 5 did not, whereas in the nonsense design only 10 of the same population reached the learning criterion and 9 did not.

The learning curves for *drawings* are generally better in both pre-operatively and post-operatively tested patients than the learning curves with the two other materials (nouns and nonsense designs). Therefore it may be concluded that visual figure learning is, *a priori*, less affected by temporal lobe damage.

Comparing the pre-operatively and post-operatively tested different populations (Figs. 30 a and b), at a first glance no significant differences are evident with respect to the learning curves of all three materials. Also such a comparison does not show significantly poorer memory in the post-operatively tested patients (excluding the anterior $^2/_3$ TL resections) compared with the pre-operatively tested patients.

It is noteworthy that 2 patients, tested post-operatively and listed in Fig. 30 b, performed very badly. They are separately plotted on the learning curves because delayed memory testing was not possible. One, who underwent a selective amygdalohippocampectomy and who had a right mesiobasal benign tumour, displayed a marked phenytoin intoxication. The other had a left "palliative" selective amygdalohippocampectomy, although his primary seizure originating site, identified by SEEG, was situated in the left parietal-temporal cortex and cingulate gyrus. Although secondary propagation to the left mesiobasal structures was seen, this patient did not profit from the operation. The reduced post-operative seizure frequency was counteracted by an impaired neuropsychological outcome. (This patient has not been included in our series of the 103 patients, because later a second operation was performed outside our hospital and no follow-up data are available at present).

Fig. 31 shows the *pre- and post-operative learning and memory performances* of 17 patients who underwent amygdalohippocampectomy. The improvement or worsening of each individual in the learning curves have been measured as the difference between the post-operative and pre-operative trials necessary to reach the criterion. The memory assessment was measured as the number of items recalled 30 minutes later. The difference between pre- and post-operatively recalled material-specific

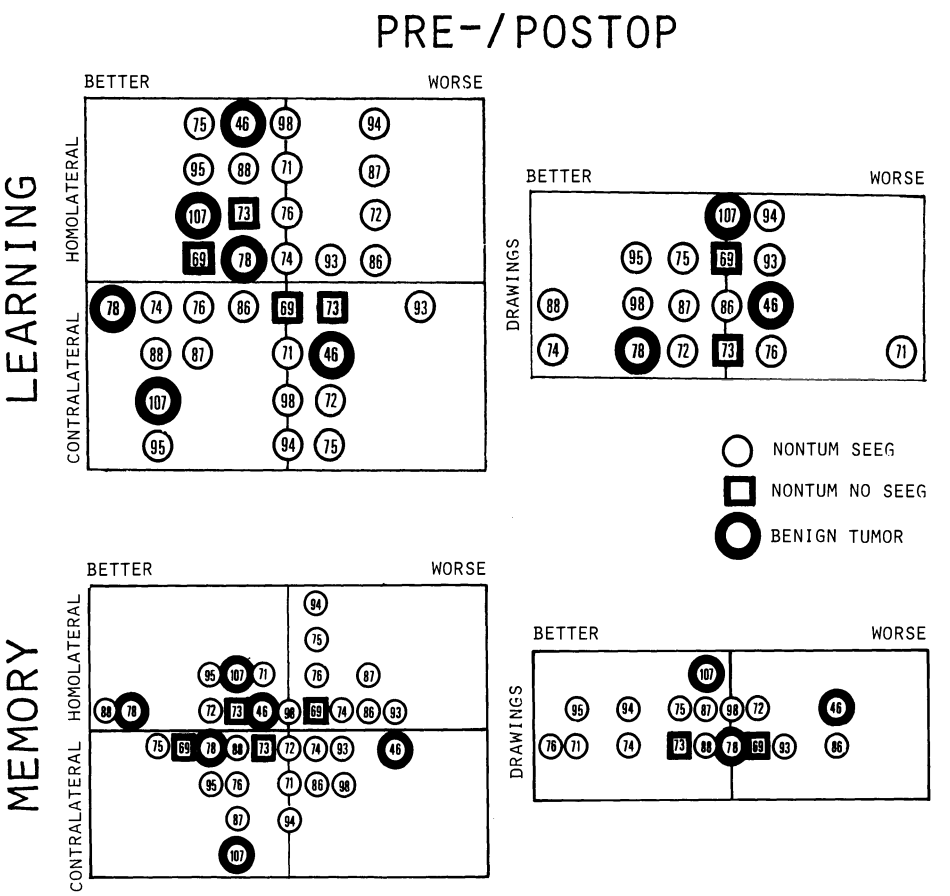


Fig. 31. Graph showing the post-operative changes of learning and memory performances relative to the pre-operative performances of those 17 patients (indicated by numbers) who were tested pre- and post-operatively with the same test procedure and at appropriate time intervals with respect to selective amygdalohippocampectomy. The code refers to the same criteria of grouping as given in Fig. 25. The comparison of pre-/post-operative learning performances was measured as described in the text

items was plotted for each patient at the bottom of Fig. 31. To simplify the presentation, the performance of a patient confronted with nonsense designs and operated at the right side is treated the same way as the performance of a patient confronted with nouns and operated on the left side, *i.e.*, both are plotted under the rubric "homolateral".

Concerning the learning performance, homolaterally $^{4}/_{17}$ of the patients are unchanged, $^{8}/_{17}$ are slightly better and $^{5}/_{17}$ perform slightly worse. Contralateral learning is unchanged in $^{4}/_{17}$, slightly better in $^{3}/_{17}$ and markedly improved in $^{5}/_{17}$ of patients. It is slightly worse in $^{4}/_{17}$ and

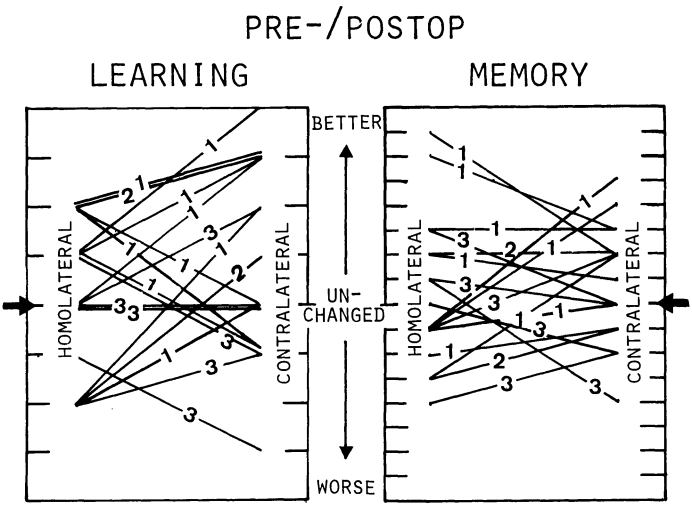


Fig. 32. This graph is essentially the same as Fig. 31. However, it better visualizes the directional change of (1), the individual post-operative performance with respect to the pre-operative results and (2) it emphasizes the relative changes of both hemispheres of a given patient according to his or her seizure outcome (*1* seizure-free, *2* rare seizures, *3* worthwhile improvement). Note that post-operative performance (as compared to the pre-operative one) is now indicated by the position on the y axis. The ends of the lines give the post-operative improvement (upper half) or worsening (lower half). If lines ascend, the contralateral hemisphere (= not operated) improved more (or worsened less) than the homolateral (= operated) hemisphere. Grading of y axis for the "learning graph" is the difference between pre- and post-operative trials necessary to reach the learning criterion. For the "memory graph" it is the difference between the number of pre- and post-operatively recalled items

markedly worse in $^{1}/_{17}$. Memory is more or less unchanged homolaterally in $^{7}/_{17}$, slightly improved in $^{4}/_{17}$ and markedly improved in $^{2}/_{17}$ of patients. Homolateral memory is slightly worse in $^{3}/_{17}$ and markedly worse in $^{1}/_{17}$. Contralateral to the operated hemisphere, memory is more or less unchanged in $^{6}/_{17}$, slightly better in $^{6}/_{17}$, and markedly improved in $^{2}/_{17}$ of patients. Contralateral memory is slightly worse in $^{2}/_{17}$, and markedly worse in $^{1}/_{17}$ of the patients.

The overall trend of these patients in the learning and memory performances for the *drawings* is that of a post-operative improvement.

In Fig. 32 we use the same style of presentation as in Fig. 31, but emphasize *the individual* interhemispheric performance changes and include also the post-operative *seizure outcome*. This figure shows that learning as well as the memory performances of the hemisphere opposite to the side of operation are post-operatively generally improved. This contralateral

improvement is especially marked in cases with seizure outcome category 1, *i.e.*, being seizure-free. It is also evident that learning is relatively more improved contralaterally than homolaterally. This is visualized by ascending (10 patients) versus descending (5 patients) lines. With regard to memory this trend is not as clear (8 patients with ascending and 7 patients with descending lines).

3. The Bear-Fedio Personality Inventory and TL Epilepsy

In 1975, Waxman and Geschwind reported that "... a distinct syndrome of interictal behaviour changes occurs in many patients with temporal lobe epilepsy. It is characterized by alterations in sexual behaviour, 'religiosity', and a tendency toward extensive and, in some cases, compulsive writing". Bear and Fedio (1977) then devised a personality inventory in which 90 questions sampled 18 "traits" that were supposed to be characteristic of TLE, and 10 others were taken from the Minnesota Multiphasic Personality Inventory (MMPI) L scale. Bear and Fedio studied 24 patients with TLE, 9 with neuromuscular disorders, and 12 normal controls, and concluded that the study identified "... psychologic features, self-reported or observed, which reliably distinguished patients with TL foci". The study was strongly endorsed by Geschwind (1977), has been widely quoted, and published in textbooks (Fenton 1981, Lechtenberg 1982).

However, subsequent studies (Hermann and Riel 1981, Mungas 1982, Rodin and Schmaltz 1984) called into question the characteristics that define the syndrome.

In the study of Hermann and Riel (1981), who contrasted patients with primary generalized epilepsy against those with TLE, the TLE group scored significantly higher in terms of "personal destiny", "dependence", "paranoia", and "philosophical interest", but none of the other 15 comparisons approached significance.

Following Standage and Fenton's (1975) use of a reliable psychiatric interview technique, Mungas (1982) even found no significant differences between patients with TLE and psychiatric disorders, patients with other mixed neurological diseases and behaviour disorders but no epilepsy, and psychiatric patients without neurological disorder. Rodin and Schmaltz (1984) administered the Bear-Fedio inventory to normal controls and to patients with epilepsy, chronic pain, and psychiatric disorders. The trait scores showed a progressive increase with the severity of psychiatric symptoms. There were, however, no significant differences between epileptic patients with diffuse spike wave discharges and those with focal temporal EEG abnormalities. Also, there were no significant differences in patients with left versus right temporal foci. Therefore, these authors concluded that "the test in its current form measures overall psychopathology rather than a specific syndrome". Moreover, from their study it becomes clear that the inventory is markedly influenced by intellectual factors and, to some extent, by gender and anticonvulsant drug levels.

In the context of our mesiobasal-limbic epilepsy series, the study of Nielsen and Kristensen (1981) must be mentioned. Comparing patients with mesiobasal TL foci (as revealed by sphenoidal electrode recordings) and patients with lateral-temporal spikes, they found that their patients with mesiobasal foci had significantly more total positive answers, particularly for four categories: hypergraphia, elation, guilt and paranoia. Patients with left-sided foci scored higher on aggression and on a combined depression-elation score, than patients with a right-sided focus. Regarding the problem of lateralization of personality functions using the Bear-Fedio inventory (Seidman 1980, Bear *et al.* 1982), all authors found the left TLE group more disturbed. A consistent trait profile, however, did not emerge (Rodin and Schmaltz 1984).

Since 1982 we have administered the Bear-Fedio personality inventory, as part of the routine work-up, candidates for epilepsy surgery. Sixty-three patients, all of whom had depth-electrode studies, were analyzed using self-reporting. By means of a stepwise discriminant analysis we correlated the exact localization of the primary epileptogenic focus as well as other "clinical variables" including sex, age, handedness, age at seizure onset, average seizure frequency per month, post-operative outcome, education, socio-professional background, drug therapy, etc. (see Table 17), with the trait scores of the inventory (see Fig. 34).

Table 17 summarizes the results of this stepwise discriminant analysis using the BMDP 7 M programme*. As can be seen, only the following traits, listed according to their discriminating power, entered the discriminant analysis: "altered sexual content" correlated with left handedness. The next most definitive correlation was "aggression" in patients with post-operative complications. "Emotionality" and "hypermoralism" correlated with sex (females stronger with "emotionality", and males more strongly with "hypermoralism").

"Altered sexual content" and "hypergraphia" correlated with a marked desire for medico-social professions, *i.e.,* patients exhibiting this "Helfer-syndrom" scored low in the sex-trait but high in hypergraphia. "Humorlessness", a trait retained in Bear's second study (Bear *et al.* 1982) and thought to be specific for TLE, correlated with the environmental living conditions in our study, with a discriminating power of 50%, *i.e.,* the urbans represented more strongly in this trait than the rurals. With 25% discriminating power, "humorlessness" also correlated with the localization of the epileptic focus; but contrary to other studies (Bear *et al.* 1982), in our study the frontal group exhibited the highest adherence to this trait (see also Fig. 35). With 39% discriminating power "dependence, passivity" correlated with the profession (being highest in the unemployed). With 32%

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* BMDP-79 Biomedical Computer Programs P-Series (Dixon, W. J., Brown, M. B., eds.). Berkeley-Los Angeles-London: University of California Press. 1979.

discriminating power "sadness, depression" correlated with the age at seizure onset (being highest with a seizure onset below 5 years).

A few further trends also emerged. These were: patients reported themselves as the more severely affected (1) the younger they were, (2) the shorter their education, (3) the higher their actual seizure frequency, (4) the worse their post-operative outcome, and (5) the higher their actual anticonvulsant drug therapy.

Since the original publication by Bear and Fedio (1977) and a subsequent publication by Bear (1977) had suggested that the categories measure discrete personality traits, intercorrelation of the 19 inventory traits and the clinical variables (*i.e.*, sex, age, education, etc.) was carried out by a cluster-analysis using the BMDP programme. Fig. 33 shows these results. The majority of the traits are highly intercorrelated and the correlative adherence of the traits to the analytic "clinical variables" is low. However, it is obvious even from Fig. 33 that within the traits two clusters can be seen.

Using a rotated factor analysis, this subdivision of the traits can be visualized more clearly, as shown in Fig. 34. Factor 1 is the strongest and includes "anger and hostility", "stickiness" and "aggression" as its most characteristic traits, whereas factor 2 includes "hypergraphia" and "philosophical interest" as its most characteristic traits. *A clear-cut correlation of these factors with the location of the epileptic focus, however, is not possible* (see Fig. 35) *although the traits "hypergraphia" and "philosophical interest" have a certain but weak adherence to the clinical variable "localization"* in the cluster analysis of Fig. 33.

The trait scores for the patients with different localizations of epileptic focus are graphically presented in Fig. 35. From this figure it can be seen that patients with *right-sided foci* (n = 18) are more strongly represented in the traits *"hypermoralism", "humorlessness"* and *"sadness, depression"*. Patients with *left-sided foci* (n = 18) have higher trait-scores in *"hypergraphia", "altered sexual content"* and *"religiosity"*.

From the trait profiles of the differently localized patient-groups (Fig. 35, middle section), it is obvious that the frontal group (n = 16) is reporting more severely in all traits and especially severely in "humorlessness". The *"circumstantiality"* score is *highest in the temporal limbic* group. Also high in this group are the scores for *"hypermoralism", "anger and hostility"* as well as *"stickiness"*. "Stickiness", however, has similar high scores in the other subgroups. The influence of the post-operative outcome (Fig. 35, right) has already been mentioned above. *Patients with a poor surgical outcome gave more positive answers* than those who were seizure-free post-operatively.

In *conclusion, our study with the Bear-Fedio inventory* does not support the original thesis by Bear and Fedio or Bear's later views (1979, 1983) that

Table 17. *Synopsis of Stepwise Discriminant Analysis of the 18 Traits of the Bear-EEG Exploration in View of Surgery.* The discriminating power of the 18 traits has no trait entered, the trend

CLINICAL VARIABLE	SUBGROUPING & RELATIVE FREQUENCY	STEPWISE DISCRIMINANT ANALYSIS BEAR-FEDIO INVENTORY, TRAIT ENTERING	DISCRIMINATING POWER CORRECTLY CLASSIFIED % OF PATIENTS
SEX	M:F = 37:26	EMOTIONALITY ↑ FEM HYPERMORALISM ↑ MALES	68
AGE	<23 YR :17 23-30 YR :17 30-37 YR :16 >37 YR :13 $\bar{x}$:30,7 (SD 10) MAX:57, MIN:10	NO (TREND: THE YOUNGER THE STRONGER IN ALL TRAITS)	
EDUCATION (YRS.AT SCHOOL)	<9 YR :15 9-10 YR :30 10-11 YR : 6 >11 YR :12 $\bar{x}$:9,4YR (SD 2,5) MAX:13,MIN Ø	NO (TREND: THE SHORTER THE EDUCATION THE STRONGER IN ALL TRAITS)	
PROFESSION	GRADUATE : 2 SKILLED :21 UNSKILLED :23 UNEMPLOYED :17	DEPENDENCE & PASSIVITY ↑UNEMPLOYED, ↑UNSKILLED (TREND: THE BETTER THE JOB, THE WEAKER IN ALL TRAITS)	39
MARKED DESIRE FOR MEDICO-SOCIAL PROFESSIONS	NO : 49 YES+ : 9 YES+++ : 5 "HELFERSYNDROM"	ALT. SEX. CONT.(↓HELFERSYNDROM) HYPERGRAPHIA (↑HELFERSYNDROM) (TREND FOR ALL TRAITS [EXC. AGGRESSION & DEPRESSION] TO BE STRONGER IN "HELFERSYNDROM")	66
HANDEDNESS	RIGHT: 55 LEFT : 8	ALT. SEX. CONT. (↑LEFT) (TREND: ALL TRAITS STRONGER IN LEFT HANDED PERSONS)	79
CIVIL STATE	SINGLE :47 MARRIED: :13 DIVORCED: : 3	NO (TREND: DIVORCED ↓ IN ALL TRAITS)	
MODE OF LIVING	SINGLE :19 WITH FRIENDS :11 WITH SPOUSE :13 IN INSTITUTIONS: 4	NO	
ENVIRONMENT	URBAN :18 SUBURBAN :20 RURAL :25	HUMORLESSNESS URBAN ↑ (TREND: URBAN ↑ IN ALL TRAITS)	50
ADMITTANCE TO PSYCHIATRIC A/O NEUROLOGICAL HOSPITALS	MORE THAN TWICE A/O >1 YR 14 ONCE 9 NONE 38	NO	
ALCOHOL, DRUGS	YES : 2		

