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# A Reappraisal of the Ascending Systems in Man, with Emphasis on the Medial Lemniscus

**With 24 Figures and 1 Table**

Springer

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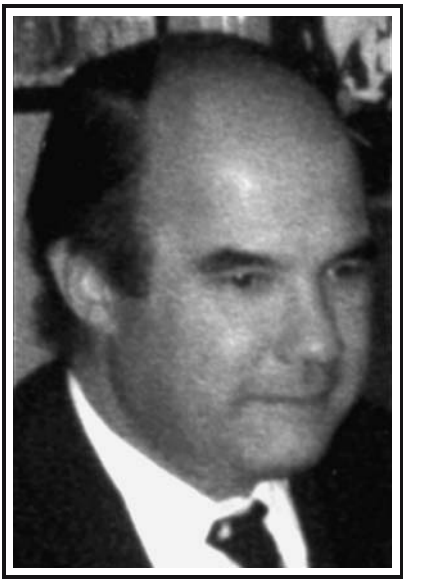

**Jaap H.R. Schoen**
**(20.10.1930 – 29.06.1981)**

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# Abbreviations

(The abbreviations apply to all figures.)

| | |
|---|---|
| bc | Brachium conjunctivum |
| bci | Brachium colliculus inf. |
| bcs | Brachium colliculus sup. |
| C | Nucl. interstitialis Cajal |
| CE | Nucl. cuneatus ext. |
| CGM | Corpus geniculatum med. |
| Ci | Capsula interna |
| CM | Center median |
| CND | Nucl. centralis griseus dors. |
| CNV | Nucl. centralis griseus ventr. |
| CNS | Nucl. centralis sup. |
| CP | Commissura post. |
| cp | Pedunculus cerebri |
| cr | Corpus restiforme |
| Ctt | Tractus tegmentus centralis |
| CU | Nucl. cuneatus int. |
| Cun | Nucl. cuneiformis |
| dbe | Decussatio bc |
| dp | Decussatio pyramidalis |
| drV | Ramus descendens NV |
| dsc | Tractus dorsospinocerebellaris |
| DV | Nucl. vestibularis descendens |
| DX | Nucl. dorsalis vagus |
| fa | Fasciculus anterior |
| fatl | Fasciculus antero-lateralis |
| FL | Fasciculus lat. |
| flm | Nucl. fasciculus longitudinalis med. |
| fp | Fasciculus posterior |
| frt | Fasciculus reticulo-tectalis spinalis |
| GC | Griseum centrale mesencephali |
| Gc | Nucl. reticularis gigantocellularis |

| | |
|---|---|
| GR(N) | Nucl. gracilis |
| g VII | Genu nucl. facialis |
| ia | Fibrae arcuatae internae |
| IC | Colliculus inf. |
| Icol | Nucl. intercolliculare |
| ll | Lemniscus laterale |
| ml | Lemniscus mediale |
| mlf | Fasciculus longitudinalis med. |
| MV | Ramus mesencephalicus NV |
| MV | Nucl. vestibularis med. |
| N | Substantia nigra |
| nc | Tractus cuneocerebellaris |
| NIII | Nucl. occulomotorius |
| NVI | Nucl. abducens |
| NVII | Nucl. facialis |
| NXII | Nucl. hypoglossus |
| Oc | Tractus olivocerebellaris |
| p | Tractus pyramidalis |
| P | Promontorium |
| Pc | Nucl. pontocaudalis |
| pf | Fasciculus praedorsalis |
| pl | Area paralemniscale |
| Pmd(s) | Promontorium, marginalis disseminatus |
| PR | Nucl. praepositus hypoglossi |
| Pul | Pulvinar thalami |
| PV | Nucl. princeps NV |
| R | Nucl. ruber |
| Rp | Repagulum |
| S | Tractus solitarius |
| SC | Colliculus sup. |
| SO | Nucl. oliva sup. |
| Ssp | Substantia (nucl.) supraspinalis |
| Sth | Tractus spinothalamicus |
| Tppc | Nucl. tegmenti pedunculo pontinus pars compacta |
| Vsc | Tractus spinocerebellaris ventralis |
| vma | Velum medullare ant. |
| VPL | Nucl. ventralis posterior lat. |
| VPM | Nucl. ventralis posterior med. |
| II | Tractus opticus |

# Preface

This volume of Advances in Anatomy, Embryology and Cell Biology is based on material assembled by Dr. Jaap H.R. Schoen. Jaap Schoen published his results only partially himself (see Schoen's references in the preface of Usunoff et al. 1997). After his sudden death, due to a diving accident, Jan Voogd and Hans Feirabend of our Neuroregulation group encompassed his cerebellar results in the chapter on the cerebellum and precerebellar nuclei in Paxinos' The Human Nervous System (Voogd et al. 1990), while Kamen Usunoff and myself grouped Schoen's trigeminal results and presented them together with the background of the outcome of recent animal trigeminal experiments in Advances in Anatomy, Embryology and Cell Biology 136 (Usunoff et al. 1997).

Jaap Schoen described his series thoroughly and worked them out in serial drawings of the most important sections. Numerous scientists have consulted this material. Together with the abstracts of the Dutch Anatomical Society and half-finished descriptions of the different parts of the central nervous system for his thesis, the pattern of his results emerged.

A large series of results are available that still have to be published. Since Jaap Schoen "was one of the few neuroanatomists to apply the Nauta method to human material" (Voogd et al. 1990), his results are highly important for human neuroanatomy. This monograph contains part of his material. Some repetition, especially of figures, is inevitably due to the dispersed publication of Schoen's results in various books, monographs, articles, and abstracts (see Usunoff et al. 1997).

I acknowledge Jan Voogd for the correction of the part on spinal ascending systems of this monograph and Kamen Usunoff for correcting the whole manuscript. Madame Tineke Schoen-Obink is thanked for permission to use the results of her late husband's work.

January 2005 Enrico Marani

# 1 Introduction

In cats it was demonstrated that after reimplantation of the ventral rootlets (Hoffmann et al. 1993,1996), or after reimplantation of an autologous transplant between spinal cord and ruptured nerve (Holtzer 2003), regeneration of the motoneurons in the cervical spinal cord occurs. To reimplant rootlets or transplants into the spinal cord, a small longitudinal incision has to be made in the motor pathway area, whereby the rootlets leave the spinal cord (Hoffmann 1993; Holtzer 2003). Gaining insight into the consequences of such a longitudinal wound in the human spinal cord is necessary before reimplantation of avulsed rootlets or an autologous transplant can be performed in man (Thomeer et al. 2002). A reexamination of the ascending systems in the human anterolateral funiculus, therefore, is one of the prerequisites to be carried out before adapting animal transplantation or reimplantation operations to man.

A second, more technical, approach in the restoration of damage in the human central nervous system is Functional Electrical Stimulation (FES). Cortex and nucleus subthalamicus stimulation in Parkinson's disease or spinal cord stimulation in chronic, intractable pain of neurogenic origin are examples in which FES is now applied in man. Renewed interest in the involved ascending (and of course descending) systems is noted here too. For dorso- and dorsolateral columns in man, see Feirabend et al. (2002); for the subthalamic nucleus see Hamani et al. (2003); and see Manola et al. (2005) and Peyron et al. (2000) for human cortical stimulation. In addition, cranial nerve stimulation is now applied in patients with epileptic seizures. Vagus nerve stimulation is an accepted therapy in patients that are refractory to antiepileptic medications (Schachter 2001). This cranial nerve stimulation brought renewed interest in the human nucleus and tractus solitarius and its thalamic and brain stem connections; notice has been especially taken of the locus ceruleus (Theodore and Fisher 2004)

Both approaches for the restoration of nervous system function are in need of further elucidation of the *human* connections in the central nervous system, in general, and especially in the spinal cord.

A large body of literature exists on ascending spinal systems (for review see Schoenen and Grant 1990). However, the number of papers concerning these systems in the human nervous system is limited to only a few (Mehler 1962,1966; Bowsher 1957, 1962; Schoen 1964, 1969; Smith 1957; Smith and Deacon 1981; Voogd et al. 1990; Usunoff et al. 1997), and to these in which silver impregnation methods for degenerating axons were used: (Nauta Gygax 1951; Nauta and Ebbesson 1970; and for a review of the application of the Nauta technique in human brain see Mesulam 1981; Miklossy et al. 1991). Despite the frequent occurrence of artifacts in immersion-fixed human material, the Nauta method remains the method of choice for the study of fiber connections in the human brain. In this paper a combination of the Nauta and the Häggqvist stains (Sie Pek Giok 1956; Verhaart and Sie Pek Giok 1958) were used. For cases with chronic lesions of the spinal cord only the

Häggqvist method allows the study of the topographical relations of the ascending spinal tracts to other, non-degenerated components of the ventrolateral funiculus, the dorsal columns, and the restiform body. Moreover, the characteristic fiber pattern of a certain tract in normal Häggqvist sections may sometimes give an indication of its position amidst other systems (for instance olivocerebellar fibers against other components of the restiform body; see Voogd et al. 1990) or the localization of the fiber systems within the white matter of the medulla oblongata and the cervical cord in man (Sie Pek Giok 1956; Van Beusekom 1955). With the Nauta method, the localization and termination of the spinobulbar, spinotectal, and spinothalamic fibers can be determined in more detail. Special attention has been devoted to the spinal projections to the small cell groups in and around the restiform body (described by Braak 1970, 1971), the spinal-thalamic projections, and especially to the medial lemniscus.