Fedio Personality Inventory Administered to 63 Patients Who Underwent Depth-
been analyzed for the different clinical variables as listed in the left column. Where
has been noted in brackets

CLINICAL VARIABLE	SUBGROUPING & RELATIVE FREQUENCY	STEPWISE DISCRIMINANT ANALYSIS BEAR-FEDIO INVENTORY, TRAIT ENTERING	DISCRIMINATING POWER CORRECTLY CLASSIFIED % OF PATIENTS
AGE AT SEIZURE ONSET	<5 YR :14 5-11YR :21 >11YR :28 $\bar{x}$=12,2 (SD 9,6 MAX 49, MIN 1	SADNESS, DEPRESSION (↑<5 YR) (TREND: THE EARLIER SEIZURE ONSET THE STRONGER IN ALL TRAITS)	32
SEIZURE FREQUNCY (PER MONTH, LAST YEAR PRIOR TO SEEG)	<8 :19 8-15 :12 15-30 :15 >30 :17	NO (TREND: THE MORE SEIZURES PER MONTH THE STRONGER IN ALL TRAITS)	
LATERALIZATION OF EPI-FOCUS	R :18 L :18 BILAT :25 ? : 2	NO (TREND: R:HYPERMORALISM ↑, HUMORLESSNESS ↑, L:RELIGIOSITY ↑ HYPERGRAPHIA ↑, ALT, SEX, CONT ↑)	
LOCALIZATION OF EPI-FOCUS	T LIMB :10 T NEOC : 6 T LIMB+NC:23 F :16 C-P : 5 O : 3	HUMORLESSNESS ↑ IN FRONT (TREND: ALL TRAITS ↑ IN FRONT., IN TLIMB ↑ : CIRCUMSTANTIALITY HYPERMORALISM	25
SURGERY	YES 43 NO 14 (WAITING LIST 6)	NO (TREND: NO SURGERY: ↑ HYPER-MORALISM, ↑ HUMORLESSNESS)	
POSTOPERATIVE YEARS	<2 14 2-5 12 5-8 7 >8 10	NO REPORT THEMSELVES MORE SEVERELY IN ALL TRAITS → SELECTION!	
POSTOPERATIVE RESULTS	SEIZUREFREE 22 IMPROVED 12 UNCHANGED 9	NO (TREND: UNCHANGED ↑ IN ALL TRAITS, SEIZUREFREE ↓ IN ALL TRAITS)	
POSTOPERATIVE NEUROLOGICAL DEFICITS	YES: 7 NO: 36	AGGRESSION ↑ IN PTS WITH COMPLICATIONS (→ TREND: ↑ EMOTIONALITY, ↑ RELIGIOSITY, ↑ DEPENDENCY)	77
POSTOPERATIVE ANTICONVUL-SANTS	WITHOUT DRUGS 3 REDUCED 11 ± UNCHANGED 29	NO (TREND: REDUCED: ALL TRAITS ↓)	
TRANSGRESSION OF LAW	YES, DUE TO: -AGGRESSION : 2 -ACCIDENT LINKED TO SEIZURE } 4	NO (TREND: ↑ AGGRESSION ↑OBSESSIONALISM, ↓ RELIGIOSITY)	
SUICIDE ATTEMPTS	REPEATED 2 ONCE 11 NONE 50	NO (TREND: REPEATED ATTEMPTS: EMOTIONALITY ↑ & CIRCUMSTANTIALITY ↑)	

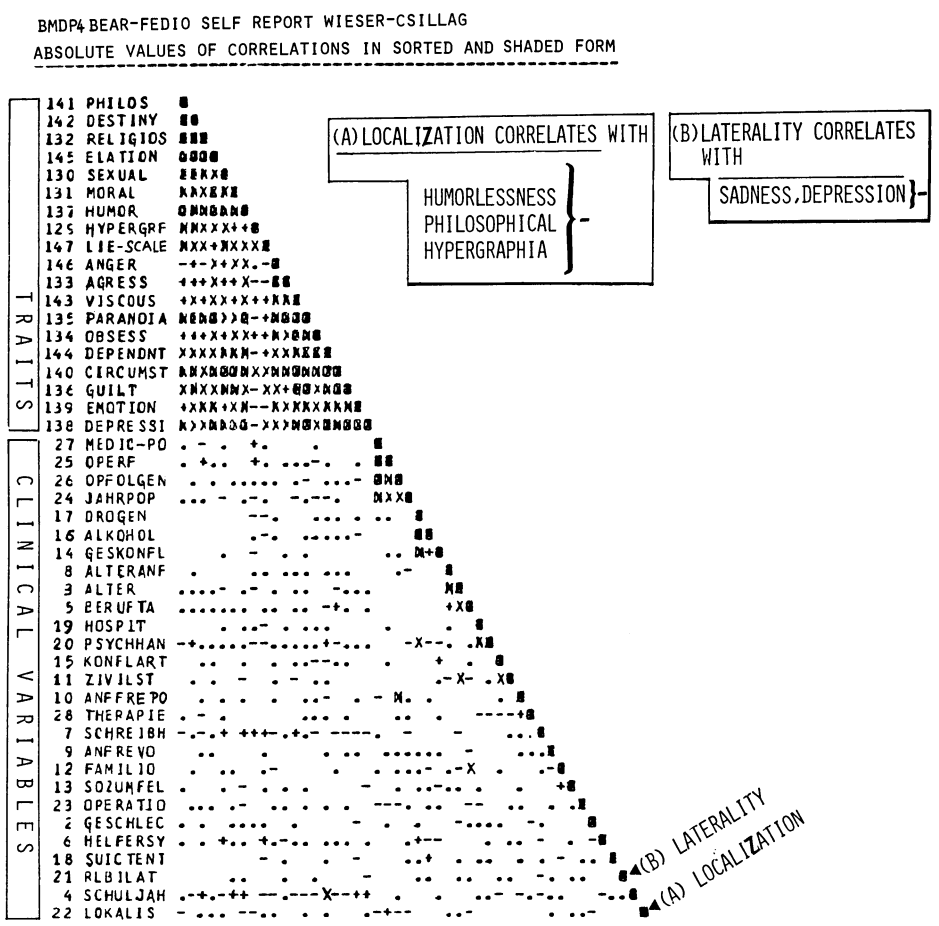


Fig. 33. Cluster analysis of the 18 personality traits (listed in Fig. 34) as reported by 63 patients in the Bear-Fedio inventory, and the clinical variables (listed in Table 17). Method BMDP: this programme forms clusters of variables based on the correlation coefficient between the variables. The criterion used to combine the variables into clusters (the amalgamation rule) was the maximum similarity (single linkage). Note that the 18 personality traits, in general, show a relatively high intercorrelation but only a low correlative adherence to the clinical variables. The variables "laterality" and "localization" of the epileptic focus are indicated with their highest traits

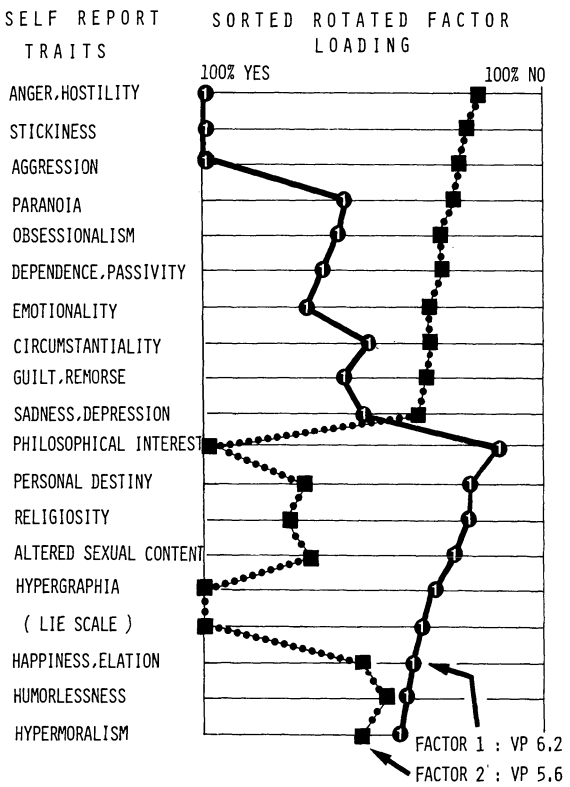


Fig. 34. Rotated factor analysis with the 18 personality traits reported by 63 patients in the Bear-Fedio inventory. The first two factors are presented with their loadings. Method PMDP: this programme creates factors, *i.e.*, synthetic variables, formed from the original measured variables. The factors account for the correlations among the variables. By using oblique rotations (= factor analysis) more complete explanation of the variance is possible, but the resulting factors are no longer independent. Note that some traits originally reported to constitute a distinct syndrome of interictal behaviour changes in patients with TLE (such as hypergraphia, philosophical interest, alterations in sexual behaviour, and religiosity) are represented in the personality profile of factor 2

the inventory detects personality traits that are specific for patients with TLE and can distinguish those with right or left TL foci. It agrees with the recent study of Rodin and Schmaltz (1984) that the inventory is markedly influenced by gender and intellectual factors. The test, although non-specific for TLE (Brumback 1983), is, however, a useful measure of overall psychopathology and therefore allowed us to quantify a few aspects of personality changes associated with, or at least seen more often in, patients with TLE. It appears quite likely that patients with a long-lasting epileptic dysfunction due to an irritative lesion within the limbic system, or to

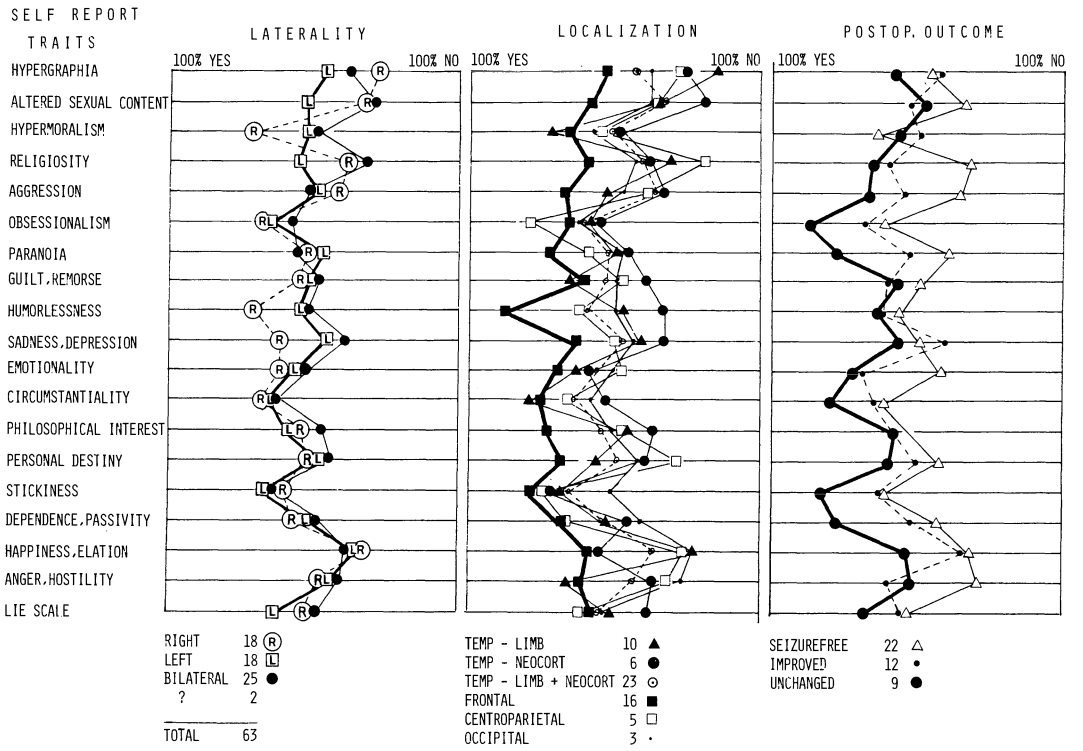


Fig. 35. Personality profiles for patients subgrouped according to laterality, localization, and post-operative outcome. Note that with the exception of "humorlessness" (which is severely reported by frontal patients), no other traits were effective predictors when discriminate function analysis (see Table 17) was used. Some trends, however, are obvious: the trait scores show general increase in the frontal group and in patients with unsuccessful post-operative outcome (see also Table 17 and text)

repetitive bombardment of these structures, may be more susceptible to emotional-ideational disorders (Stevens and Hermann 1981, Rodin and Schmaltz 1984). It is, however, unlikely that these disorders should take the same form in each patient, and also unlikely that basic personality characteristics of each individual and normal psychodynamics should be of merely minor importance. Our findings show that many social, economic and intellectual problems, as expressed by the patients, are observed on the personality inventory as long as self-reports are considered. We wish to emphasize that this report included only self-reports. Comparing self-reports with ratings by a family member or closely connected person, it was seen that patients with right sided TLE under-reported some qualities while over-reporting others. The opposite was true for patients with left TLE (Bear and Fedio 1977).

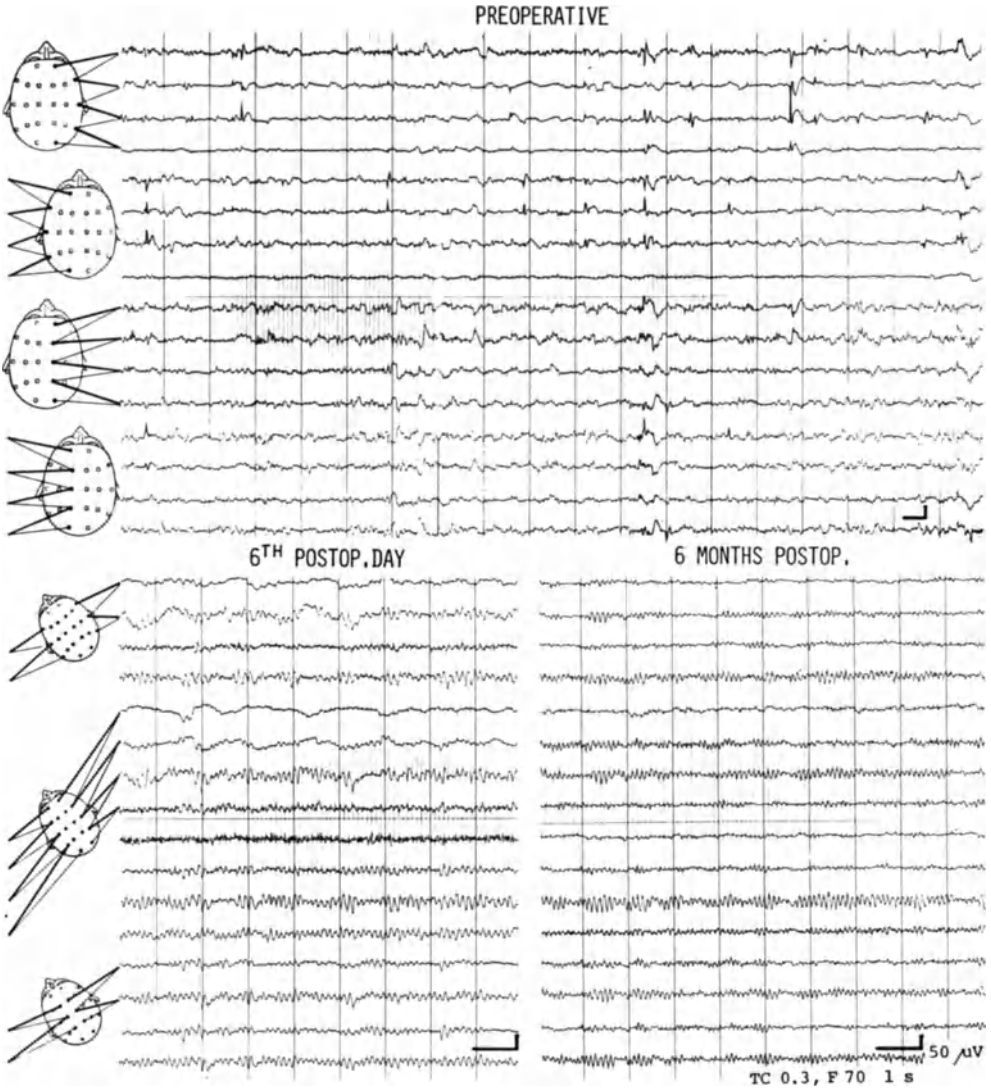


Fig. 36. Pre-operative and follow-up (6 days and 6 months post-operatively) electroencephalograms in a patient who underwent right selective amygdalohippocampectomy

4. Post-Operative EEG Controls

Post-operative EEG controls were carried out in *all* patients of these series (n = 103) at least on days 6–12 and 3 and 6 months after operation. Most patients were followed beyond this time with EEGs recorded once a year. Almost all patients with an amygdalohippocampectomy resulting in complete control of seizures (55 patients with seizure outcome 1 a) have completely normal EEGs taken one year after the operation (see Fig. 36).

When auras but no overt seizures persist (7 patients with seizure outcome 1 b), usually rare spiking, mostly in the midtemporal region homolateral to operation, persists as well. When only an improvement (27 patients with seizure outcome 3) resulted from the removal of the mesiobasal TL structures, in more than 60% of these patients the EEG is improved but usually interictal temporal spiking persists. In nearly 20% interictal temporal spikes are bilateral.

Table 18. *Post-Operative EEGs Correlate Well with Epileptological Outcome* (Non-tumoural SEEG group). Coding of seizure outcome is the same as used previously (see Fig. 25). The number of patients with "palliative" interventions (P) is indicated in brackets

	Seizure-free without aura (1 a)	Seizure-free with persist. auras (1b) or for $\geqslant$ 2 years (1c) and Rare Seizures (2)	Worthwhile Improvement (3)	Total
Normalized EEG	13 (1 P)	1	1	15
Improved EEG	2 (2 P)	1	4 (3 P)	7
Unchanged EEG	—	2 (2 P)	7 (7 P)	9
Total	15	4	12	31

Partly in collaboration with Hans Aebersold and Carlo Albani (Aebersold *et al.* 1983), we have studied the prognostic value of the post-operative EEG in the 31 patients of this series without tumours who underwent SEEG exploration. In 16 patients the amygdala and/or hippocampus were proven as the site of seizure origin by SEEG ("causally" operated "non-tumoural SEEG group"). Fifteen patients had temporal limbic *and* homolateral neocortical ($^{11}/_{15}$) or bilateral mesiobasal-limbic foci ($^{4}/_{15}$), thus falling into the "palliatively" operated "non-tumoural SEEG group". The results are given in Table 18. As can be seen, the post-operative EEG correlates well with the epileptological outcome and therefore is of definite prognostic value.

It is also obvious that in most palliatively operated patients the EEG is in accordance with the seizure outcome, *i.e.*, in the category 1 a (seizure-free without aura) 1 patient with a palliative amygdalohippocampectomy has a normal and two an improved EEG. Within the categories, 1 b, 1 c and 2, the 2 palliatively operated patients have unchanged EEGs, *i.e.*, homolateral spiking persists. In category 3 (worthwhile improvement) all of the patients

with unchanged EEGs and $^3/_4$ of the patients with improved EEGs had "palliative" operations.

5. Post-Operative Visual Field Examinations Using the OCTOPUS

Based on visual field defects in patients with tumours of the TL, Cushing (1922) was able to confirm that some visual fibres from the thalamus proceed forward and laterally over the temporal horn before they project back to the occipital lobe. This detour into the TL had been described earlier by Meyer (1907) and is now referred to as Meyer's loop (see Fig. 37). This lateral fibre contingent represents the lower retina and a portion of it passes through the core of the parahippocampal gyrus (Polyak 1957).

In 1965, Cuenod *et al.* recording from units in squirrel monkeys, found 4% of 56 units in the subiculum or prosubiculum responding to photic stimulation with latencies of 225–275 ms and to electrical stimulation of the lateral geniculate with latencies of 37–60 ms. In later studies MacLean (1968) and MacLean *et al.* (1968) recorded responses from 6.5% of 279 cells located in the posterior hippocampal gyrus. The mean latency for all responses was 58.7 ms. In rats, Vastola (1982) has reported findings compatible with an oligosynaptic visual projection to the rat hippocampus.

In 1964, Brazier with implanted bipolar electrodes recorded responses to photic stimulation in the pes hippocampi of epileptic patients. She reported them with a latency to onset of 25–30 ms and a total duration of 150 ms.

Babb *et al.* (1982) and Wilson *et al.* (1983) have studied the retinotopic organization of fibres in the *human* geniculostriate pathway and showed that this pathway may have considerable variability in the anterior and ventral course through the TL. Recording neuronal and field potentials in response to diffuse retinal illumination, they found clear short-latency responses in the parahippocampal gyrus. They concluded that these visual afferents in the mesial TL stem from both subcortical and cortical visual areas. Furthermore they found an asymmetry in the ventral trajectory of the geniculostriate pathway as evidenced by asymmetric neuronal field potential responses to brief flashes in right vs. left hippocampal gyrus and by post-operative incongruous defects following anterior TL resections with the extent of visual loss greater for the eye ipsilateral to the TL removed.

Our pre-/post-operative comparison of visual fields, as carried out by routine Goldmann perimeter examination, did not reveal any significant additive post-operative deficits in the non-tumoural cases with selective removal of amygdala and hippocampus. Because of evidence (Babb *et al.* 1982, Wilson *et al.* 1983) which suggests that collaterals from the optic radiation go into the hippocampal gyrus, since 1983 we have started more exact studies using the OCTOPUS. To date 13 patients have been examined pre- and post-operatively.

In the 13 patients studied using the OCTOPUS since 1983, visual field defects have been documented pre-operatively in 3 of these patients. The

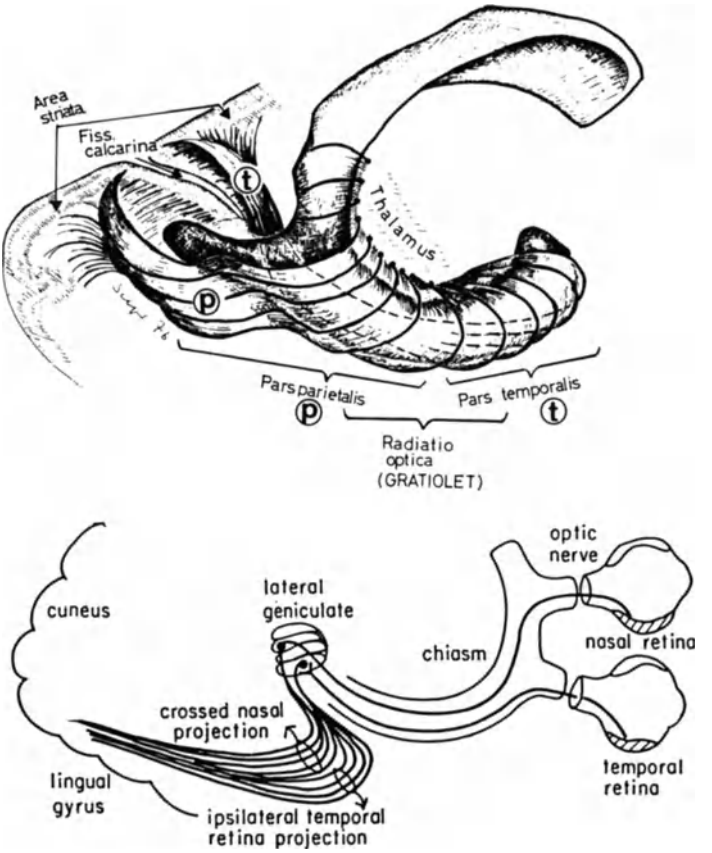
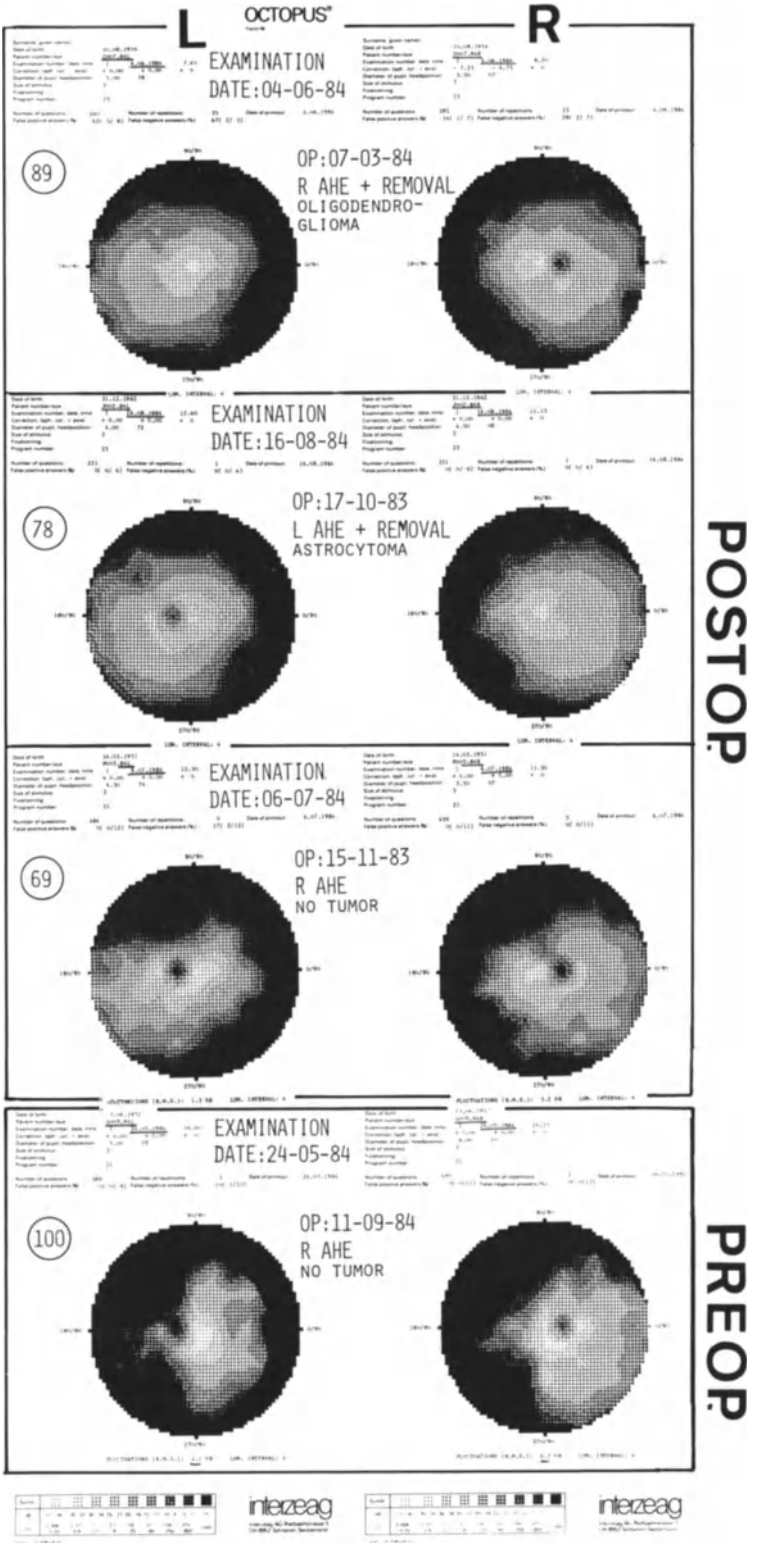


Fig. 37. Schematic drawing (top) of the visual pathway showing that some visual fibres from the thalamus proced forward and laterally over the temporal horn, before they project back to the occipital lobe. This detour into the temporal lobe is referred to as Meyer's loop (Meyer 1907) or pars temporalis. [From Seeger (1978) who refers to Pfeifer (1925). With kind permission of the author and Springer Verlag, Wien-New York.] The proposed retinotopic organisation of Meyer's loop is shown in the bottom section. [From Babb *et al.* (1982). With kind permission of the authors and Springer International, Berlin-Heidelberg-New York]

Fig. 38. Post-operative (patients nos. 89, 78, and 69) or pre-operative (patient no. 100) OCTOPUS findings of 4 patients. The 2 upper patients (89 and 78) have normal visual fields. Patient 69 shows a slight defect in the left upper quadrant with indentations. These, however, were already present pre-operatively. Patient 100 shows an incongrous left visual field defect, the macula being spared, due to an old posterior right occipital infarction. The SEEG evaluation, however, revealed right hippocampal seizure onset. L = left eye, R = right eye


L
OCTOPUS
R
EXAMINATION
DATE:04-06-84
89
OP:07-03-84
R AHE + REMOVAL
OLIGODENDRO-
GLIOMA
EXAMINATION
DATE:16-08-84
78
OP:17-10-83
L AHE + REMOVAL
ASTROCYTOMA
POSTOP.
EXAMINATION
DATE:06-07-84
69
OP:15-11-83
R AHE
NO TUMOR
EXAMINATION
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100
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R AHE
NO TUMOR
PREOP.
interzeag
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Fig. 38

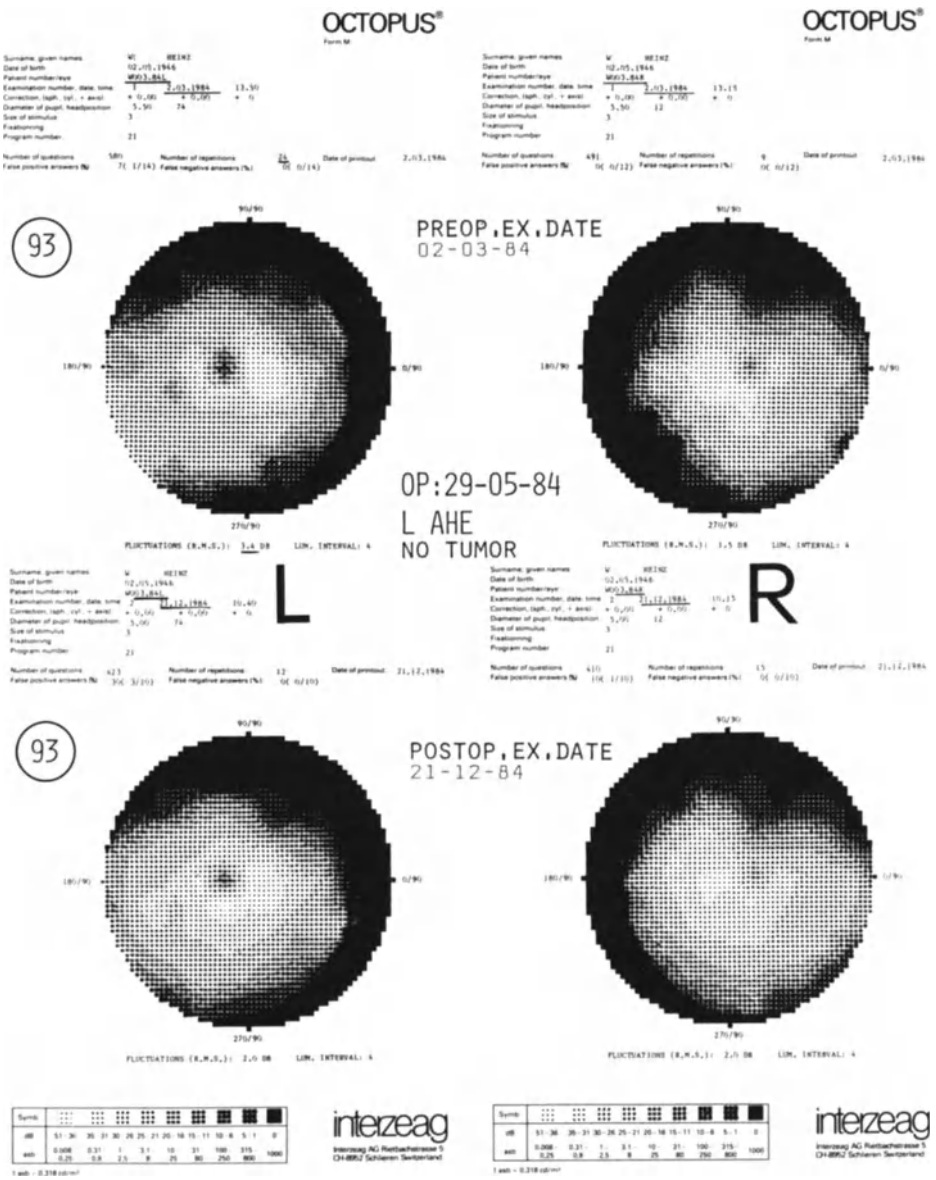

Fig. 39. Pre-operative (top) and post-operative (bottom) visual field of patient 93. As can be seen, there is no additive visual field defect post-operatively. In both examinations, however, the right upper quadrant shows a slight indentation

most severe (patient no. 100) is shown in Fig. 38 at the bottom. In contrast to anterior TL lesions, this patient demonstrated an incongruous defect greater for the eye *contralateral* to the affected TL due to an old right occipital infarction. As can be derived from the lower part of Fig. 37, temporal anterior lesions may produce an incongruous defect with the

extent of visual loss greater for the eye *ipsilateral* to the lesion. This is because the ipsilateral temporal retina projection fibres are located more anteriorly and ventrally.

Slight indentations in the sense of an incomplete quadrantanopsia were seen in 2 of these 13 cases. One of them (patient no. 69) is shown with its post-operative visual fields in Fig. 38, and the other with its pre- and post-operative visual fields in Fig. 39.

In *conclusion,* as yet we have not found any additive post-operative visual field defect resulting from selective amygdalohippocampectomy. All visual field defects identified in the 13 patients studied with the OCTOPUS were present pre-operatively. We therefore have no direct evidence that collaterals from the optic radiation go into the hippocampal gyrus.

6. Concluding Remarks

"Modern" resective surgical therapy after careful case selection and guidance by EEG as a means of treating medically intractable epilepsy is nearly half a century old (Penfield and Jasper 1954). Anterior temporal lobectomy has been by far the most commonly performed resection for epilepsy, and thousands of procedures may have been carried out, so that this operation has been considered a "standard" procedure (Hansebout 1977). Whereas resections guided by electrocorticograms (and electrical stimulation if no general anaesthesia was applied) were initially limited to the lateral cortex, a concept subsequently developed that a critical amount of anterior temporal lobe should be removed in all patients. Resections that included mesial structures were found to be more effective (Green *et al.* 1951) and the results of surgery were better the larger the resections were (van Buren *et al.* 1975). The *en bloc* resection (Falconer 1953, Crandall *et al.* 1963) reflected this concept, allowing also for more careful pathological analysis than the early piecemeal resections, usually performed by suction.

Greater precision in the identification of the epileptic focus enabled surgeons to perform more tailored procedures. This greater precision was developed through better understanding of brain physiology (Stephan and Andy 1982, Creutzfeldt 1983) and through the advent of modern pre-operative and intra-operative diagnosis. Stereoelectroencephalography (Bancaud *et al.* 1965) allows precise and safe stereotactic implantation of many depth electrodes into critical brain areas. Subdural electrode recording techniques (Wyler *et al.* 1984, Goldring and Gregorie 1984) used in the pre-surgical evaluation programme, as well as sophisticated intra-operative recording and stimulation techniques (Ojemann 1983), contributed considerably to this development. Simultaneous advances have been made in X-ray computed tomography which cannot only identify such local structural

abnormalities as small tumours or AVMs, local calcification or atrophy, but may also often indicate the focus by a relative enhancement after intravenous injection of Conray®. The enhancement probably reflects an alteration in the blood-brain barrier in the locally gliotic tissue (Oakley *et al.* 1979, Ojemann 1983). MRI or CSF enhancement using metrizamide helps identify mesial temporal herniation and sclerosis. Techniques for functional imaging of the human brain promise even greater diagnostic capabilities. Metabolic changes related to an epileptic focus include locally increased blood flow during a seizure, detectable by inert or isotopic xenon (Hougaard *et al.* 1976). Local changes in glucose metabolism may be identified by positron emission scanning, with an increase in metabolism during a fit and a relative lowering in the interictal phase (Engel *et al.* 1982 d, 1983 a).

However, none of these techniques can replace the appropriate EEG in the identification of epileptiform abnormalities. As epilepsy is best understood by studying ictal events, long-term EEG telemetry and video monitoring as well as appropriate recording and analysis techniques are very important. Careful analysis of interictal epileptiform abnormalities is equally important, and indeed there is renewed recognition of its value (Ojemann 1983).

The need for even greater precision in the pre-operative identification of the epileptic focus remains one major contemporary problem. However, development of appropriate microsurgical techniques (Yaşargil 1984 a, b) has enabled the progress in diagnosis to be translated into surgical procedures from which patients profit.

It is clear that in many epileptics no simple and narrowly confined epileptic focus is detectable, but rather a more diffuse, poorly defined region or even regions. In these cases, if surgery is feasible only large resections offer a real chance of cure. It is also true that in many patients with recurrent complex partial seizures there exists a well-localized mesiobasal TL focus. This concept of mesiobasal-limbic epilepsy has not only gained substantial support from pre-operative depth recordings (Wieser 1983 a) but also from careful analysis of the surgical outcome and histological findings of the "standard" surgical TL approach (Lieb *et al.* 1984, Walsh and Delgado-Escueta 1984).