## 2
## Material and Methods

### 2.1
### Häggqvist and Nauta-Gygax Stain

The material used for this study is summarized in Table 1 (lesions, gender, age, and stains) and the Appendix (description of the pathological cases). Usually the brain and spinal cord were fixed by immersion in 10% formalin within 18 h after death and directly after autopsy. After several days or weeks the brain stems were dissected out. The tissue blocks and selected spinal cord segments were post-fixed for a variable period in Baker's fixative (prior to Häggqvist staining, 6 weeks to 2 months) or in neutral formalin (for Nauta staining, 2 weeks to 1 month). For the Häggqvist method (Häggqvist 1936) the blocks were mordanted in several changes of a 10% solution of potassium dichromate, embedded in paraffin, and transversely sectioned at 6 μm. After deparaffination the sections were immersed in 10% phosphomolybdic acid for 30 min, stained in Mann's solution (methyl blue, 0.26%; eosin, 0.06% ethanol solution in water), differentiated in ethanol 70%, 96%, and 100% and cover-slipped (Sie Pek Giok 1956; Verhaart and Sie Pek Giok 1958). For the Nauta method 25-μm sections were cut on a Jung freezing microtome and stored in 10% neutral formalin for 1–7 days. The silver impregnation in the protocols of Nauta and Gygax (1951) and Nauta and Ebbesson (1970) were used with Laidlaw's silver carbonate solution (for a discussion of the modifications of the Nauta method, see Voogd and Feirabend 1981).

### 2.2
### Häggqvist and Klüver-Barrera Staining

Alternate sections were mordanted for 3 days in 5% potassium dichromate at room temperature. After thorough rinsing in tap water the sections were treated with

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**Table 1** Summary of the pathological cases, age, gender, lesion(s), and the staining methods applied

| Number | Sex | Age (years) | Lesion | Left | Right | Survival | Staining methods | Remarks |
|---|---|---|---|---|---|---|---|---|
| H3382 | M | 50 | Lumbar spinal cord | Upper lumbar | Upper lumbar | 3 Weeks | Hag | Lesion medial lemniscus |
| H3655 | M | 66 | Transverse | C1 | | 6 Months | Hag | Mes- and diencephalon not available |
| H3977 | M | 46 | Medial lemniscus | | | 3.5 Months | Hag | Lues, softened pons and small spinal cord |
| H4477 | M | 17 | Cordotomy | C4/5 | C4/5 | 4 Months | Hag | Lesion extends to C2 |
| H4685 | F | 60 | Cordotomy | T2/T3 | T2/T3 | 6 Weeks | Hag | |
| H5017 | M | 58 | Brain stem, cerebellum | Tegmentum, pontine and midbrain | Tegmentum, pontine | 4 Months | Hag + Nissl | Lesion N.V, partially, lesion medial lemniscus |
| H5151 | M | 51 | Pons, cerebellum, cortex | | All lesions | 8 Days | Nau + Hag | Softening right cerebellar hemisphere and right occipital lobe |
| H5379 | M | 32 | Transverse | T10 | | 10 Months | Hag | |
| H5412 | M | 37 | Cordotomy | T2 and T4 | T3 | 4 Weeks | Nau + Hag | Infarcts in dorsal columns at T2 |
| H5517 | M | 65 | Wallenberg syndrome | | All lesions | 9 Months | Hag | Recent softening pontine tegmentum, old large vascular forebrain lesion |
| H5554 | M | 54 | Dorsal rhizotomy | C1/C2 | | 3 Weeks | Nau + Hag | Rami dorsalis C1 and C2, tractotomy N.V |
| | | | Tractotomy NV | Tract NV | | | Klu + Bodian | |
| H5579 | M | ? | Wallenberg syndrome | Cerebellar peduncle | Pontine tegmentum | 6 Weeks | Nau + Hag + Klu | |
| H5631 | M | 60 | Cordotomy | T2 | T2 | 4 Weeks | Nau + Hag | Recent compression thoracic cord |

**Table 1** (continued)

| Number | Sex | Age (years) | Lesion | Left | Right | Survival | Staining methods | Remarks |
|---|---|---|---|---|---|---|---|---|
| H5671 | F | 56 | Cerebrovascular cortical | | | 6 Weeks | Nau + Hag | Softening temporal, frontal, precentral insula, lentiform nucleus, and corona |
| H5747 | M | 67 | Temporal lobe, brainstem (small) | Temporal lobe | Medial lemniscus | 6 Weeks | Nau + Hag + Klu | |
| H5800 | M | 69 | Transverse | T7 | | 1 year | Hag | |
| H6688 | F | 65 | Cordotomy | T4 | T4 | 6 Years | Hag | Preoperative lesions, lumbar cord |
| H6995 | M | ? | Wallenberg syndrome | | | 1 Month | Hag | |
| H7085 | F | 55 | Cordotomy | T5 | | 3 Weeks | Nau + Hag | |
| H7228 | M | 68 | Rhizotomy | C6–C8/T1 | | 3 Weeks | Klu | Only demyelinization studied |
| H7251 | M | 42 | Arterial occlusion, right | | Cortex | 2 Years | Hag | Pyramidal atrophy |
| H7980 | M | 60 | Olivopontocerebellar atrophy | | | 7 Years | Hag | |

Hag, Häggqvist staining; Nau, Nauta Gygax degeneration technique; Klu, Klüver-Barrera staining. Description of these stainings, also of Bodian and Nissl, can be found in Voogd and Feirabend (1981)

phosphomolybdic acid for 30 min and stained in Mann's solution. Finally the sections were differentiated in ethanol 70% and 96% and mounted from phenol-xylene on glass slides, dried with tissue paper, and cover-slipped. Additional sections were stained with the Nissl or Klüver-Barrera stain. In most cases some hematoxylin-eosin sections were used to quickly determine the area of injury (Voogd and Feirabend 1981).

### 2.3 Interpretation of the Stains

In Häggqvist-stained sections, axons are colored blue and myelin light red. Cell nuclei, cytoplasm, dendrites, and glia are stained in different shades of blue. In degenerated fibers the axon has disintegrated or disappeared, and the myelin stains a vivid red, swells, and becomes vacuolated. Häggqvist's stain was originally developed by Alzheimer as a glial stain (see Voogd and Feirabend 1981). The gliosis and the compound granular cells that predominate in chronic degeneration, therefore, can be studied at advantage. In the silver-impregnated sections, increased argyrophilia, fragmentation, and vacuolization are considered as signs of degeneration of the axon. The presence of a meshwork of fine, degenerated axons in a nucleus is taken as a sign of termination and called "preterminal" to distinguish it from bouton degeneration, which cannot been seen. Different kinds of artifacts were frequently encountered. Dust-like precipitates, "myelin cuffs", and irregular, fusiform enlargements of apparently normal fibers generally could be distinguished from true axonal degeneration.

## 3 Spinal Ascending Systems

### 3.1 Ascending Fiber Degeneration in the Whole Spinal Cord

Ascending degeneration in the spinal cord after a cordotomy was studied in Häggqvist-stained and Nauta Gygax sections. In most cases, with exception of H7085 and H4685, ascending degeneration is present in the dorsal columns. In H5631 a unilateral, right-sided ventrolateral cordotomy at T2, is combined with bilateral ascending degeneration of the fasciculi gracilis, probably due to a more

**Fig. 1A, B** Anterolateral cordotomy T2–T4 (H5412). **A** *Stippled outline* of the Nauta degeneration through the brain stem and thalamus. **B a** *Stippled* drawing of the section involved in the localization of **b** and **c**. **b** Preterminal degeneration of the spinothalamic fibers in the nucleus VPL-thalami, medial near the CM nucleus (×170). **c** Preterminal degeneration of spinothalamic fibers in a cluster-like appearance in the latero-dorsal nucleus VPL-thalami (×170). **d** Detail taken from the left lower comer of **c** (×425)