To date, two surgical resective procedures have taken into account the operative consequences of this concept. They are the selective removal of amygdala and hippocampus either by the transventricular route (Niemeyer 1958, Niemeyer and Bello 1973), or by our approach, and the standard anterior temporal lobectomy (4.5 cm) with removal of the more posterior hippocampus (Spencer *et al.* 1984).

Niemeyer has given no detailed clinical long-term follow-up data for his entire series, but reported satisfactory results in 74% of 27 patients followed

from 6 months to 10 years and good post-operative EEG outcome. Spencer *et al.* (1984) have recently reported their series (consisting of 19 patients) in detail. Our preliminary report on 27 patients who had undergone selective amygdalohippocampectomy (Wieser and Yaşargil 1982a, b) did not consider details. This report on 127 operated patients attempts to fill this gap and reports the outcome data of 103 patients with a minimum follow-up of 1 year.

In summarizing the results obtained in this series, we should try to answer the question as to what extent the goals of surgical epilepsy therapy as described on p. 48 have been reached. With respect to *seizure control* the results of this series (62% of 103 patients being seizure-free, 5% with rare seizures, 26% having worthwhile and 7% having no worthwhile improvement) are good and at least in the upper range of the figures found in the literature (Talairach 1974, Jensen 1976a, b, Rasmussen 1977, 1980, 1982, Kawamura *et al.* 1982, Fisher and Uematsu 1982, Ward 1983, Niedermeyer 1983, Crandall *et al.* 1983, Ojemann 1983, Aird *et al.* 1984). Disregarding malignant tumours and "palliatively" operated non-tumoural cases, 75% are seizure-free, 4% have rare seizures, 16% have worthwhile and 4% have no worthwhile improvement (n = 73). In the non-tumoural group, from those patients who were operated on the basis of an unequivocally and strictly focal seizure onset on SEEG ("causally" operated, n = 16), as many as 88% are seizure-free. The remaining 12% show worthwhile improvement, and there is no single patient who has not improved. Thus one can say that a morphological lesion is not necessarily a pre-condition for a good post-operative outcome. The success rate is better in those cases with no obvious morphological lesion, where SEEG localization of unilateral seizure foci is narrowly confined to mesiobasal structures, than in cases with or without tumour and no depth electrode evaluation. Even the 3 patients with tuberous sclerosis have results good enough not to exclude further patients with this diagnosis, especially when the oligosymptomatic form is present (Perot *et al.* 1966).

Functional and behavioural improvement by review of the medical records and as reported from patients and families was achieved in 85% of patients. Only 1 benign tumour case has worsened post-operatively. Apart from the 2 patients who died as a consequence of having acquired Creutzfeldt Jakob disease during the pre-surgical evaluation procedure, in the non-tumoural cases none has worsened and only 2 patients failed to improve. Our post-operative neuropsychological results of this series are much better than with large anterior temporal lobectomy. A special role has been attributed to the hippocampus for memory (Milner 1958, 1963, 1968, 1974, Milner *et al.* 1968, Penfield 1952, Penfield and Milner 1958, Penfield and Mathieson 1974) or, at least, it has been argued (Squire 1982). Our findings that detailed learning and memory studies could not detect any significant

additional learning and memory deficit after unilateral removal of amygdala and hippocampus are therefore very significant. They do not support the hippocampal memory hypothesis but are in line with several recent suggestions that the lateral temporal cortex is at least as important to recent memory (Horel 1978, Ojemann 1983, Ojemann and Dodrill 1985, Creutzfeldt 1983) as the hippocampus, or both amygdala and hippocampus (Mishkin 1978, 1982, Mishkin *et al.* 1982). Our results are in full agreement with those recently published by Spencer *et al.* (1984) and Luczywek and Mempel (1980). However, testing of post-operative learning and memory in most patients was carried out 3 to 6 months post-operatively when the possible beneficial consequences of a successful operation were manifest, *i.e.,* under different psychosocial and drug conditions as compared to the pre-operative state. Most patients were by then seizure-free and therefore in an highly optimistic and sometimes even euphoric state. They felt themselves highly motivated not only to start "a new life" but also to perform well in the tasks. In addition, many of them had considerable reduction of their anticonvulsant medication. The latter might well contribute to the general trend for improved neuropsychological performances (Trimble and Thompson 1983). Along with these factors, a certain learning effect in those patients where a pre-/post-operative comparison was made with the same type of tests (even if different versions were used) cannot be ruled out completely.

Thus, although different factors might be involved, the final improvement—whether it be a predominant consequence of lowering the drug regimen or of the psychosocial implications of "being cured", or whatever—is primarily dependent on a successful removal of the epileptic focus being as radical as necessary, yet at the same time as careful and selective as possible. Studying those patients in whom post-operative seizure control was absent and in whom subtle but detectable post-operative learning and memory deficits developed, we are inclined to link intellectual status to the degree of post-operative seizure relief. Lieb *et al.* (1982) derived similar conclusions, although they stated that post-lobectomy changes in intellectual status are not necessarily exclusively attributable to the amount of seizure relief.

Definitive conclusions cannot be offered in *prevention of kindling-like mechanisms* and *interruption of the otherwise continuing epileptic process.* Despite the popularity of kindling with researchers as a model of epilepsy and of non-epileptic plastic changes of the brain (Wada 1981), evidence that kindling is relevant clinically remains circumstantial. A few retrospective studies suggested that the larger the delay in surgery from the time of seizure onset the poorer the results, perhaps because distant areas of brain have become epileptogenic (Adamec *et al.* 1981). The well-known fact that bilateral abnormalities may appear in the EEG years after onset of clinically

and electroencephalographically localized seizure discharges is not always accepted as an argument that kindling has taken place, because other latent foci may have independently matured. On the other hand, there are several findings supporting the suggestion that amygdala and hippocampus are especially prone to kindling-like mechanisms. Removal of a focus situated in this part of the brain with intense pathways to structures of the homolateral and contralateral hemisphere may be more important for preventing kindling than removal of foci in other regions of the TL; *i.e.*, the insular cortex (Silfvenius *et al.* 1964, Rasmussen 1982).

More experimental work is necessary to determine whether or not chronically recurrent focal seizures can generate distant epileptic foci or harm initially healthy brain. Recent work has found strong evidence that this is really the case, at least in rabbits and cats. For example, when chronic epileptiform discharges were induced in the occipital cortex of baby rabbits, after maturation visual field maps were found to be significantly abnormal (Baumbach and Chow 1981). Majkowski and Kwast (1981) have found changes in somatosensory evoked potentials after having established kindling by daily stimulation of the hippocampus in cats.

From our data several findings can be used as strong evidence that successful removal of the epileptic focus prevents (kindling-like) continuing functional disturbance of remote brain areas. Perhaps the strongest evidence derives from the neuropsychological learning results, which indicate that the contralateral hemisphere usually improves quantitatively better and more rapidily than the ipsilateral, provided surgery results in complete seizure relief and normalization of the EEG.

Thus from the evidence of this series we conclude that in patients with strictly localized, drug resistant, recurrent mesiobasal-limbic seizures, selective amygdalohippocampectomy is to be preferred to the "standard" anterior temporal lobectomy.

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Spinal Cord Astrocytomas of Childhood

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With 13 Figures

Contents

Intramedullary spinal cord astrocytomas are a relatively uncommon neoplasm, accounting for only 4% of central nervous system tumors of childhood[1,2]. Because of its rarity, individual neurosurgeons have relatively little experience with surgical management and long-term follow-up of afflicted patients. There has been little impetus to modify the traditional treatment of biopsy, dural decompression and radiation therapy despite the recognition that after a relatively short remission serious disability or death ensues.

This must be regarded as particularly tragic as most of these neoplasms are low grade gliomas and microscopically identical to their "sister" tumors which occur in the cerebellum, and are surgically curable. It was this perspective that encouraged the author to explore the technical feasibility of radical excision of spinal cord astrocytomas. In this endeavor, 120 children have undergone gross total excision of spinal cord astrocytomas over the past four years. This unusual series has provided a unique opportunity to study the biology of the tumor as well as its response to traditional, as well as recently introduced more radical surgical techniques.

Clinical Presentation

In most cases, the clinical evolution was indolent and, almost invariably, parents became aware of a problem long before there were objective signs of neurological dysfunction. In a significant number of patients the onset of symptoms was related to some apparently trivial injury, while in others parents described exacerbations and remissions which may be related to varying degrees of peritumoral edema.

The most common early symptom was local pain along the spinal axis. Other symptoms included motor disturbance, radicular pain, paresthesias, dysesthesias and, rarely, sphincter dysfunction.

Weakness of the lower extremities was usually first manifest as an alteration of a previously normal gait. This was often extremely subtle, and only obvious to a parent who noted a tendency to fall more frequently or walk on the heels or toes. In young children, there was commonly a history of being a "late walker", and in the youngest (under 2 years) there was often a history of motor regression, *i.e.*, starting to crawl again instead of walking, or refusing to stand.

70% of patients experienced severe pain along the spinal axis which was secondary to distension of the dural tube, and was most acute in the bony segments which were directly over the tumor. Characteristically, the pain was worse in the recumbent position as venous congestion further distended the dural tube and resulted in typical night pains. It was common to discover that patients had been on long-standing analgesics, including narcotics, after a nondiagnostic orthopedic evaluation.

Radicular pain occurred in 10% of cases, and was usually limited to one or two cervical or lumbar dermatomes, similar to root pain from a variety of disease processes.

Painful dysesthesias occurred in 10% of cases, and was generally described as painful hot or cold sensations in one or more extremities. In rare circumstances, this was the primary symptom, and not associated with objective signs of neurological dysfunction.

Paresthesias were occasionally associated with the dysesthetic pain, and both of these symptoms were more common with neoplasms in the cervical than in the thoracic spinal cord.

Cervical Tumors

The most common early symptoms were nuchal pain and head tilt with torticollis. Mild upper extremity monoparesis was the next most common symptom, and was often extremely subtle during the early stages of the illness. Very often, in young children, the first manifestation of weakness was switching "handedness" in right- or left-handed patients. Neoplasms in the caudal cervical spinal cord commonly caused weakness and atrophy of the intrinsic muscles of the hand in contradistinction to tumors rostral to C 5 which were less likely to cause significant weakness until relatively late in the clinical course. Interestingly, weakness of the lower extremities only evolved months or, rarely, two to three years after the first symptoms, and bowel and bladder dysfunction was rarely present at the time of primary diagnosis.

Sensory abnormalities were generally limited to one upper extremity, and a discrete sensory level was only noted very late in the course of the disease and, then, only in association with severe neurological disability.

In most patients, there was increased reflex activity in the lower extremities with or without extensor plantar signs and clonus.

Thoracic Tumors

Mild scoliosis was the most common early sign of an intramedullary thoracic cord neoplasm. Pain and paraspinal muscle spasm commonly occurred before there were objective signs of neurological dysfunction, and were commonly assumed to be secondary to the evolving scoliosis. Insidious progressive motor weakness in the lower extremities was first manifest by "awkwardness" and, only later, by frequent falls and an obvious limp. Early sensory abnormalities were uncommon although dysesthesias and paresthesias were occasionally present. Increased reflexes and extensor plantar signs, with or without clonus, occurred relatively early in the neurological course.

A presenting complaint of bowel and bladder dysfunction was most

unusual, and was diagnostic of neoplasm extending into the conus. In general, these symptoms evolved only late in the clinical course if the tumor was rostral to the conus medullaris.

Neurodiagnostic Studies

Spinal cord astrocytomas may be divided into two general categories: holocord and focal.

Holocord Astrocytoma

"Holocord" widening occurred in 60% of pediatric patients, and was manifest by expansion of the entire spinal cord from the medulla or cervicomedullary junction to the conus (Fig. 1).

These neoplasms were invariably cystic astrocytomas in which the solid component of the neoplasm spanned a variable length of the cord, and was associated with huge non-neoplastic rostral and caudal cysts which expanded the central canal above and below the tumor (Fig. 2).

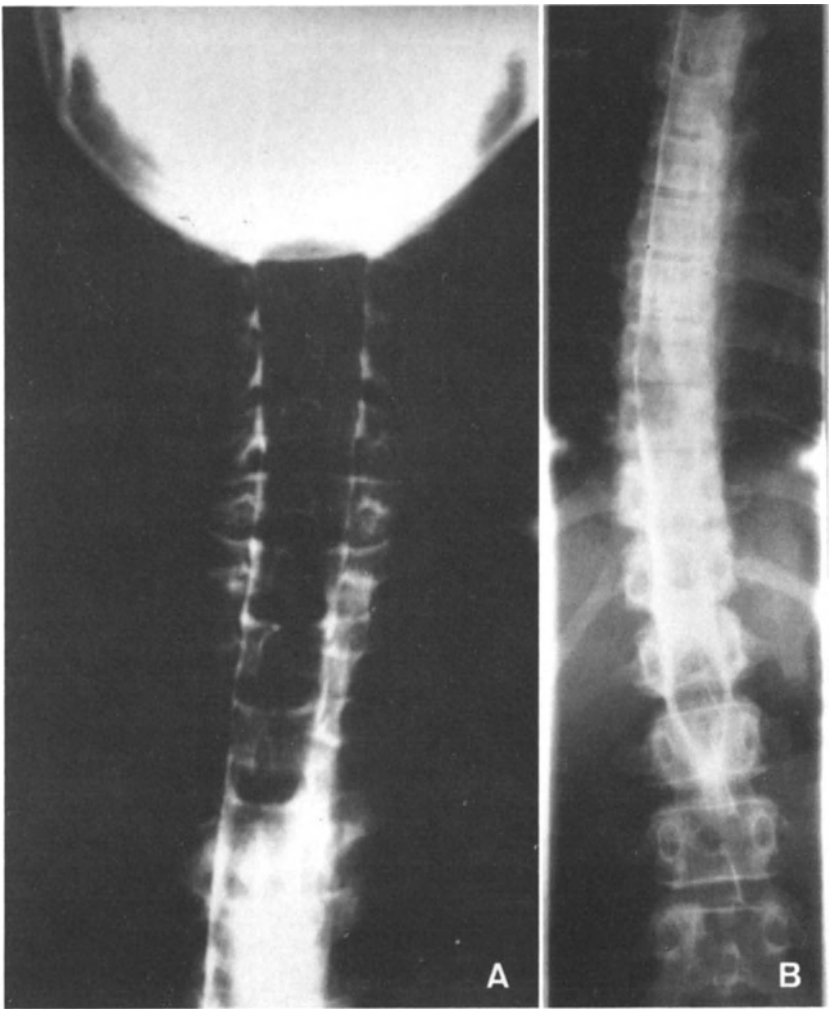
Plane spine X-rays commonly disclosed a diffusely widened spinal canal with relatively localized erosion or flattening of pedicles. Whereas the former was secondary to long-standing expansion of the entire spinal cord, the latter occurred only adjacent to the solid component of the neoplasm.

Although there were occasional early case reports of holocord widening, its relative frequency was probably not recognized because of the tendency to terminate the neurodiagnostic study when a lumbar myelogram disclosed a complete block secondary to an intramedullary neoplasm[2, 5, 17, 18]. In the first patients in this series a cervical puncture was employed to identify the rostral extent of cord widening. It was subsequently recognized that although not apparent on the myelogram, a small amount of Metrizamide almost invariably "trickles" past the block and is obvious on the immediate or delayed spinal CAT scan which, therefore, defines the rostral extent of the expanded cord[6—10]. It is for this reason that the availability of Computerized Axial Tomography (CAT) of the spine is an invaluable adjunct to the neurodiagnostic evaluation of spinal cord tumors.

A 24-hour delayed spinal CAT scan was a mandatory study as rostral and caudal, as well as occasional intra-tumor cysts were identified as the Metrizamide diffused within them.

Holocord expansion caused by a spinal cord tumor may be confused with hydromyelia, and it is important that this differential diagnosis be firmly established prior to surgery. There are four major observations which will contribute to making the correct diagnosis:

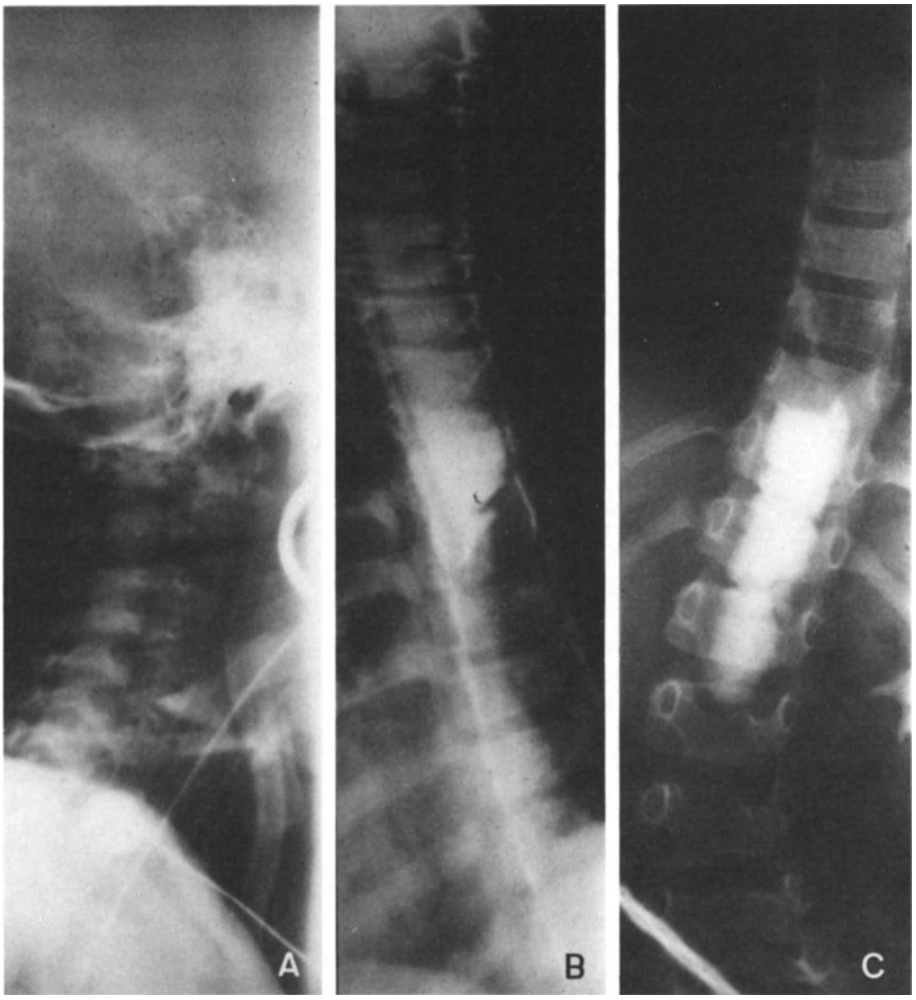
1. Plane spine X-rays often disclose erosion of pedicles adjacent to a tumor, while this is rarely present in hydromyelia. Both of these entities may be associated with a diffusely widened spinal canal.



Figs. 1 A and B. Myelogram disclosing holocord expansion from cervicomedullary junction to the conus. At surgery tumor was typical cystic astrocytoma with mid portion of solid component at T 9—10. Retrospectively it was apparent that this coincided with the region of maximal cord widening on the myelogram

2. While 95% of spinal cord astrocytomas are associated with a complete subarachnoid block there is, very rarely, an obstruction to the flow of Metrizamide in the presence of hydromyelia.

Even in the rare absence of a complete myelographic block, a spinal cord astrocytoma is associated with some distinct focal widening, while hydromyelia usually causes diffuse widening of the spinal cord without one area being significantly more widened than another.



Figs. 2 A–C. Inadvertant intracyst injection of metrizamide discloses that the cystic component of the neoplasm extends from the medulla to the conus. B delineates the solid component of the neoplasm as it deforms the intracyst contrast

3. Hydromyelia is invariably associated with an Arnold-Chiari-I malformation and, for this reason, it is essential that in the presence of any diagnostic uncertainty that the contrast study include the cervicomedullary junction.

4. In the presence of hydromyelia the delayed Metrizamide spinal CAT scan discloses homogeneous enhancement of the entire hydromyelic cavity, while cystic tumors have relatively localized collections of intracyst contrast.

Focal Astrocytoma

Focal spinal cord astrocytomas were generally four to eight segments in length, and commonly associated with flattening of pedicles immediately adjacent to the neoplasm. In some cases, plane film changes were as precise as the myelogram for tumor localization (though obviously never a substitute).

Focal astrocytomas were associated with a total subarachnoid block in 90% of cases and, for this reason, an immediate and delayed CAT scan was necessary to define the rostral extent of cord expansion. Intra-tumor cysts were rarely present in the previously unoperated and non-radiated patient.

Patients who had received a full course of spinal radiation (4,500 R) commonly had multiple cysts within the tumor which were obvious on the delayed CAT scan or ultrasonography (see below).

It has become evident that MRI scanning will relegate most invasive neurodiagnostic studies to history. The MRI scan provides an excellent image of intramedullary neoplasms, and it is often unnecessary to carry out other studies if the scan is satisfactory. It is essential to obtain a mid-sagittal view which may occasionally be impossible in the presence of severe scoliosis (Figs. 3 A and B).

Transcutaneous Ultrasound

In patients who have had an earlier laminectomy, transcutaneous ultrasonography may be employed to visualize the spinal cord and the neoplasm. Utilizing this technique (real-time unit with triple frequency: 3.5 and 7.5 MHz) the cord may be studied in both sagittal and transverse projections, and the presence of significant expansion will be immediately obvious[3, 11, 15].

Transcutaneous ultrasonography may be more informative than conventional myelography or Metrizamide spine CT scanning as it gives a direct view of the interior of the spinal cord. In occasional cases, the tumor may be echogenic, affording a dramatic view of the neoplasm and its relationship to the spinal cord. The presence of cysts either within the tumor or in relation to the rostral and caudal pole of the neoplasm is evident (Fig. 4). Eighteen months or longer, following radiation therapy, there are commonly multiple intra-tumor cysts which are "swiss cheese" like in appearance. The technique is limited by the length of the laminectomy, and it is not possible to visualize the spinal cord rostral or caudal to the laminectomy defect.

Surgery

It is desirable to carry out a limited laminectomy over the solid component of the neoplasm, but not to unnecessarily extend it rostrally or caudally.

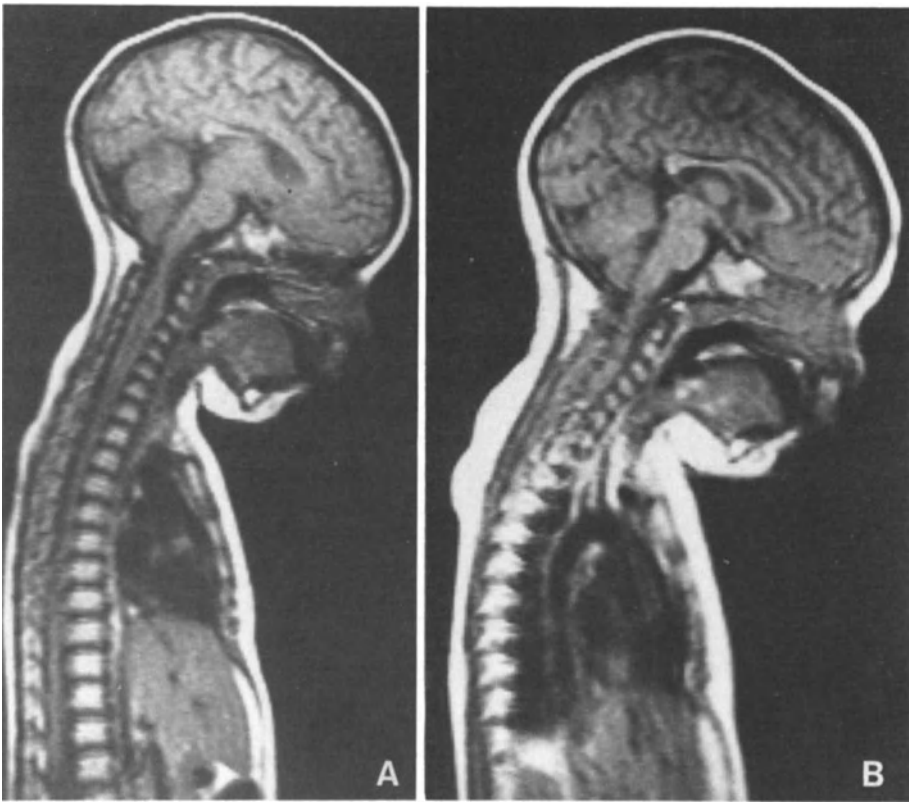


Fig. 3 A. MRI scan discloses cystic tumor within cervical cord
Fig. 3 B. 12 months following surgery the cord appears relatively normal

In our first surgical experience with "holocord" widening, a total laminectomy from C 1–T 12 was carried out. It was subsequently recognized that it was not necessary to expose the spinal cord over the rostral and caudal cysts and, for this reason, it was important to define as accurately as possible the location of the solid component of the neoplasm vis-à-vis the cysts.

The approximate location of the solid component of the neoplasm may be estimated on the basis of the clinical and radiographic findings.

Clinical Indications of Tumor Location in the Presence of Holocord Expansion

In the presence of holocord widening associated with a cystic astrocytoma, it is the solid component of the neoplasm that is responsible for primary neurological dysfunction while the rostral and caudal cysts which expand the remainder of the spinal cord remain asymptomatic in the early stages of the disease.

Therefore, neurological symptoms in one or both upper extremities in the presence of holocord widening suggests that the solid component of the neoplasm is within the cervical cord.

Conversely, progressive scoliosis and/or neurological dysfunction limited to the lower extremities are strongly suggestive of solid neoplasm within the thoracic cord, while bowel and bladder dysfunction indicates extension of neoplasm into the conus.

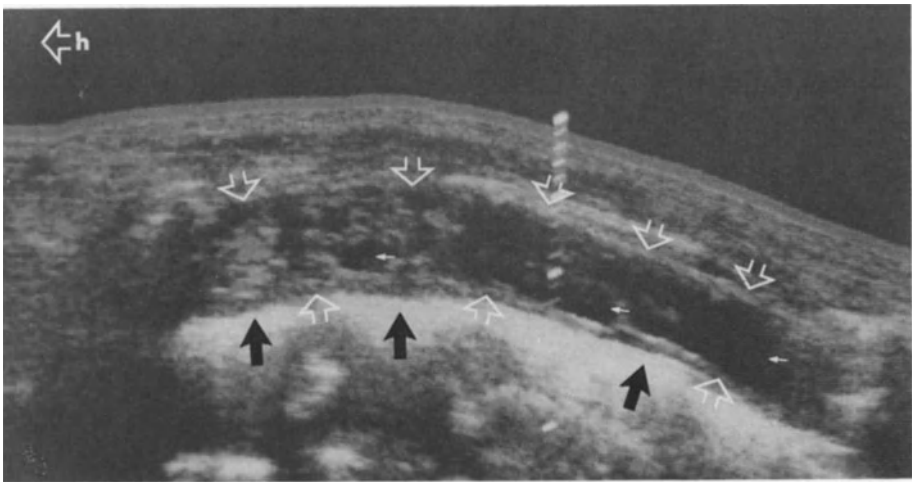


Fig. 4. Transcutaneous ultrasonography discloses a sagittal view of an expanded spinal cord (open arrows) with multiple small intratumor cysts (small arrows). Closed black arrows indicate posterior surface of vertebral bodies. This patient received 4,500 R of spinal radiation which induced formation of small cysts resulting in typical postradiation "swiss cheese" appearance of tumor

In the presence of normal bowel and bladder function, an expanded conus, in our experience, is invariably associated with a cyst.

Spinal cord ependymomas do not adhere to this clinical pattern as they may expand any length of the spinal cord with a relative paucity of signs and symptoms referrable to the segmental involvement. It is tempting to speculate that this is directly related to the primary anatomic location of the tumor in the region of the central canal which causes very gradual compression of adjacent neural structures as the tumor increases in volume. This may be analogous to the rostral and caudal cystic component of the spinal cord astrocytomas, which are also in the region of the central canal and asymptomatic at the time of primary diagnosis. The origin of the solid component of the astrocytoma is probably relatively asymmetric and may cause symptoms as a result of both compression and infiltration of adjacent neural tissues.

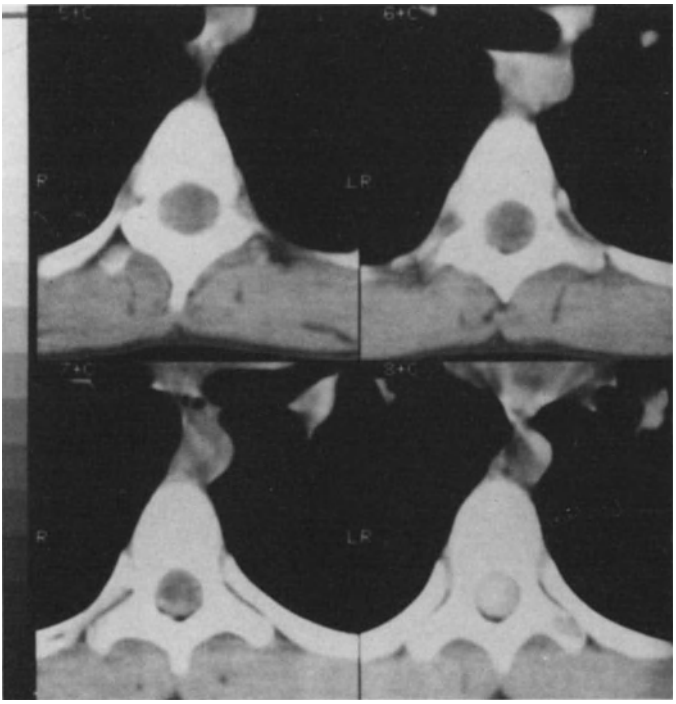


Fig. 5. Delayed spinal CAT scan carried out 12 hours after myelogram discloses expanded spinal cord in three views and adjacent caudal cyst in one view. (The cyst is filled with contrast.) This identifies the tumor-cyst interface and delineates the segmental location of the solid component of the neoplasm

Radiologic Indicators of Tumor Location in the Presence of Holocord Expansion

While the entire spinal canal may be widened in the presence of a "holocord" astrocytoma, erosion of pedicles occurs only immediately adjacent to the solid component of the neoplasm. In addition, the myelogram and myelo-CAT scan disclose a disproportionate widening adjacent to the midportion of the neoplasm (most commonly associated with total subarachnoid block).

Finally, the delayed Metrizamide spinal CAT scan may disclose the rostral and caudal tumor-cyst junction as the contrast diffuses into the latter (Fig. 5).

Surgical Instrumentation

Spinal cord astrocytomas are firm, often contain microscopic foci of calcium, and only rarely have a cleavage plane to facilitate an en bloc resection. In the overwhelming majority of cases it is necessary to remove

the tumor from inside-out until the almost invariably present "glia-tumor interface" is recognized as a change in color and consistency between the tumor and adjacent normal neural tissues.

In the past, neurosurgeons were limited to traditional suction-cautery techniques for removal of neoplasms and, whereas that was often satisfactory for brain tumors, it was extremely hazardous in the spinal cord. This was because of the transmitted heat and movement through the tumor to the adjacent normal spinal cord which was invariably firmly adherent to it. As a result of these technical limitations there was a significant morbidity associated with intramedullary spinal cord surgery.

The development and application of the CUSA system was a significant improvement over the conventional systems, and made a major contribution to spinal cord surgery[12, 13].

It is important to briefly describe the CUSA in order to fully appreciate its impact on intramedullary spinal cord surgery.

The CUSA system incorporates three major systems at the handpiece to provide maximum efficiency in removing tissue. The three systems are:

1. Vibration: The surgical tip is caused to vibrate longitudinally, thereby fragmenting tissue in contact with its distal annular end. The level of vibration is adjustable.

2. Irrigation: Sterile irrigating solution is routed from an IV source hanging from the console to the coaxial space between the outer surface of the surgical tip and the inner surface of the flue. The fluid exits near the tip, enters the operating field, and suspends the fragmented particles.

3. Suction: A suction pump contained in the console applies the suction to the hollow surgical tip. Fluid and particulate matter are aspirated at the distal end of the tip and subsequently deposited in a cannister. The suction available at the tip is adjustable from 0 to 24 inches of mercury (0–24 inches Hg).

The ultrasonic dissecting system is capable of discrete removal of a broad range of tissue. It is important to emphasize that the primary value of ultrasonic dissection is the fragmentation of tissue by the vibrating tip of the handpiece.

If it were possible to observe the operation of the instrument in slow motion, there would be these events: a) tissue fragmentation within 1 ml of the vibrating tip; b) suspension of fragmented tissue in the irrigation; c) aspiration of the tissue-irrigation solution.

Because the suction removes an emulsion of tissue and irrigation, there is no movement of adjacent tissue. This is an important divergence from conventional suction-cautery technique in which there is a great deal of transmitted movement.

Laboratory studies of the CUSA system have demonstrated that normal electrical conduction in neural tissue is maintained beyond a 1 ml radius of

the vibrating instrument tip. For this reason, dissection with the ultrasonic instrument may be carried out immediately adjacent to vital structures with little attendent risk.

The CUSA is the ideal instrument to rapidly "debulk" and remove all but residual fragments of a spinal cord neoplasm. The neurosurgical laser is equally ideal to remove the residual fragments as it may be employed with great precision along the length of the glia-tumor interface.

Although the laser may be employed in place of the CUSA, it is extremely tedious and time-consuming when directed towards a very voluminous intramedullary neoplasm. In addition, the resulting laser "char" makes it difficult to recognize the "glia-tumor" interface, and mandates frequent interruptions of the ongoing dissection as the blackened tissues are gently removed with a small caliber suction.

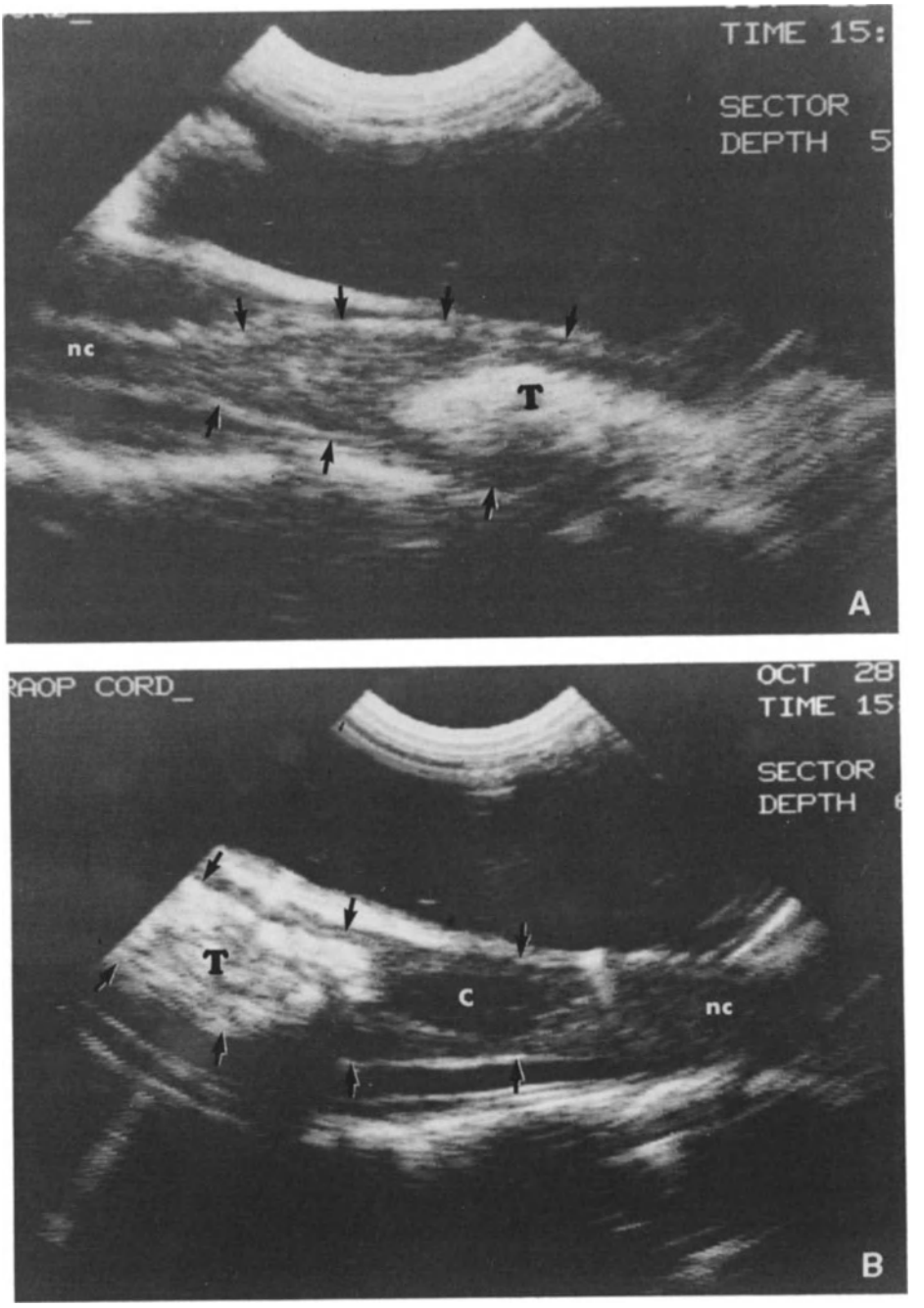
Surgical Technique

In patients who have not been previously operated on, an osteoplastic laminectomy is carried out. This permits replacement of the bone which is a nidus for subsequent osteogenesis and posterior fusion. Replacement of the bone does not prevent the postsurgical evolution of spinal deformity, but offers protection against future local trauma.