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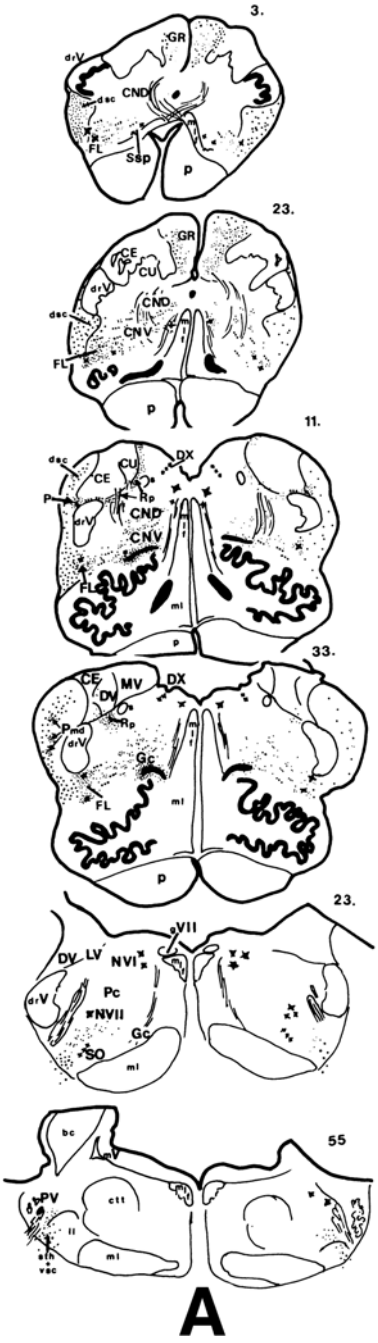
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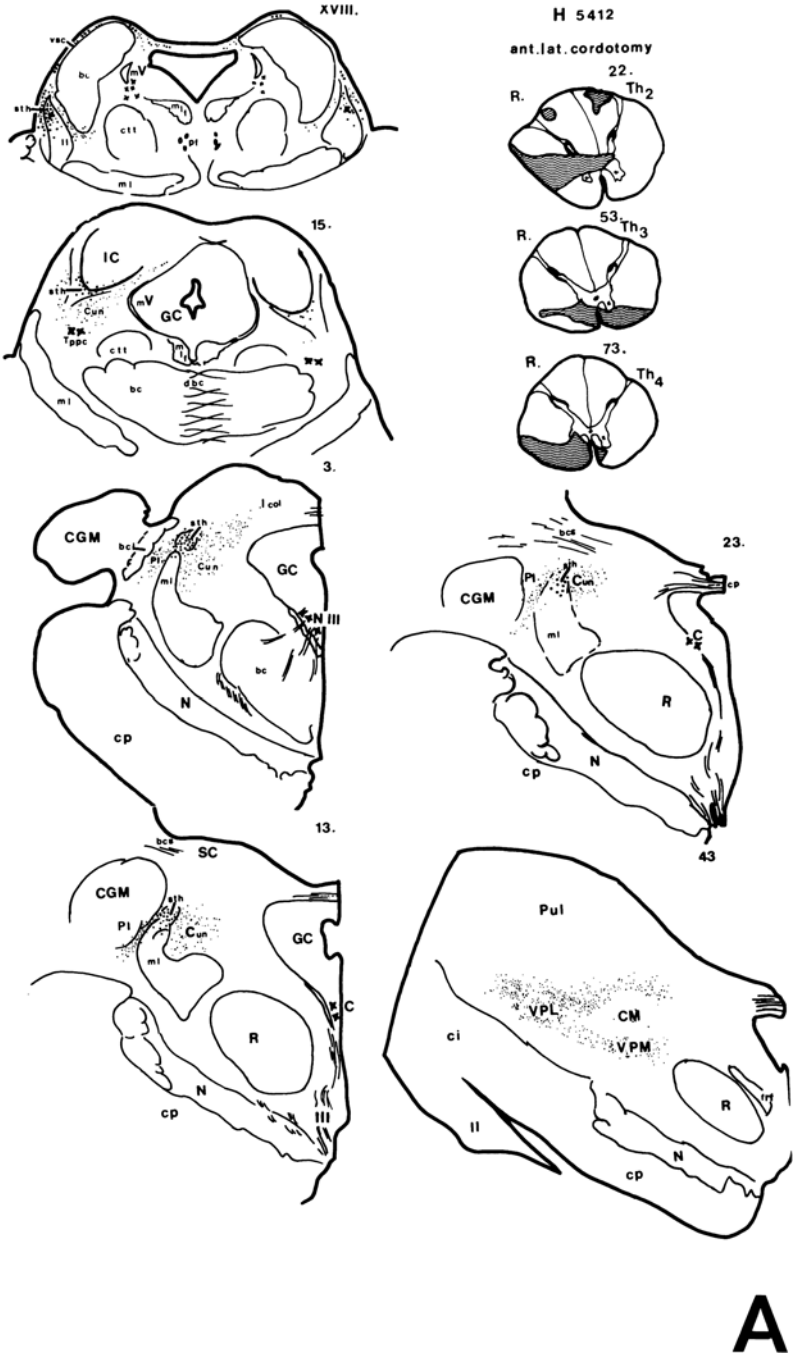
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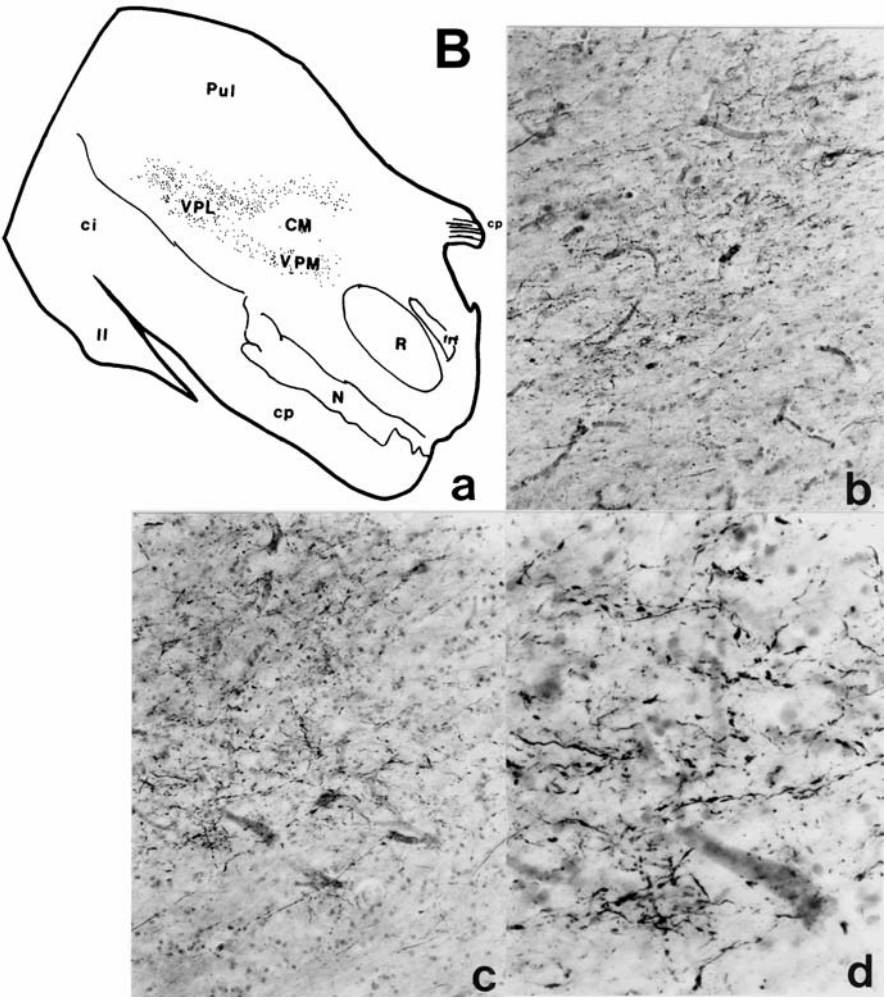
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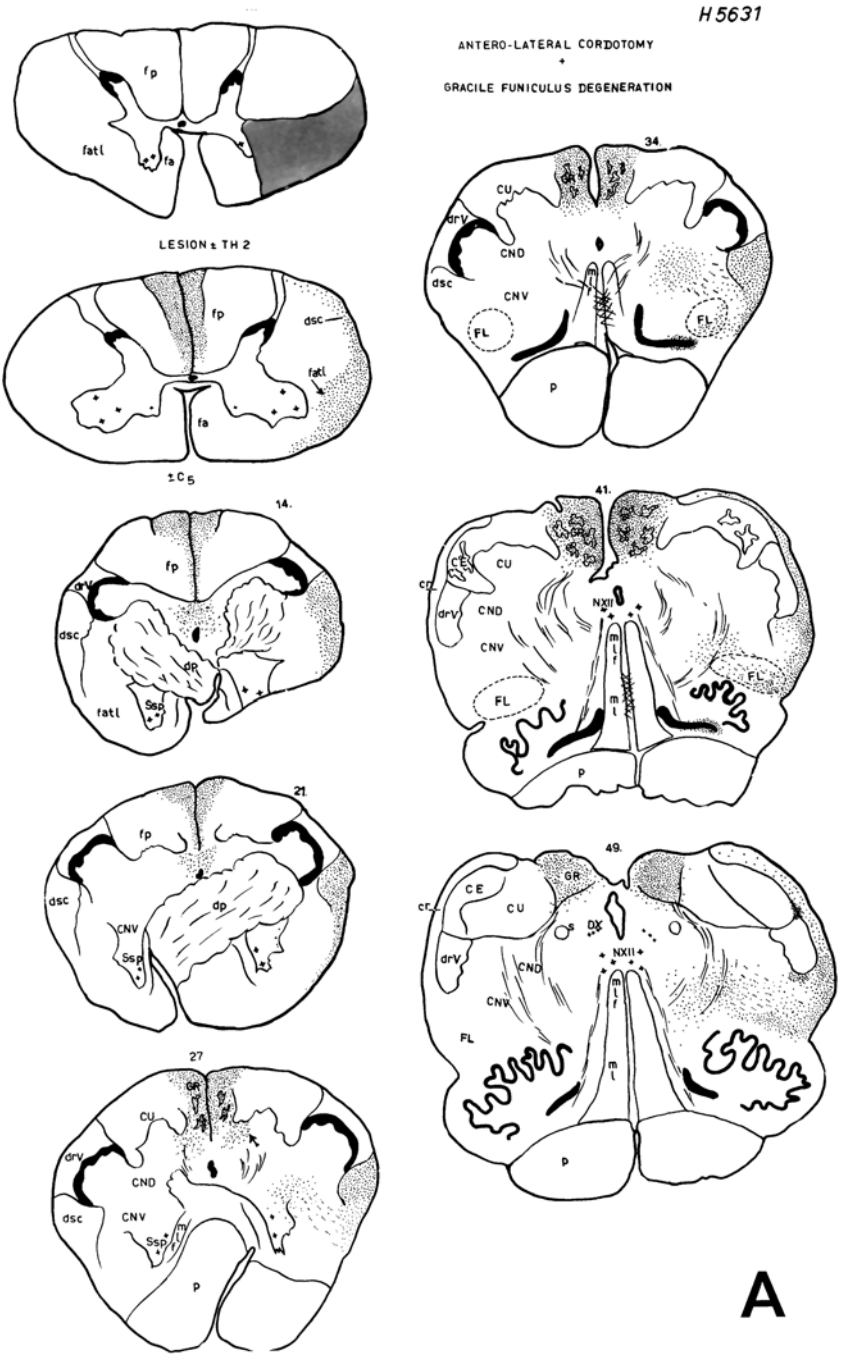
recent compression of the cord by tumor metastases in the thoracic vertebrae. In H5412 ascending degeneration is present bilaterally in the ventrolateral and dorsal funiculi. In this case softenings in the dorsal columns are responsible for the degeneration in the fasciculi gracilis.

In the caudal medulla the fibers of the posterior columns terminate in their nuclei. In Nauta-stained sections (H5412, Fig. 1A) the degeneration in the nucleus gracilis is mainly located in the nuclei found at the periphery of the clustered cells ("shell localization"; See Snow and Wilson 1991). At these levels the degeneration in the gracile fascicle extends beyond the territory of the nucleus into the adjoining part of the central gray matter, dorsal to the central canal (H5631, Fig. 2A). This extension into the central gray was confirmed in case of commissural myelotomy (see Goedhart et al. 1984). At the same level collaterals from degenerating dorsal root fibers of the upper two cervical roots (H5554) terminate in Cajal's nucleus intermedius ("group a" of Meessen and Olzsewski 1949, Olzsewski and Baxter 1954), which is located just dorsal to the pyramidal decussation in the lateral part of the central gray matter. Part of these fibers traverses the pyramidal decussation to end in the supraspinal nucleus. These fibers are also found degenerated after high cervical transverse lesions of the cord. After thoracic lesions such degeneration in the intermediate and supraspinal nuclei could not be found in the Häggqvist- or Nauta-stained material.

After thoracic-ventrolateral cordotomies degeneration was always found to be present in the dorsolateral part of the ventrolateral funiculus and in the coarse fibers of the spinocerebellar tracts. In the case of a complete transverse lesion of the thoracic cord (H5800, Fig. 3) the degeneration of the dorsal spinocerebellar tract is more complete, and degenerated fibers extend along the periphery of the ventral funiculus. At low bulbar levels these degenerated fibers of the ventral funiculus have moved into the ventrolateral funiculus and numerous coarse degenerating fibers shift dorsally from the periphery of the ventrolateral funiculus into the area of the dorsal spinocerebellar tract. A few coarse degenerated fibers, which more rostrally will join the dorsal spinocerebellar tract, are still located in the lateral pyramidal tract at C5. At cervical and low bulbar levels it is impossible, therefore, to draw a distinct border between the ventral and dorsal spinocerebellar tracts, or between the ventral tract and the deeper parts of the ventrolateral funiculus.

**Fig. 2A–D** Anterolateral cordotomy at T2 and gracile funiculus degeneration (H5631). **A** *Stippled outline* of the caudal brain stem down to the nucleus N.XII, enlarged as compared to **B** (see text). **B** *Stippled outline* of the rostral brain stem above the nucleus N.IV. **C a** *Stippled* drawing of the section through the thalamus involved in **b** and **c**. **b** One burst of preterminal degeneration in the VPL at its caudal extent (×110). **c** Enlargement of **b** (×300)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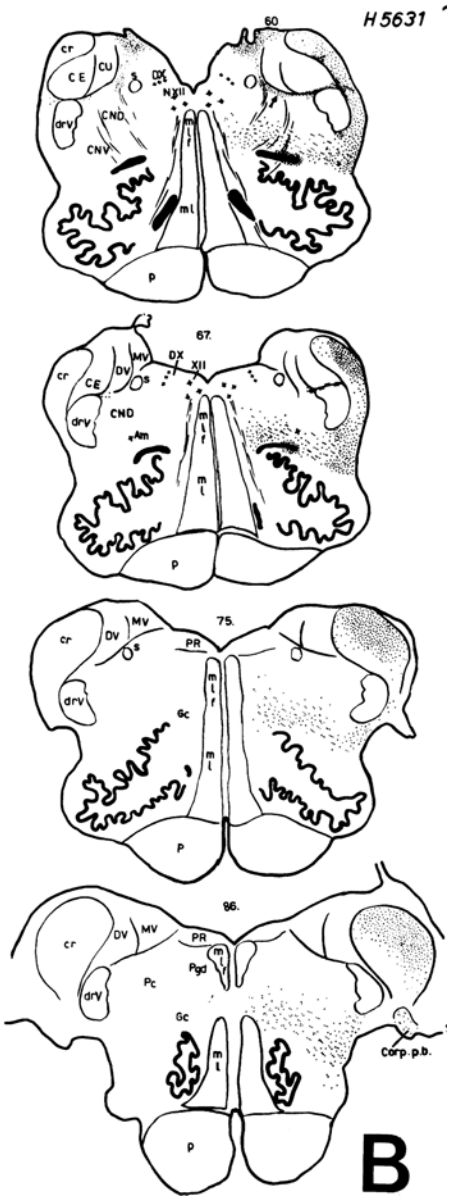

H 5631
60
cr
CE
CU
DX
NXII
drV
CND
CNV
ml
p
67.
MV
DV
XII
Am
75.
PR
Gc
86.
Pc
Pgd
Corp. p.b.
B


H5631
ANTERO-LATERAL CORDOTOMY
GRACILE FUNICULUS DEGENERATION
6.
cr
DV
MV
mlf
drV
NVII
ctb
ml
51.
bc
Pbm
Coe
mlf
ll
Poo
Cns
ml
17a.
cr
LV
gVII
mlf
drV
ctb
SO
ml
63.
lV
bc
Coe
ll
mlf
Poo
Cns
ml
24a
drV
MV
mlf
Poc
ll
ml
bc
40
Pbm
Coe
Subc.
mlf
ll
Poo
Ppl
ml
B