Even following careful consideration of the clinical and neuroradiologic examination, it is not possible to be certain that the laminectomy is of sufficient length to expose the entirety of the solid component of the neoplasm. For this reason, transdural ultrasonography is utilized to further define the location of the tumor vis-à-vis the bone removal.

Therefore, after laminectomy is carried out, the wound is filled with saline and the head of the transducer probe is placed into gentle contact with the dura. Utilizing this technique, the spinal cord is viewed in both sagittal and transverse sections. The rostral and caudal limits of the tumor, as well as the presence or absence of associated cysts are immediately obvious. Occasionally, an echogenic tumor provides a striking ultrasound image though, most commonly, the solid component of the neoplasm is only manifest as a widened spinal cord (Figs. 6 A and B). If the laminectomy is not sufficiently long to expose the entirety of the solid component of the neoplasm it is lengthened, segment-by-segment, until the ultrasound discloses that the entire tumor mass is exposed. Only at this juncture is the dura opened, and this is limited to overlay the expanded spinal cord—it is not extended rostrally or caudally over normal spinal cord. In addition, it is not necessary to open the dura widely over the rostral or caudal cyst, as these are easily drained as the solid component of the neoplasm is excised.

It is rarely helpful to utilize intra-operative ultrasound after the dura is opened as numerous surgical artifacts obscure the image.



Figs. 6 A and B. Intraoperative transdural ultrasonography discloses echogenic tumor (*T*) expanding spinal cord (arrows). A small rostral cyst (*C*) is apparent as is the normal appearing spinal cord (*nc*) above and below the neoplasm

It is important to emphasize that the "swollen" spinal cord is commonly rotated and distorted, and it is essential that careful inspection identify normal landmarks prior to placing the myelotomy. Since the posterior median raphe is generally obliterated, the only sure way of recognizing the posterior midline is by identifying the dorsal root entry zones bilaterally. Rotation of the cord may occasionally make this difficult, and even surprising, in terms of the distorted location of the midline. In any event, this is important as otherwise it is possible the myelotomy may be placed away from the median raphe and sever multiple nerves along the dorsal root entry zone.

In In the presence of holocord widening associated with rostral and caudal cysts, the ultrasound will have clearly defined the junction of cyst and neoplasm over the rostral and caudal poles of the tumor. It is in the "junctional" regions that the midline myelotomy is started.

The carbon dioxide laser utilized at 6–8 watts is an ideal instrument for placing the myelotomy as the cord is incised and hemastasis obtained simultaneously. Although neurosurgeons are loathe to interrupt blood vessels on the surface of the spinal cord, it is tedious and time-consuming to preserve these vascular channels, not at all essential to the preservation of neurological function, and they are almost inevitably disrupted during the course of the procedure, even if primarily preserved.

After the cyst is entered, inspection of the cavity will localize the rostral or caudal neoplasm which extends into it. It is not necessary, in most cases, to extend the myelotomy over the cyst as it is easily drained as either pole of the neoplasm is identified and removed. Because the cyst fluid is produced by the tumor, it is unlikely to reaccumulate following gross total excision of the neoplasm.

After identifying the rostral and caudal cyst-tumor junction, the myelotomy is continued over the midline of the cord between the previously placed incisions (Figs. 7 A and C).

Following completion of the myelotomy, there is usually 1 to 2 mm of white matter overlying the neoplasm which is removed with the laser or bipolar cautery and a very fine suction. Most astrocytomas are grey or pink in color, and may be distinguished from adjacent white matter.

At this juncture, it is essential that pia traction sutures be utilized to open the myelotomy incision and further expose the intramedullary tumor. It is satisfactory to utilize any fine suture material, and it the author's practice to simply "hang" small clamps on the sutures rather than suturing the pia to adjacent tissues.

It must be emphasized that in the presence of an astrocytoma, there must be no effort to define a plane of cleavage around the tumor. These neoplasms must be removed from "inside out" until a "glia-tumor interface" is recognized by the change in color and consistency of the

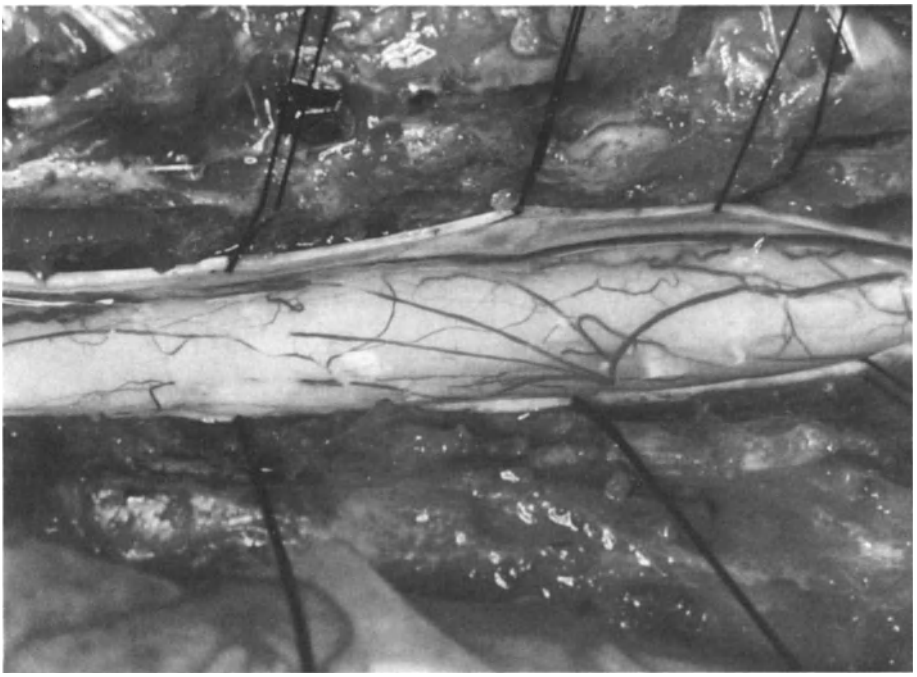


Fig. 7 A. External appearance of expanded spinal cord. Note stretching of surface blood vessels

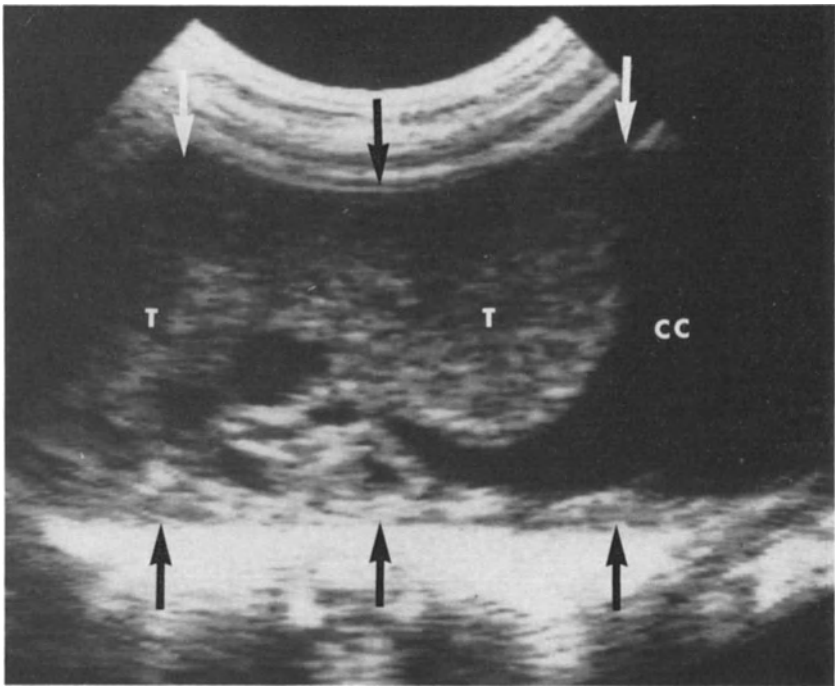


Fig. 7 B. Ultrasonogram (carried out prior to opening dura) discloses the anterior and posterior dura (black arrows), the tumor (*T*) with a few small cysts and the caudal cyst (*CC*). The white arrows identify the posterior surface of the spinal cord. Note that the relationship of the caudal pole of the tumor to the caudal cyst is well defined. It is over the tumor-cyst junction that the first myelotomy incision is placed

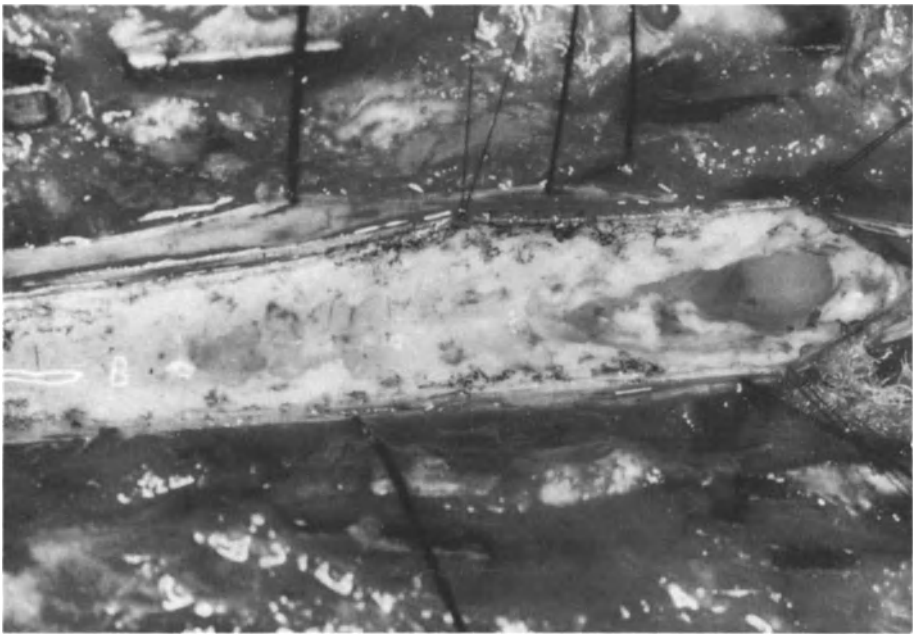


Fig. 7C. Following myelotomy the caudal pole of the tumor and caudal cyst are evident

Fig. 7D. Tumor has been removed

adjacent tissues. There is rarely a true plane of dissection, and futile efforts to define its presence only results in unnecessary retraction and manipulation of functioning neural tissue.

In the presence of cystic holocord neoplasms, tumor removal is initiated either at the rostral or caudal pole of the neoplasm in the region of the tumor-cyst junction.

As tumor excision continues, it is helpful to recognize that the anterior extent of the neoplasm is only very rarely ventral to the anterior wall of the cyst. The bulk of the tumor is most often in the posterior two thirds of the spinal cord (as viewed in cross section), and the general dimensions of the tumor may be roughly conceptualized following inspection of the rostral and caudal cyst.

The excision of the solid noncystic astrocytoma is initiated in the midportion rather than the rostral or caudal pole of the neoplasm. This is because there is no clear rostral or caudal demarcation of the tumor as occurs when there are rostral and caudal cysts. In addition, the "poles" of the neoplasm are the least voluminous and, for this reason, removal of this part of the neoplasm may be the most hazardous as normal neural tissue may be easily disrupted.

The CUSA is utilized to remove the bulk of the neoplasm, following which, the carbon dioxide laser is employed to vaproize the visible remaining fragments. The dura is closed primarily as it is unnecessary to utilize a dural substitute for decompression if tumor excision has been grossly complete (Figs. 8–10).

Evoked Potential Monitoring

Sensory-evoked potentials are monitored throughout the majority of the operative procedures. This monitoring is only valuable if the information is immediately available and utilized by the surgeon to modify the operative dissection. Therefore, it is essential that the data be continuously updated and communicated. Information that is updated every two minutes only informs the surgeon that some event in the dissection has already occurred at some unknown time and, therefore, allows neither corrective steps nor assessment as to the responsible manipulation.

The conventional averaging systems such as the Tracor or Nicolet, are only capable of updating information every two minutes, and require an evoked-potential amplitude in the order of 0.25 MV. Since evoked potentials (EP) from a spinal cord compressed by a tumor, are often less than 0.10 MV in amplitude, these instruments are not helpful surgical adjuncts for intramedullary spinal cord sugery.

This is quite a different situation from scoliosis surgery or spinal cord angiography in which more conventional monitoring systems may provide valuable information inasmuch as after the straightening of the spine or

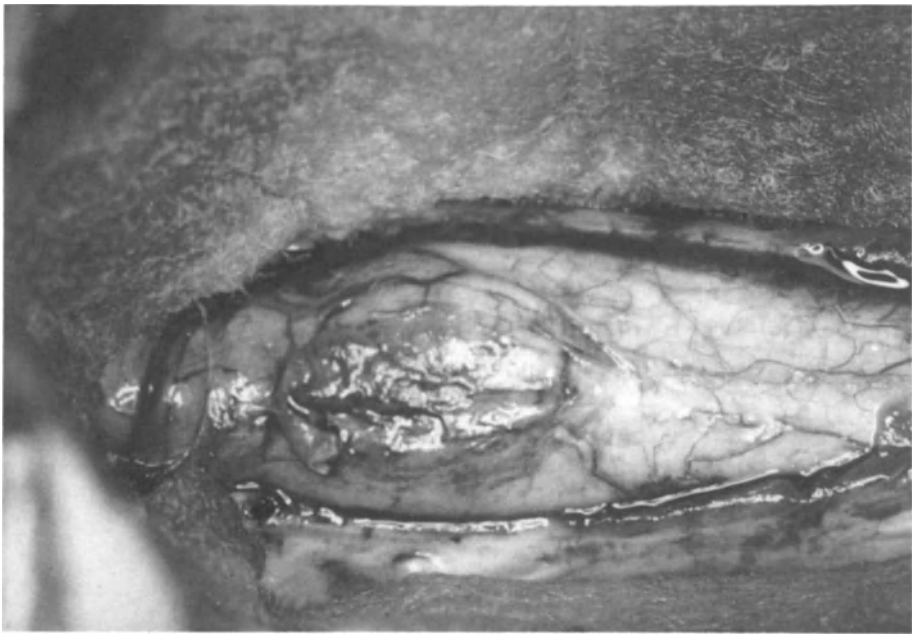


Fig. 8 A. External appearance of spinal cord (C 4–C 8). Tumor is fungating through a small biopsy incision carried out a few weeks earlier

Fig. 8 B. Following myelotomy and insertion of pia traction sutures the tumor is well visualized and it is unnecessary to retract neural tissues

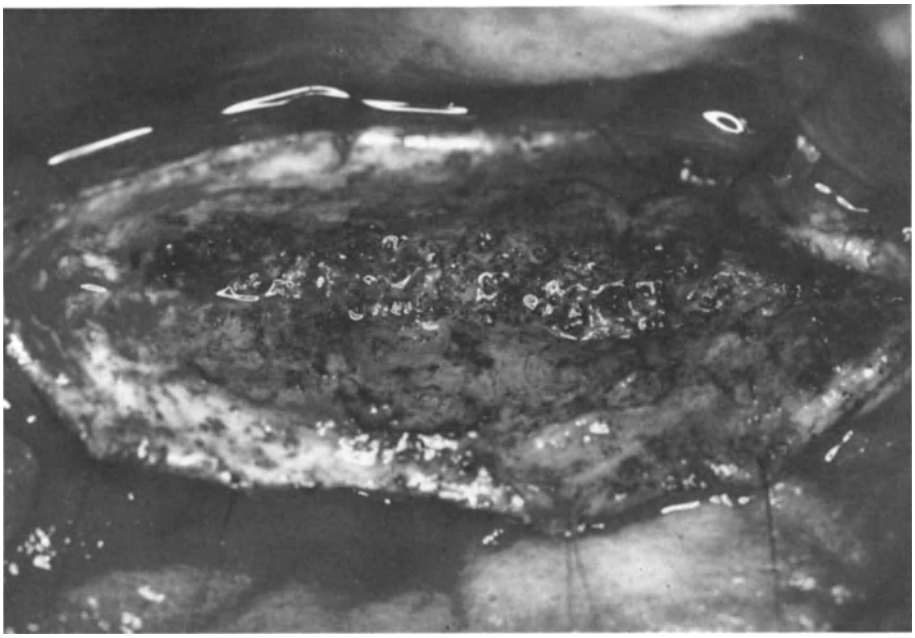


Fig. 8C. Following tumor removal there is invariably a huge residual intramedullary cavity

Fig. 9A. External appearance of spinal cord (C2–C7). Note abnormal surface vasculature over rostral part of exposed cord

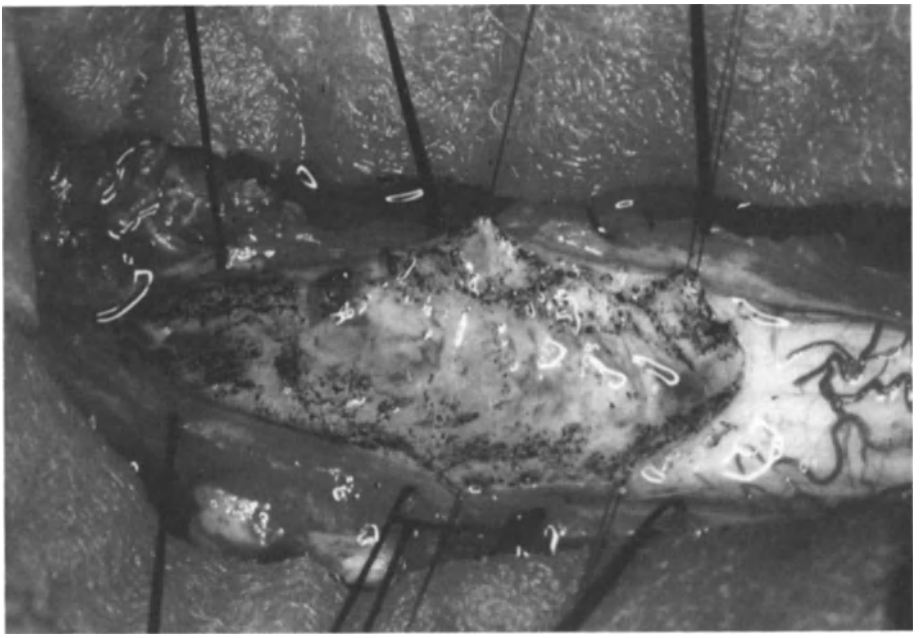


Fig. 9 B. Following myelotomy and placement of pia traction sutures the tumor is exposed. The black particulate matter is laser "char"