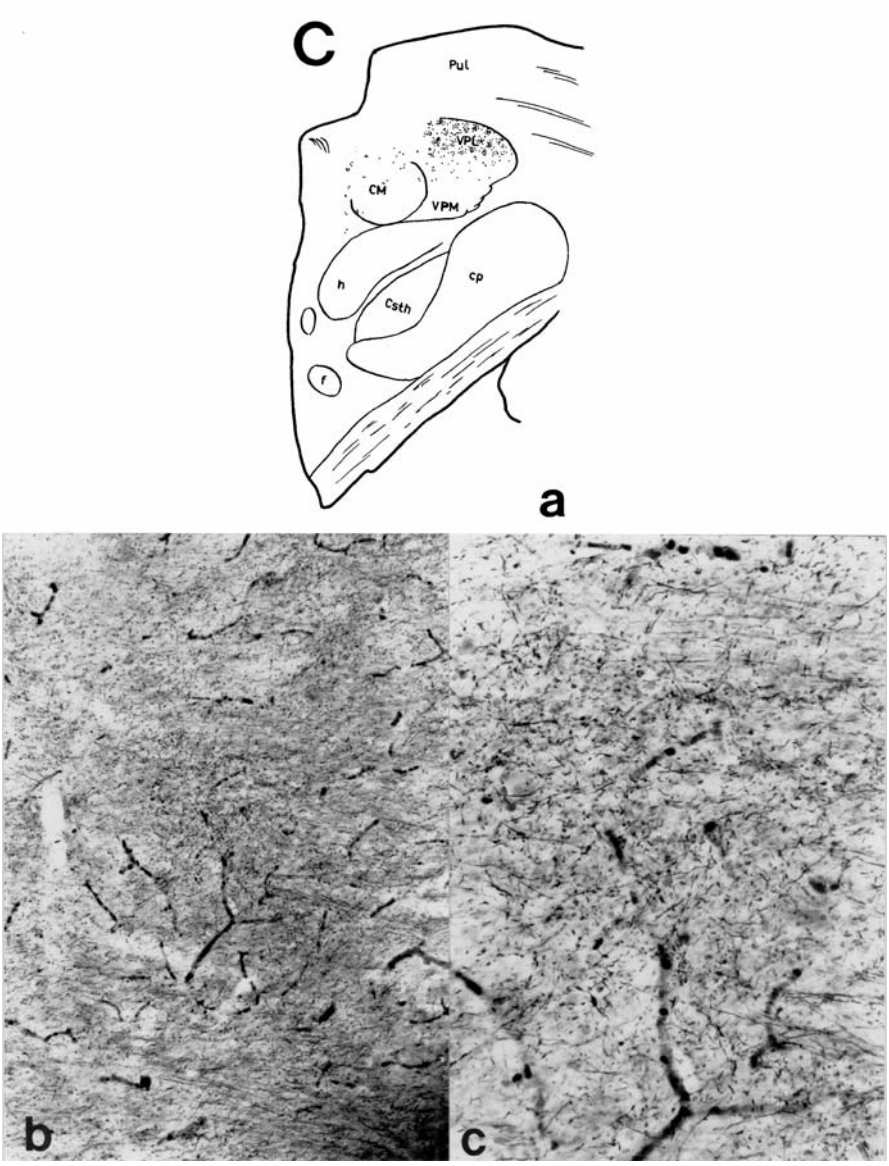
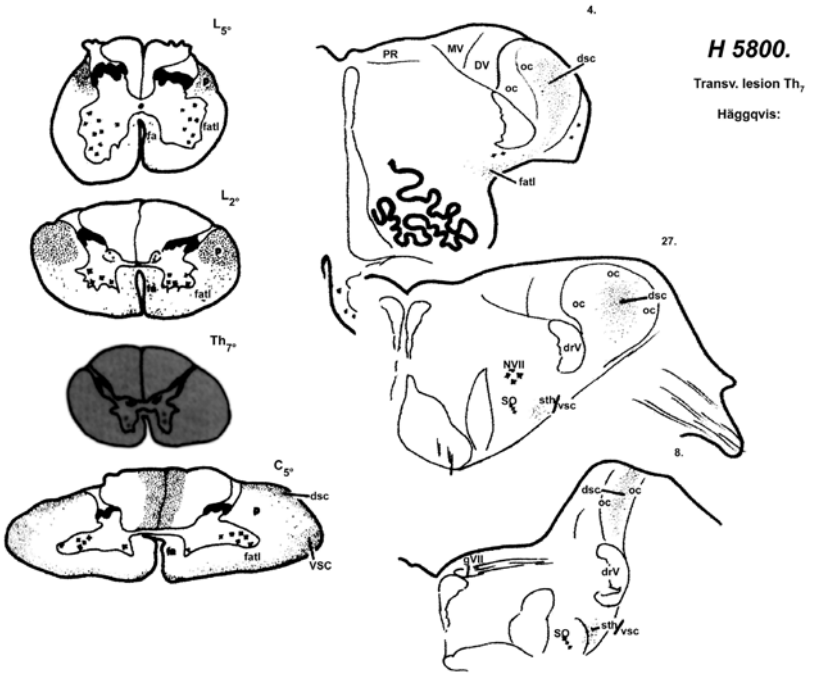
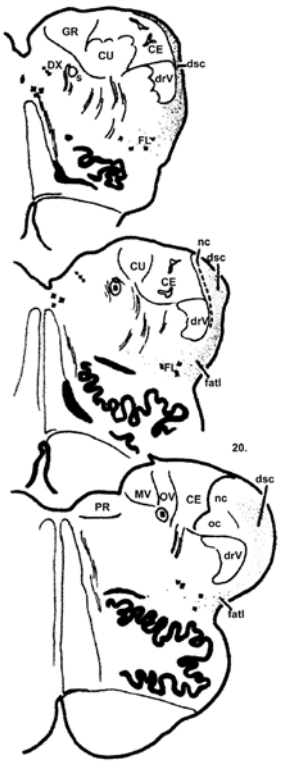



**Fig. 3A, B** *Stippled outline* of the degeneration of a transverse spinal cord lesion at T7 (H5800)


L5°
fatl
fa
L2°
fatl
Th7°
C5°
dsc
fatl
VSC
4.
PR
MV
DV
oc
oc
dsc
fatl
H 5800.
Transv. lesion Th7
Häggqvis:
27.
oc
dsc
oc
oc
drV
NVII
SO
stV
vsc
8.
dsc
oc
oc
NVII
drV
SO
stV
vsc


GR
CU
CE
dsc
DX
drV
FL
nc
dsc
CU
CE
drV
FL
fatl
20.
dsc
MV
OV
CE
nc
PR
oc
drV
fatl


H 5800.
31.
Transv. lesion Th7
Häggqvis:
IC
sth
mV
ml
ctt
SC
sth
bct
ml
mV
NIII
ctt
Pul
2.
CP
sth
CGM
ml
pc
R
N

## 3.2
## The Ventrolateral Funiculus in the Medulla Oblongata

### 3.2.1
### Normal Description

In the medulla the borders of the ventrolateral funiculus are rather vague. More dorsally the coarse fibers of the dorsal spinocerebellar tract are sharply delimited dorsally and medially. At caudal bulbar levels it is possible to divide the ventrolateral funiculus into three concentric layers. In the deepest layer, which includes the reticulated area lateral to the supraspinal nucleus, only very few spinal fibers are found, even in high cervical lesions. It contains fibers of varying diameters of the dorsal reticulospinal system that degenerate after lesions of the medial reticular formation (H5554). Ascending spinal fibers occupy the intermediate and superficial layers. The intermediate layer stands out by the prevalence of very fine fibers. In the superficial layer the coarse fibers intermingle with numerous medium-sized and small fibers. In the ventrolateral periphery of the funiculus we often detect the densely packed, uniform 1–2-μm-thick fibers of Helweg's area (containing olivocervical fibers that do not descend beyond $C_5$), the presumed caudal prolongation of olivo-cervical, reticulospinal, spinoreticular, and vestibulo-spinal fibers (see Sie Pek Giok, 1956, for discussion). At this level large numbers of corticofugal fibers detach from the lateral aspect of the pyramidal decussation and break up the homogeneity of the dorsal spinocerebellar tract, to terminate on small clusters of slender, fusiform cells located at the very periphery of the section.

Slightly more rostrally, at the level of the medial decussation of the lemniscus, the caudal pole of the lateral reticular nucleus makes its appearance in the center of the ventrolateral funiculus. At this level the nucleus is still circumscribed; more rostrally its cells become dispersed over the lateral funiculus into several subnuclei (Braak 1971).

### 3.2.2
### Results of Degeneration

In Häggqvist-stained sections the ascending degeneration is restricted to the bundles of fine fibers in the lateral part of the lateral reticular nucleus and to the coarse, medium, and fine fibers in the superficial part of the funiculus. The coarse degenerated fibers of the dorsal spinocerebellar tract constitute a compact, comma shaped bundle, immediately ventral to the spinal trigeminal tract. Some of these fibers shift dorsally, lateral to the spinal trigeminal tract, to constitute the incipient restiform body. Ventrolaterally the area of degeneration of the ventrolateral funiculus touches the amiculum of the inferior olive. Some of the coarse ventrally located spinocerebellar tract fibers still shift dorsally to join the dorsal spinocerebellar tract in its course toward the cerebellum through the restiform body.

No degenerated fibers are present in the fiber bundles in the medial portion of the lateral reticular nucleus, or in the reticular formation medial to it. In the

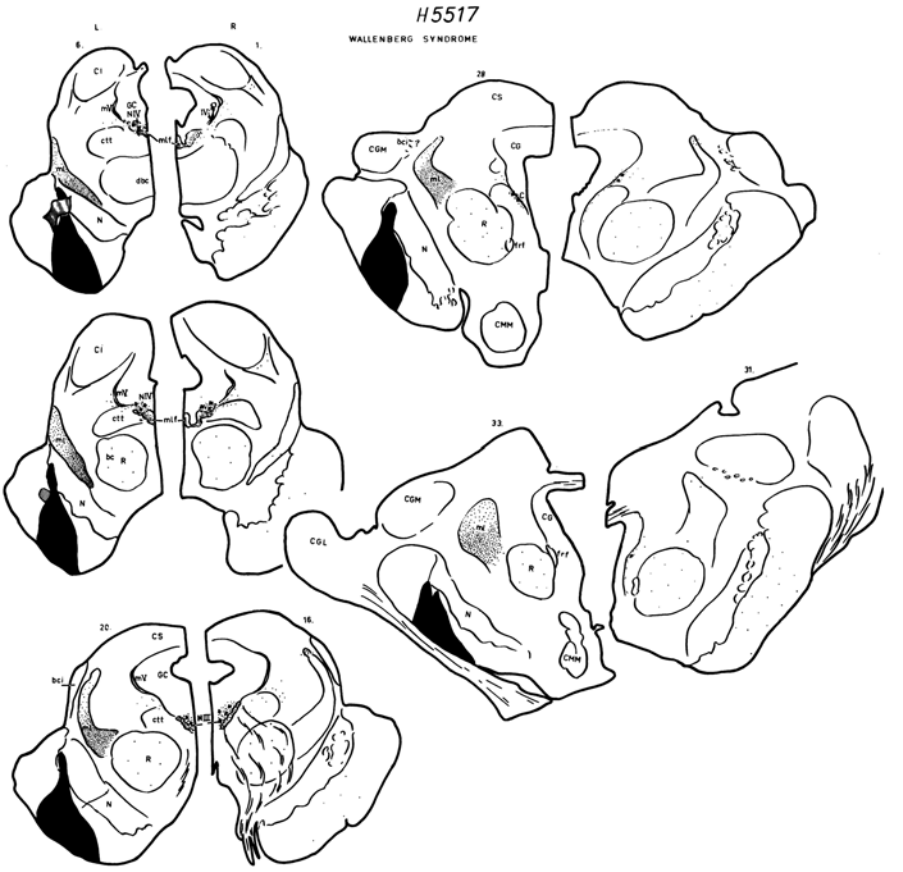
Nauta-stained sections preterminal degeneration in the reticulated neuropil of the lateral reticular nucleus is restricted to the lateral half of this nucleus, and large numbers of degenerated fibers are seen to enter the reticular formation. In cases of high cervical transverse lesions of the cord (H3655, H4477) the degeneration in the ventrolateral funiculus appears to be almost complete, practically no intact fibers being left. In the cases of a longstanding transverse lesion of the thoracic cord (H5379, H5800, Fig. 3) a number of fibers demonstrates their somatotopical arrangement in the ventrolateral funiculus.

## 3.3 The Restiform Body

The use of Häggqvist-stained sections facilitates the study of the topography of the restiform body, because the olivocerebellar component, with its characteristic uniform pattern of 2-µm-thick fibers, can be easily distinguished from the larger spinocerebellar, cuneocerebellar, and reticulocerebellar fibers (see Voogd et al. 1990). High cervical lesions (H3655, H4477) can be used to distinguish between the reticulo- and spinocerebellar fibers. Degeneration of both the spinocerebellar and the reticulocerebellar fibers, with preservation of the olivocerebellar component was present in a case of Wallenberg's syndrome (H5517, Fig. 4). The reverse is seen in a case of an olivopontocerebellar atrophy (H7980), in which both the reticulocerebellar and the olivocerebellar contingents have disappeared, and the spinocerebellar and cuneocerebellar tracts have been preserved.

– In cases H4477 and H3655, in the caudal medulla the degenerated fibers of the *dorsal spinocerebellar tract* (Fig. 5) move dorsally, immediately lateral to the spinal trigeminal tract. Slightly more rostrally, the spinocerebellar degeneration becomes separated from the spinal trigeminal tract by normal *reticulocerebellar fibers*. These fibers can first be noted in the rostral half of the lateral reticular nucleus. At this site they are joined by external arcuate fibers that curve dorsally along the outer surface of the pyramidal tract and the eminentia olivaris. The concepts of an origin of reticulocerebellar fibers from the lateral reticular nucleus and of external arcuate fibers from the arcuate nucleus find support in the disappearance of these nuclei in cases of olivopontocerebellar atrophy, which bodies also display a loss of reticulocerebellar fibers. Reticulocerebellar fibers are only slightly smaller than the spinocerebellar ones and therefore are difficult to discern from them in normal Häggqvist-stained material.

**Fig. 4A,B** *Stippled outline* of the degeneration in series H5517 characterized by Wallenberg syndrome


H5517
WALLENBERG SYNDROME
L
R
6
1
C1
nV
GC
nVT
ctt
mlf
ml
dbc
N
28
CS
CGM
bci
7
CD
ml
R
rrf
N
CMM
C1
nV
nVT
ctt
mlf
ml
bc
R
N
33
CGM
CGL
ml
CD
rrf
R
N
CMM
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bci
nV
GC
ctt
nVT
R
N
16