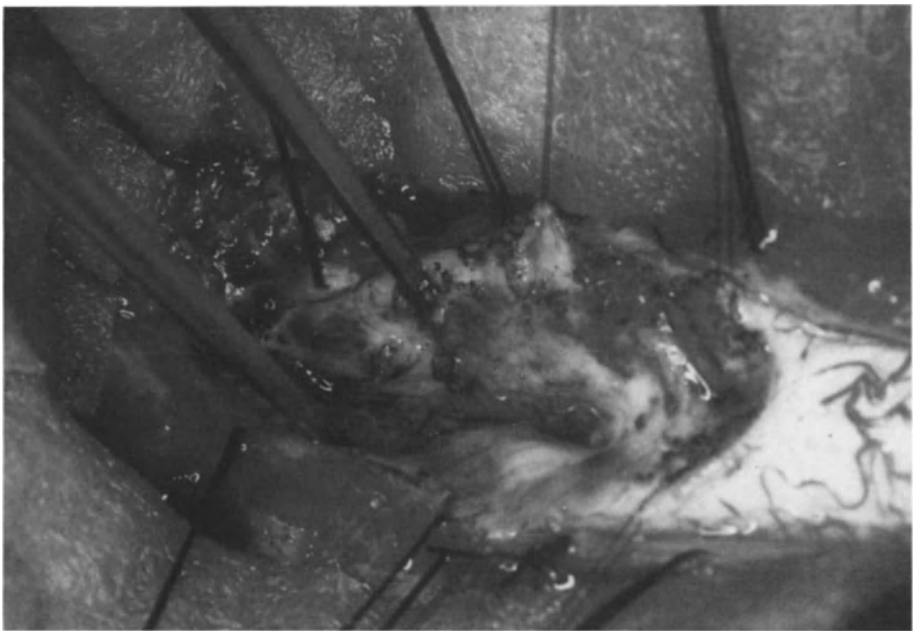


Fig. 9 C. Following removal of the tumor which extended to the ventral surface of the cord the anterior arachnoid is visualized. Note the excellent white matter-tumor interface

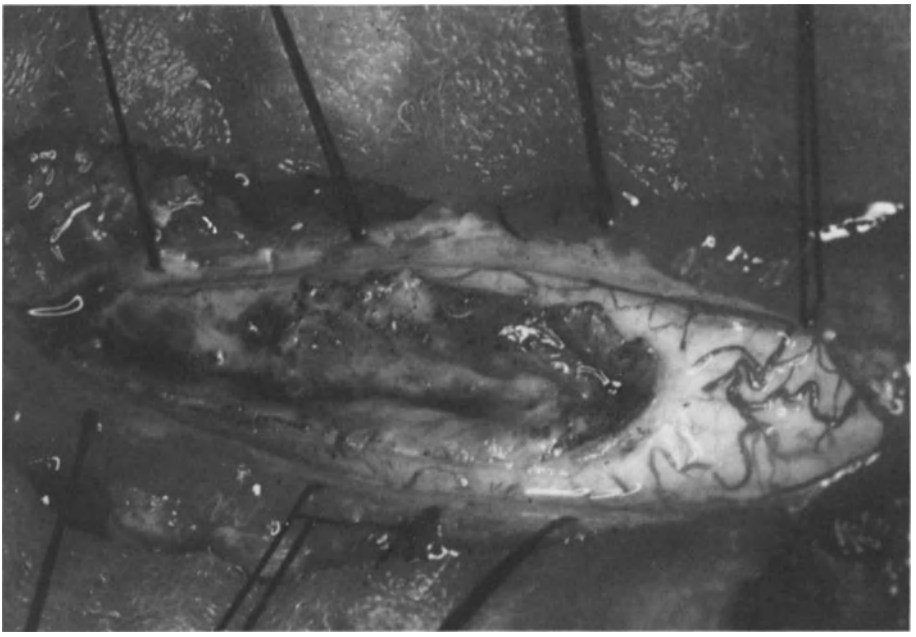


Fig. 9 D. Pia traction sutures have been removed permitting the cord to "collapse" around the residual cavity

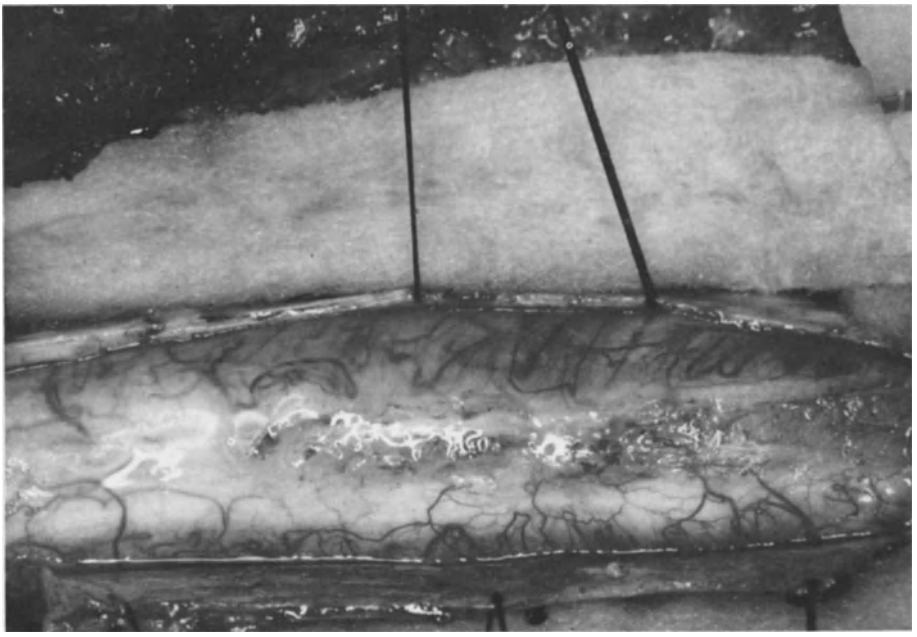


Fig. 10 A. External appearance of markedly swollen spinal cord. Note that identification of the dorsal root entry zones clearly defines the expanded midline where tumor is evident beneath the pia

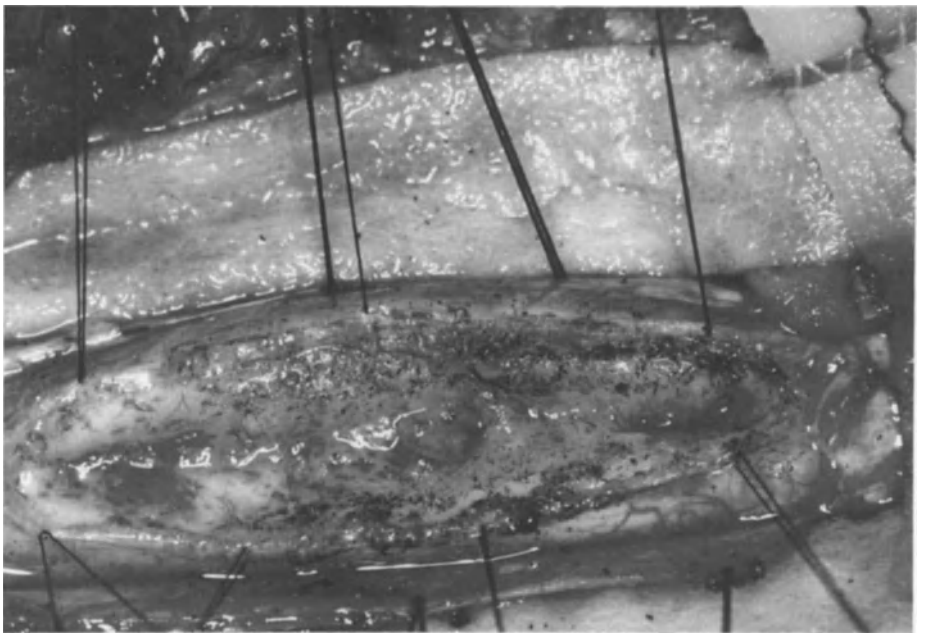


Fig. 10 B. Myelotomy and pia traction sutures have exposed the tumor

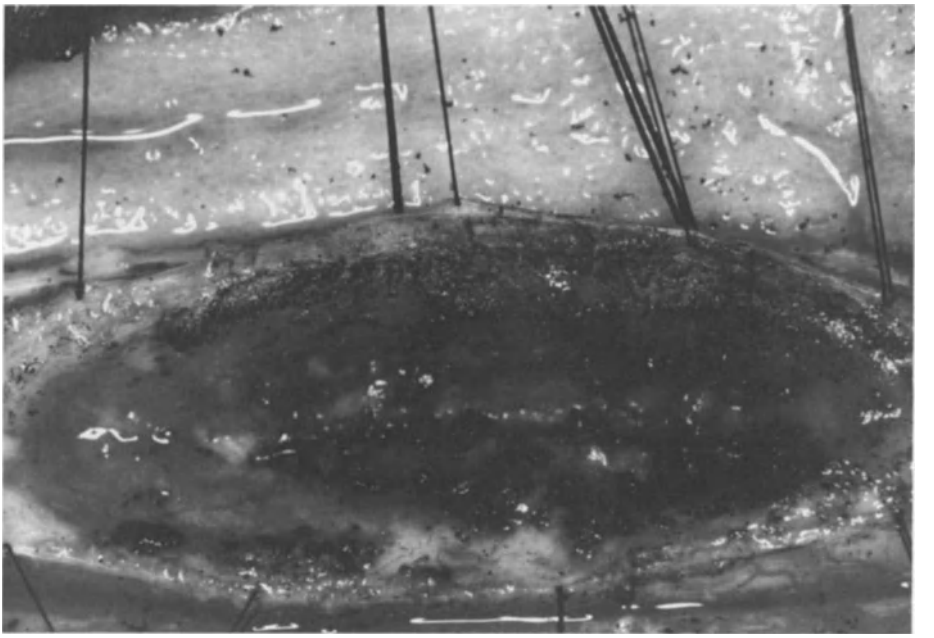


Fig. 10 C. Tumor has been removed. There is abundant laser "char" where residual tumor fragments have been "vaporized"

injection of the contrast media, the surgeon may pause to be updated on the status of the spinal cord. The hiatus in time is not important inasmuch as the event and its place in time is well-established. Since neither of these procedures is expected to adversely effect electrical conductivity, if electrical changes are observed, it may be advisable for the orthopedist to release the instrumentation, or the angiographer to delay further instillation of contrast material until there is electrical recovery.

In our early experience, 24 patients were monitored via the Tracor instrument systems. In no situation was this either prospectively or retrospectively helpful and, in fact, we temporarily abandoned monitoring utilizing conventional averaging technique.

In our last 66 consecutive patients, monitoring has been performed with the Cordis Brain-State Analyzer which utilized a new technique known as optimized digital filtering for averaging the evoked potential. This is a highly sensitive instrument which can update information as fast as every 5 to 10 seconds, and can detect an evoked-potential smaller than 0.10 mcv. For this reason, there is a continuous stream of information in real-time, and it is simple to relate this to the ongoing surgical procedure. Both brain stem (far field) and somatosensory (near field) evoked potentials are used for intraoperative monitoring. Only the near field potentials are effective when the cord is very compromised.

Several clinical correlations have been made utilizing the Cordis Brain-State Analyzer. Placement of pia traction sutures commonly result in transient decrements in the amplitude of potentials which probably occur as a result of movement of the posterior columns. Usually, the potential recovers within a few minutes. If it does not, the suture is removed and placed in another location under less tension.

If the dissection is inadvertently extended beyond the poles of the tumor, as is possible when there is no rostral or caudal cyst, there is a dramatic decrease in amplitude and increase in latency of the evoked potential. This is most likely secondary to manipulation of the posterior columns which are in their normal anatomic position, and indicates a normal cord is being disrupted.

When the laser is employed for more than 20 seconds at one time there is often an adverse, probably thermal, effect which is manifest by a decrease in amplitude and increase in latency. When this occurs, the dissection is temporarily interrupted and the cord is irrigated with cool Ringer's solution and, in most cases, electrical activity returns to "baseline" within 30 to 90 seconds.

In some cases there is deterioration of evoked-potentials as the dissection is directed towards tumor removal in specific locations. When this occurs, the manipulation is temporarily interrupted and the electrical activity permitted to recover.

It is very common to start and stop the procedure many times during the course of tumor removal.

Improved electrical conductivity following tumor removal was invariably associated with a benign postoperative course. Impaired activity as compared to the preoperative baseline was not uncommon, and it was not necessarily associated with neurological morbidity. Nevertheless, the majority of patients with deteriorated activity have had transiently greater neurological dysfunction though, in most circumstances, this has ultimately recovered. In one patient, all electrical activity was lost and, postoperatively, there was complete absence of position sense in the lower extremities.

Therefore, in summary, the Brain-State Analyzer gives meaningful information which we have utilized to modify the surgical dissection. It is too early in our experience to state that it is an indispensable adjunct but, clearly, the information is relevant, quickly available, and easily translated into surgical action.

Potential Surgical Pitfalls

In two cases, transverse myelitis was confused for an intramedullary neoplasm. These patients were 16 and 18 years of age, and it was retrospectively apparent that the clinical presentations were atypical for a spinal cord neoplasm. Subjective sensory complaints antedated motor dysfunction, and the evolution to significant neurological disability was more rapid than with the benign neoplasms in which the first symptoms often preceded diagnosis by months or even years.

In addition, in the patients with demyelinating disease the myelogram disclosed only mild spinal cord widening and no myelographic block. Therefore, rapidly evolving neurological dysfunction in the absence of significant mass was consistent with transverse myelitis, while neoplasms were associated with marked spinal cord enlargement and minimal neurological dysfunction.

Dural Substitutes

In the course of operating on 78 patients who had undergone previous surgery, we have had the opportunity of reexploring a variety of dural substitutes. These have included Gelfilm, Cargile membrane, cadaver dura, silastic, as well as many cases in which the dura was simply left open.

It has been a consistent observation that all biological material acts as a nidus for proliferation of fibrous tissue. At the time of reexploration there were dense adhesions between the spinal cord, the pseudodura which replaced the biological membrane, and the deep muscle superficial to it. As a result, the dissection was invariably tedious and prolonged. In addition, the normal anatomic landmarks along the posterior surface of the spinal cord

were distorted and there were adhesions along the lateral margins of the cord fixing it to the dural tube.

In cases in which silastic was used as a dural substitute, there were no adhesions, and only minimal thickening of the leptomeninges immediately beneath the silastic.

These observations are not intended to imply that the use of biological materials is contraindicated, or in any way deleterious to neurological function. It is only suggested that in a case in which there is a likelihood of future surgery, that silastic will invariably facilitate that procedure; whereas the biological materials will make it more difficult.

Missing Rostral or Caudal Tumor Fragment

In cases in which the entire spinal cord was expanded ("holocord astrocytomas"), it was a consistent finding that the neoplasm was associated with a rostral and caudal cyst which extended up and down the central canal but did not contain neoplasm. In three cases, a large intratumor cyst was confused with a rostral cyst, and the tumor removal was prematurely terminated on the assumption that the superior part of the tumor had been removed. In these cases, the symptoms recurred three months, six months, and 18 months postoperatively as the cysts reformed. The symptoms were rapidly evolving scoiosis in two patients, and paraspinal and cervical pain in one. In all of these cases, reexploration disclosed only residual tumor which had been neglected as a direct result of misinterpreting a large tumor cyst for a rostral or caudal cyst. It is essential that when cysts are identified over the poles of the tumor, that they be opened up widely enough to be certain that this is the cyst which is extending above or below the tumor, and not a cyst within the tumor. The former are lined by white matter, whereas cysts that occur within the neoplasm are lined by tumor tissue.

Intraoperative ultrasound may also help differentiate the rostral and caudal cyst from the intratumor cyst. The former symmetrically expand the cord, occupy two thirds of the diameter, and are smooth-walled. Intratumor cysts are eccentric and asymmetric, are of varying volume, and often have irregular walls.