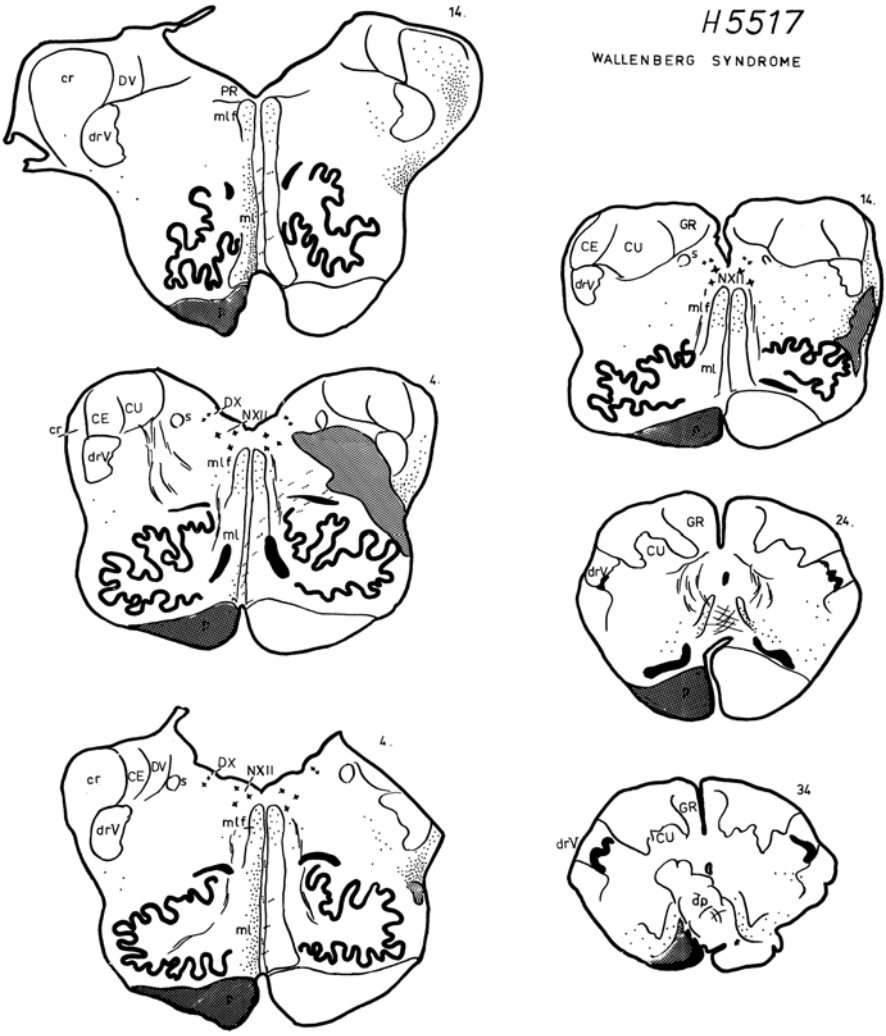
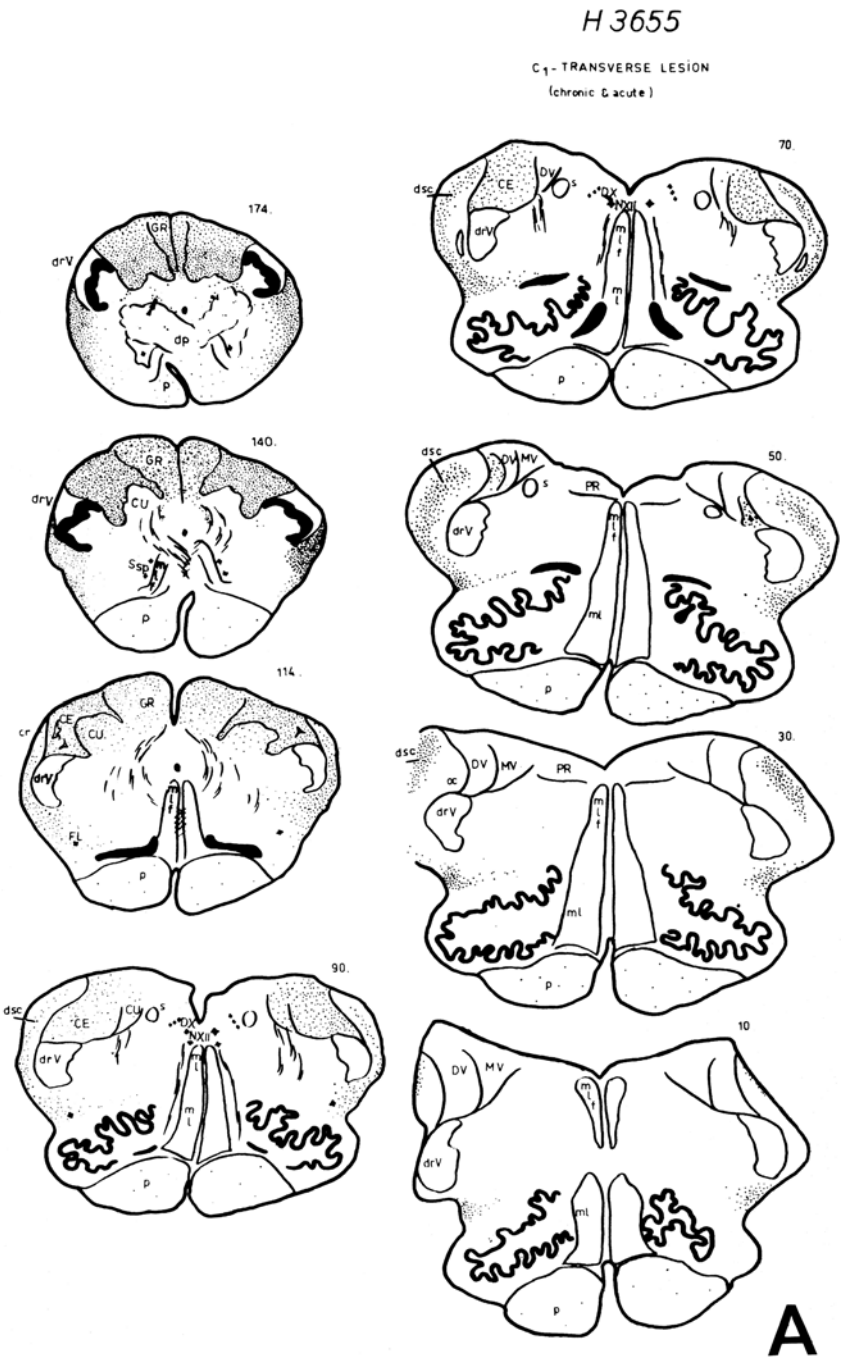
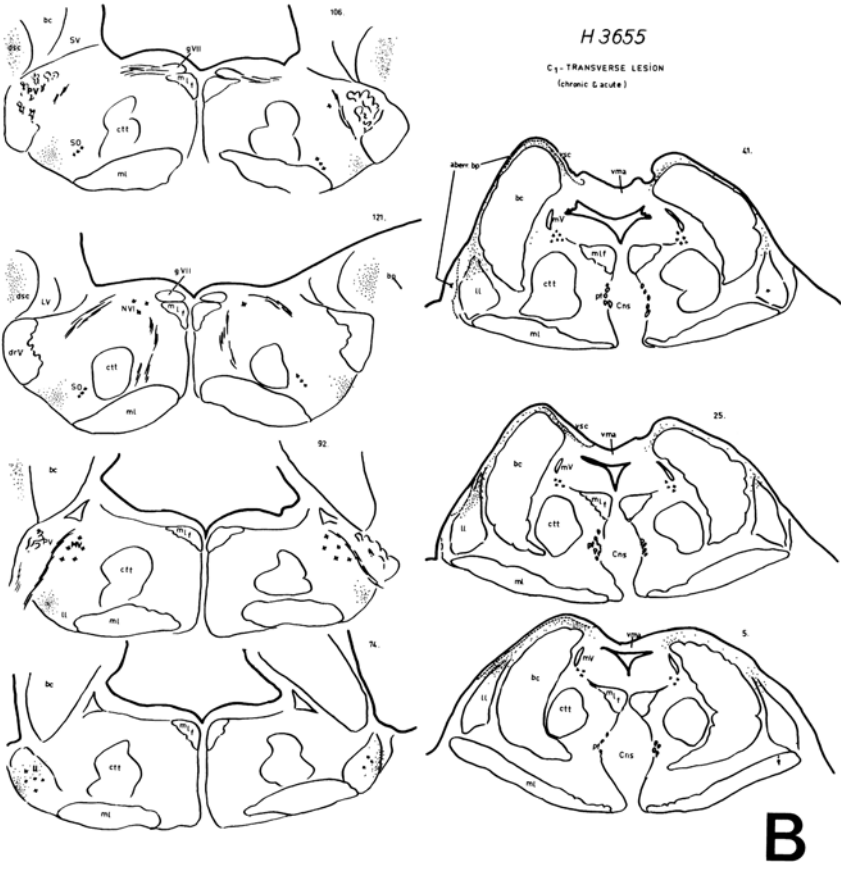



**Fig. 5A, B** *Stippled outline* of the degeneration of a C1 transverse lesion both chronic and acute. **A** Lower brain stem, **B** from genu N.VII to vma


H 3655
C1 - TRANSVERSE LESION
(chronic & acute)
174.
GR
drV
dP
p
140.
GR
drV
CU
Sp
p
114.
GR
CE
CU
cr
drV
FL
p
90.
dsc
CE
CU
DX
NXII
drV
ml
p
70.
dsc
CE
DV
DX
NXII
drV
ml
p
50.
dsc
DV
MV
PR
drV
ml
p
30.
dsc
DV
MV
PR
oc
drV
ml
p
10
DV
MV
drV
ml
p
A


H 3655
C1 - TRANSVERSE LESION
(chronic & acute)
B

After assembling in the medial part of the restiform body, the reticulocerebellar fibers break through and finally encircle the central field of spinocerebellar degeneration. Ventromedially a compact zone of reticulocerebellar fibers intervenes between the spinocerebellar fibers and the supratrigeminal area of olivocerebellar fibers. In the center of the restiform body the degenerated spinocerebellar and patches of intact reticulocerebellar fibers intermingle. When both the spinocerebellar and reticulocerebellar fibers are degenerated, as in H5517 (Fig. 4), the area of degeneration is distinctly larger than found in cases of degeneration restricted to the spinocerebellar system. Slightly rostral and lateral to the lateral vestibular nucleus, the reticulocerebellar fibers start moving dorsally into the cerebellum and their ring-like configuration becomes lost. Still more rostrally the spinocerebellar fibers are the last to turn dorsally to enter the white matter of the anterior lobe.

- Olivocerebellar fibers make their appearance rostral to the reticulocerebellar fibers as small bundles of uniformly sized 2-µm fibers penetrating from ventromedially in the rostral part of the lateral reticular nucleus. Some of them pass dorsally, immediately lateral to the spinal trigeminal tract, others pass through or medial to the spinal tract. They assemble in a triangular area, dorsal to it. At a slightly more rostral level they start to traverse and encircle the combined spinocerebellar and reticulocerebellar field. At the level of the lateral vestibular nucleus the olivocerebellar fibers are the first axons to leave the restiform body, passing dorsally into the cerebellum.
- In normal Häggqvist-stained sections cuneocerebellar fibers can be observed to leave the nucleus cuneatus in a lateral and ventrolateral direction to join the reticulocerebellar fiber contingent of the restiform body, from which they cannot be distinguished. In the case of olivopontocerebellar atrophy (H7980), the few cuneocerebellar fibers that are left (the external cuneate nucleus is partially atrophic) course through the atrophic supratrigeminal olivocerebellar area.

### 3.4
### Collateral Projections from the Spinal Cord to the Nuclei of the Restiform Body

Under this name we have assembled the groups of small cells located within the restiform body (the "pars disseminata" of the lateral reticular nucleus of Braak 1971), namely, the cells at the lateral border of the descending vestibular nucleus rostral to the external cuneate nucleus (group "X" of Brodal and Pompeiano 1957), the repagulum cuneati, and the promontorium (Braak 1971) in between the spinal trigeminal tract and the external cuneate nucleus proper. The repagulum envelops the ventral and ventromedial aspect of the rostral half of the external cuneate nucleus. Medially it reaches the solitary tract. Its cells are slightly smaller than those of the external cuneate nucleus. They give rise to typical coarse internal arcuate fibers, which after decussating join the contralateral medial lemniscus. The smaller

cells of the promontorium are located in the triangular area of olivocerebellar fibers, in between the spinal tract, the external cuneate nucleus, and the restiform body. All these nuclei, with the exception of the repagulum, have disappeared in cases of olivocerebellar atrophy (H7980).