Misinterpreting Cord Edema for Tumor or Cyst

We have operated on two very young children (ages 11 and 14 months) in which the neoplasm was associated with very extensive edema rostral and caudal to the tumor. In these cases, though the mylogram disclosed widening of most of the spinal cord, it was discovered at surgery that the edema was responsible for this appearance. We speculate that this may be related to incomplete myelinization and the immature status of the very

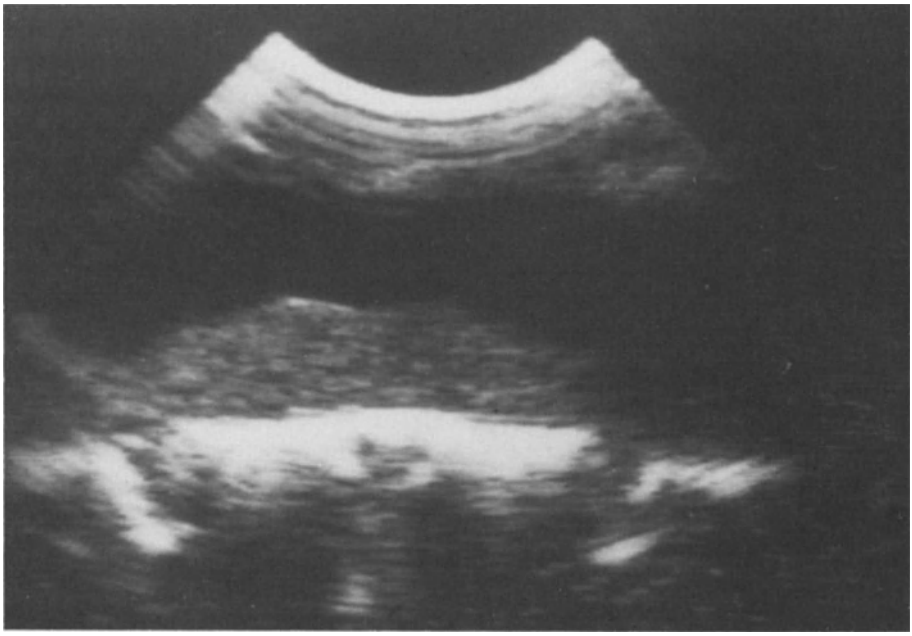


Fig. 11 A. Ultrasonogram of cystic astrocytoma. Note relationship of solid component of neoplasm to surrounding cyst

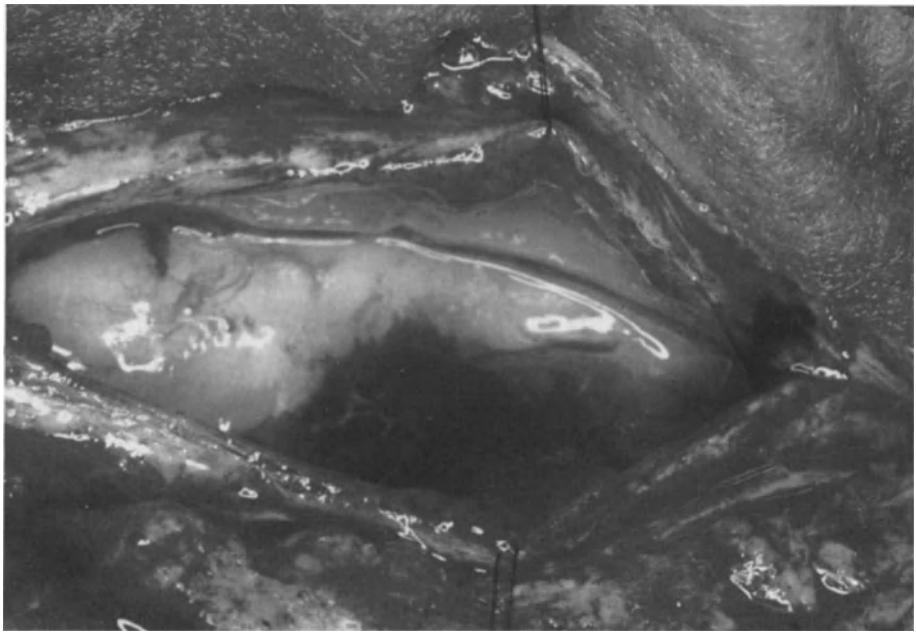


Fig. 11 B. Tumor and cyst visualized through myelotomy. Note that general appearance is very similar to cystic astrocytoma of cerebellum

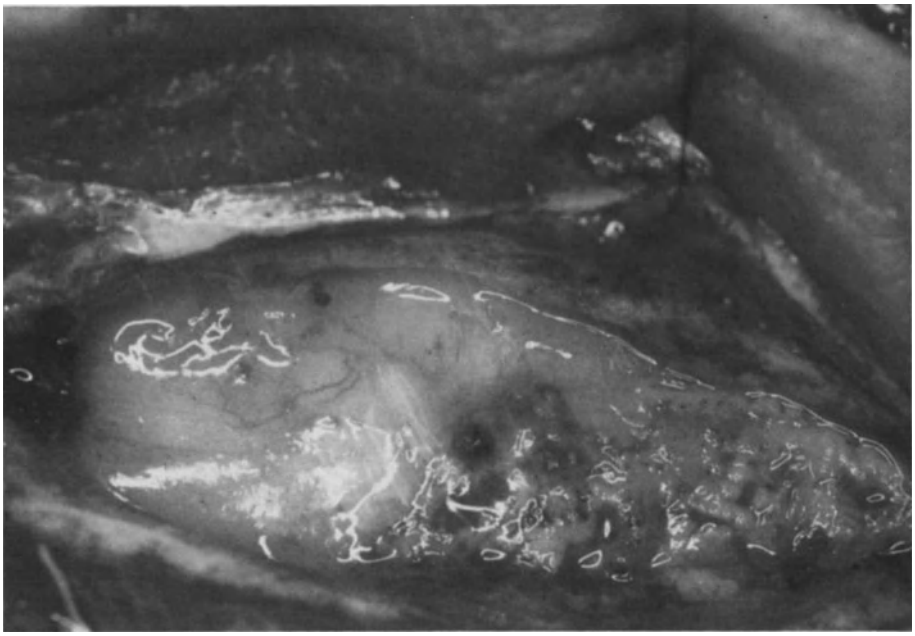


Fig. 11 C. Tumor has been removed

young child's spinal cord. It must be recognized that the ultrasound may rarely result in misinterpretation of edema for tumor, and caution must be exercized.

Anterior Subarachnoid Spinal Fluid Loculation

In six patients, there has been dramatic posterior extrusion of the spinal cord through the dural opening at some time during the tumor dissection. This was associated with a deterioration of brainstem evoked potentials, and we initially misinterpreted this as acute spinal cord swelling. We now recognize that it is not uncommon for spinal fluid to become loculated anterior to the spinal cord and result in its posterior displacement. It is effectively dealt with by retraction of the lateral margin of the spinal cord and puncturing the cyst. It has been a consistent finding that this intraoperative problem has only occurred in patients that have had previous surgery, and in which there are dense adhesions between the lateral spinal cord and the dural tube. It seems that the anterior subarachnoid space does not communicate freely with the posterior subarachnoid space, and this may be responsible for the hydrodynamics which promote this occurrence[16].

One patient in this series had a huge tumor in the lower thoracic cord, and though immediately neurologically stable, became paraplegic one week after surgery. The CT scan disclosed that the spinal cord had extruded from the spinal canal and, at surgery, there was huge anterior loculation of spinal

fluid which had displaced the spinal cord posteriorly through the dural decompression, and the cord had become incarcerated on the rostral and caudal dura with secondary infarction (Figs. 12 A and B). Retrospectively, it was apparent that the dura had been excised at the time of the first operation, and it had not been closed at the time of the tumor resection. This permitted the trapped anterior subarachnoid compartment to displace the cord out of the spinal canal with subsequent infarction. As the result of this experience, we do not leave the dura open under any circumstances, and if it has been previously excised, a suitable dural substitute is used.

Postoperative Neurological Morbidity Related to Segmental Location of Neoplasm

Postoperative neurological morbidity may be correlated with segments of spinal cord that are involved with neoplasm. Whereas an extensive dissection may be carried out with little risk in those segments of spinal cord that are largely white matter, this does not seem to be the case in the lowest segments where grey matter is most abundant.

Dissections within the cervical spinal cord are associated with little morbidity though it is not uncommon to note some anterior horn cell dysfunction as manifested by atrophy of one or more muscle groups of an upper extremity. When this has occurred, it has been permanent.

Dissections extending from the junction of the cervical and thoracic regions to T 9 are associated with remarkably little neurological morbidity.

Tumors that are located in the lower spinal cord segments from T 9 to T 12 have the greatest incidence of significant postoperative neurological morbidity. This is because neoplasms in the conus or just above it compress or infiltrate grey matter, while tumors which occur in more rostral regions of the spinal cord compress white matter tracts and, therefore, the resultant signs and symptoms are based on pathological anatomy and pathophysiology which is specific to the segmental location of the neoplasm.

Whereas an extensive intramedullary dissection may be carried out with relative impunity in white matter in the rostral cord, this is not the case in the grey matter in the region of the conus, and the surgeon must be aware of these technical limitations.

Significant preoperative sphincteric dysfunction suggests that the tumor is extending into the conus as this rarely occurs if the tumor is rostral to T 12. Conversely, the absence of bowel and bladder problems suggests that the tumor does not extend into the conus, though it may be asymptomatically expanded by a caudal cyst.

If there is not preoperative bowel and bladder dysfunction, it will occur postoperatively if the conus is disrupted. It is, therefore, essential that the myelotomy not be extended over the conus as this will invariably result in sphincter dysfunction which may be permanent.

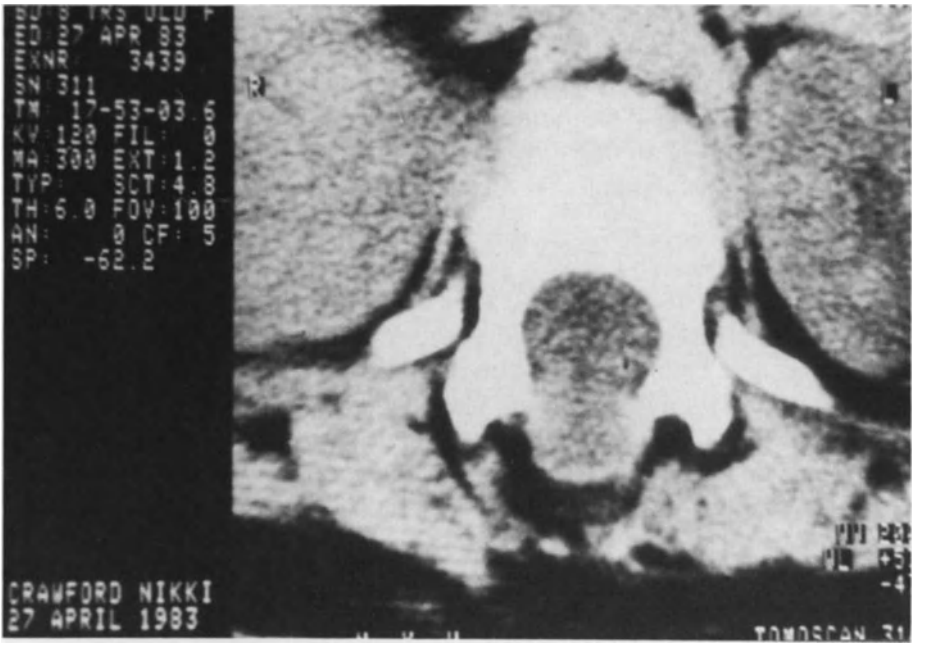


Fig. 12 A. CAT scan discloses that anterior loculation of spinal fluid has caused the extrusion of the spinal cord through the dural defect and the laminectomy

Fig. 12 B. At surgery the spinal cord was discovered to have extruded through the laminectomy. It was massively edematous and obviously infarcted

Intraoperative ultrasound is invaluable as it clearly discloses the location of the conus which may not be obvious to the surgeon as a result of distortion and rotation, as well as superimposed neural elements (Fig. 13).

It is important that the patient be advised that at least a temporary increase in neurological dysfunction is to be expected with surgery in this area, and we would assume that the long-term or permanent morbidity will also be significant.

Wound Closure

Patients that have been previously radiated are at high risk for wound dehiscence and spinal fluid fistula. In the first 14 previously radiated patients operated on in this series, nine had problems with wound-healing, and five developed meningitis. Since that experience, we have utilized plastic surgical expertise, and muscle transposition from areas outside of the radiation fields. Though this is time-consuming, and the dissection extensive, it has eliminated serious complications referable to wound healing, and we would view this as indispensable to procedures being carried out under these circumstances.

Hydrocephalus

Twelve patients developed hydrocephalus, and it was occasionally fulminating in its presentation[16]. In each of these cases, the tumor extended into the cervical cord, and we noted that there was obvious thickening of the leptomeninges overlying the cervicomedullary junction. It seems likely that this caused obstruction of the outlets of the fourth ventricle.

Pseudotumor

All patients in this series were pretreated with large doses of corticosteroids (Prednisone, Medrol, Solu Medrol 15 mg/kg). Treatment was occasionally continued 2 to 3 weeks following surgery if there was deterioration of pre-operative neurological function.

Three patients subsequently developed classical pseudotumor cerebri as the steroids were reduced. In these cases it was necessary to re-institute smaller doses and withdraw more gradually.

Two patients developed a syndrome which seems to be the equivalent of pseudotumor of the spinal cord. Increased neurological dysfunction occurred weeks after the surgery as the steroids were discontinued. In these situations it was necessary to re-institute corticosteroids and withdraw them even more gradually. Ultimately, in these cases, the steroids were discontinued and there is no correlation at this time with the length of time required to discontinue the steroids and long-term neurological dysfunction, or tumor recurrence.

Tumor Recurrence

Four patients with Grade I-II astrocytomas suffered a recurrent tumor 12 months, 18 months, 24 months, and 36 months following a primary gross total excision. In three of these cases the microscopic pathology was unchanged and there was a satisfactory neurological recovery following the second surgical procedure. In one patient the tumor extended rostrally and caudally (despite radiation therapy) and caused quadriplegia and subsequent death.

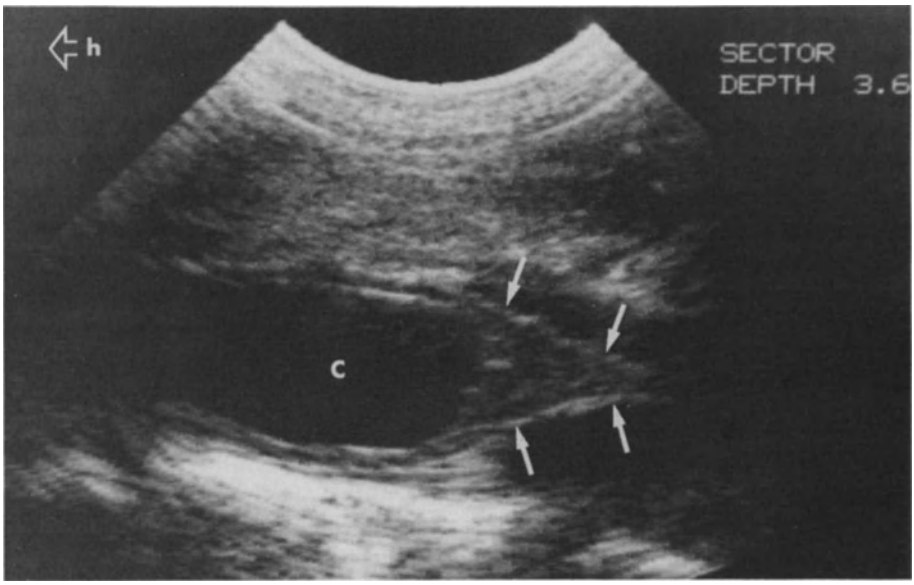


Fig. 13. Transdural ultrasonography discloses the caudal cyst (*C*) and the conus (arrows)

None of these patients received radiation therapy following the first surgical procedure but all were treated after the last operation. It is too early to suggest the future prognosis in this very small group of patients. Clearly it will be essential to analyze the incidence of recurrent tumor and relate it to the grade of the neoplasm and radiation therapy in an attempt to further define the biology of the neoplasm as well as optimal treatment.

Discussion

There are a number of important observations that are clearly relevant in terms of understanding the biology of this group of neoplasms, as well as recommending proper surgical management. It has been a consistent observation that in the presence of holocord expansion, the solid compo-

nent of the astrocytoma is often not as extensive as myelography alone suggests and, indeed, the actual location of the neoplasm may be in those segments of the spinal cord that correspond to neurological dysfunction. The lack of significant neurological dysfunction relating to spinal segments that were distended with fluid is probably directly related to the anatomical location of the cyst within the center of the cord as compared to the solid component of the neoplasm which was relatively diffuse.

The presence of cysts which were similar in appearance to those associated with the cystic astrocytoma of the cerebellum suggests that the neoplasms are congenital tumors that have their inception sometime during gestation. The fluid produced by the tumor extends up and down the spinal cord in the region of least resistance, that is, the central canal.

One might also speculate that in some cases the classical symptoms of syringomyelia may, in fact, be a late manifestation of such a cyst in which the tumor has either involuted or is not anatomically obvious. Perhaps the centrally located cyst may gradually expand over many years and compress the surrounding cord. In this regard, it is significant that a few patients with holocord widening had exceedingly small neoplasms, between 1.5 and 3 cm, and were mistakenly diagnosed as syringomyelia or hydromyelia[18, 19]. Our experience would suggest that the presence of xanthochromic cyst fluid is pathognemonic of an associated neoplasm, while clear fluid is diagnostic of hydromyelia.

It is our perspective that the presence of a widened spinal cord from the cervicomedullary junction to the conus, which is associated with a relatively slowly evolving neurological deficit, is indicative of a very slowly growing and perhaps even hamartomatous-type of lesion which has a good long-term prognosis and should be treated aggressively.

Nevertheless, it must be emphasized that despite a "gross" total tumor excision, it would be naive to assume that residual tumor fragments were not commonly left *in situ*. We have hypothesized that these remaining fragments may remain dormant, or involute, in a similar way to what has been noted to occur in many astrocytomas of the cerebellum[4, 14]. However, whether or not this is reality or "wish-fulfillment" will only be known many years from now following long-term follow-up and retrospective analysis.

In most cases of holocord tumor, the initial complaint was a weak arm, or a mildly weak leg, and associated pain somewhere along the spinal axis. The signs and symptoms were consistently relatively minor when compared to the apparently diffuse nature of the pathological process. It is perfectly understandable why neurosurgeons faced with this clinical dilemma have been most concerned about inflicting a greater neurological deficit as a result of extensive dissection within a rather well-functioning spinal cord. This rationale has been used for a temporizing surgical approach consisting of a limited laminectomy and biopsy, and relying on radiation therapy to

control tumor growth. Unfortunately, the natural history of these tumors, with radiation therapy, is slow deterioration and eventual severe neurological disability or death.

The outcome following radical resection of these tumors was directly related to the pre-operative neurological status. Although a transient increase in weakness or sensory loss was commonly present in the immediate postoperative period, only one patient had a significant permanent increase in neurological deficit following operation. Patients with paraparesis or quadriparesis, who were ambulatory before surgery had neurological improvement over several weeks. The group with severe deficits preoperatively, rarely made any significant improvement although their downhill course abated.

There is no evidence that radiation will cure benign astrocytomas of the spinal cord, and there is abundant evidence that it has a deleterious effect on the immature developing nervous system. Spinal cord astrocytomas should be recognized as potentially excisable lesions, with radiation therapy reserved for possible adjunctive use if there is a recurrence. At that time, it might be employed following a second radical surgical resection.

Intramedullary spinal cord astrocytomas are occasionally highly malignant. In these cases, the clinical course is rapid and radical surgery has not significantly improved the dismal prognosis. Unlike cranial glioblastomas, those that occured in tha spinal cord disseminated over the entire neuraxis within six months of primary surgery. For this reason, we now routinely employ total neuraxis radiation in the presence of a malignant tumor.

Children who have undergone extensive laminectomy and, in addition, have denervation of the paravertebral muscles from tumor infiltration of anterior horn cells as well as operative muscle retraction, are at risk for developing severe spinal deformities as they pass through periods of rapid growth. Close collaboration with a pediatric orthopedic surgeon experienced with kyphoscoliosis is essential in following these patients.

Summary

The author has carried out gross total excision of an intramedullary spinal cord astrocytoma in 120 consecutive patients. This experience has led to the following conclusions:

1. Holocord widening occurs in 60% of cases, and is diagnostic of a cystic astrocytoma.

2. Despite the absence of a surgical plane of dissection, these neoplasms may be removed from "inside out" until a glia-tumor interface is recognized.

3. Radical tumor excision is compatible with partial or total recovery of neurological function.

4. The success of surgery is directly related to the preoperative neurological status of the patient. Paralysis or near paralysis was never improved, while mild to moderate preoperative neurological dysfunction often recovered.

5. While this experience has established the efficacy of radical surgery, there is no information to suggest the duration of remission, or the likelihood of permanent cure. This will only become known at the time of retrospective analysis many years from now.

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Druck: Adolf Holzhausens Nfg., Universitätsbuchdrucker

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