Spinal projections to these nuclei are found in all Nauta-stained cordotomy cases. They are especially clear in H7085 (Fig. 6), which otherwise did not stain very satisfactorily. Preterminal degeneration is observed in the patches of small fusiform cells in the restiform body. From the latter cell groups small bundles of degenerated fibers run through the spinal trigeminal tract into the repagulum. Both nuclei display a meshwork of small degenerated fibers. It is unlikely that the degeneration in the repagulum in H7085 is caused by the sparse degeneration in the fasciculi gracili. Moreover, ascending degeneration in the posterior columns in H5631 is present bilaterally, but termination in the repagulum and the promontorium is found only at the right side, ipsilateral to the ventrolateral cordotomy. Within the group "X" traces of preterminal degeneration can be observed. At this level preterminal degeneration is also present in the pontobulbar body.

### 3.5
### Spino-Olivary Projections

In the Nauta-stained sections of cases H5631 and H5412 degenerated fibers terminate in the lateral half of the dorsal accessory olive, although its medial part does not remain completely free from degeneration. More rostrally the amount of degeneration in the dorsal accessory olive4 decreases, but it remains present to its rostral pole. In case H5631 a few degenerated fibers are also located around the lateral extremity of the horizontal limb of the caudal ventromedial accessory olive. In H5412 degeneration is absent at this location even though the cordotomy in this case was more extensive and included the ventral funiculus, which contains the ventral spino-olivary system (Brodal et al. 1950).

### 3.6
### The Ventrolateral Funiculus in the Tegmentum of the Pons

In the rostral medulla, where a large proportion of the spinocerebellar fibers have joined the restiform body, the ventrolateral funiculus is considerably reduced in size. At the level of the facial nerve nucleus the field is traversed by small bundles of secondary acoustic fibers, which enter the trapezoid body and the superior olive from the ventral cochlear nucleus. In the pontine tegmentum the area of degenerated fibers is located in its ventrolateral corner, bordering the medial aspect of the outgoing roots of the facial and trigeminal nerves, and is roughly quadrangular in shape. The coarse fibers of the ventral spinocerebellar tract can be found ventrally, in between the bundles of trapezoid body fibers and the dorsal most transverse fibers of the pontine pes. In between the area of spinal degeneration and the nuclei of the facial and trigeminal nerves, normal fibers, some of them

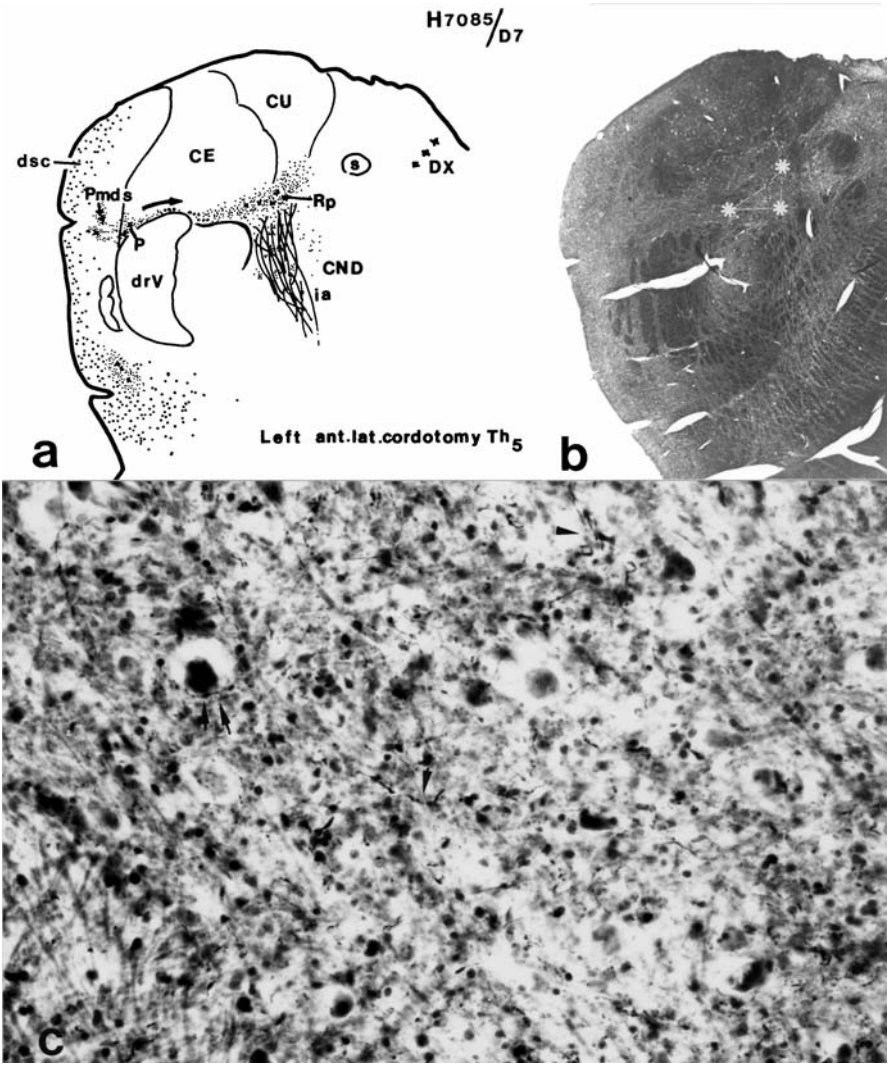



**Fig. 6a, b** Anterolateral cordotomy at T5 (H7085). **a** Schematic drawing of a section through the lower brain stem at the level of the repagulum. Degeneration is present in a line from the restiform body over the trigeminal area into the repagulum. **b** Nauta section of **a**. The repagulum is indicated by *asterisks*. **c** Detail of the preterminal degeneration in the repagulum, *arrows*

of a large caliber, are found as well as, among others, the rubrobulbospinal tract, which can be considered as part of the ventrolateral funiculus.

Still more rostrally the spinal degeneration fuses with the more medially located lateral lemniscus. The two tracts can be distinguished in Häggqvist-stained preparations by the monotonous fiber pattern and the lack of coarse fibers in the lateral lemniscus. Dorsomedially the spinal fibers merge into the reticular formation. In the rostral pons the lateral lemniscus moves dorsally, lateral to the superior cerebellar peduncle, which has made its appearance at this level. The thin degenerated fibers now are located in and around top of the lateral lemniscus, some entering the sagulum. The coarse fibers of the ventral spinocerebellar tract meanwhile have separated from them to enter the cerebellum superficially through the brachium conjunctivum. In one case (H3655) a conspicuous, aberrant bundle of thin brachium pontis fibers accompanies the degenerated ventral spinocerebellar fibers into the brachium conjunctivum (Fig. 5B, see aberr. bp in section 41).

## 3.7
## Spinoreticular Projections

Spinoreticular projections can be visualized in the Nauta-impregnated sections only; in the Häggqvist-stained material visible degeneration in the reticular formation is extremely scanty. From the area of the lateral reticular nucleus a great number of degenerated fibers enter the reticular formation. The spinoreticular projection is mostly aimed toward the caudal medulla. The fibers terminate in the ventral subnucleus of the central nucleus of the medulla oblongata and in the adjoining portion of the dorsal subnucleus. They reach but do not enter the nucleus interfascicularis of the hypoglossal nerve. No degeneration is present in the motor nucleus of the hypoglossal nerve or in the nucleus prepositus hypoglossi.

The termination of spinal fibers in the reticular formation of the rostral medulla and the pons is less voluminous and is mainly restricted to the nucleus gigantocellularis and the *adjoining* part of the nucleus paragigantocellularis. Fewer fibers can be traced into the parvocellular reticular formation. The nucleus ambiguus is negative for this degeneration. At the level of the pons the degeneration in the reticular formation is restricted to the ventrolateral funiculus. The motor nuclei of the facial, abducens, trochlear, and trigeminal nerves remain definitely free from degenerated fibers, as does the oculomotor nucleus.

At the pontomesencephalic junction decreasing amounts of degenerated fibers are still concentrated around the dorsal tip of the lateral lemniscus, with preterminal degeneration in the sagulum, the dorsal parabrachial nucleus and, in H5631 (Fig. 2B), in the ventral parabrachial nucleus, which lines the superior cerebellar peduncle on its ventromedial side. In this case a small number of degenerated fibers can be seen passing through the ventral limb of the superior cerebellar peduncle, to distribute to the reticular formation immediately ventromedial to it (Fig. 2B). In case H5412 this degeneration cannot be noted, owing to the presence of artifacts in the sections of the rostral pons. In the caudal mesencephalon of this case, how-

ever, preterminal degeneration is observed at approximately the same site, among the cells of the subnucleus compactus of the nucleus tegmenti pedunculopontinus (Fig. 1A). In case 5631, with a right sided cordotomy, the spinoreticular projection is completely ipsilateral. From case H5412, with bilateral incisions of the cord, no conclusions as to the laterality of the spinoreticular projection can be drawn.

### 3.8
### Spinomesencephalic and Spinothalamic Projections

In the caudal mesencephalon the ascending spinal fibers keep their position dorsally in the lemniscus lateralis, spreading along the ventral side of the inferior colliculus. In Nauta-stained sections no degeneration can be found to enter the inferior colliculus. Modest projections are found to the nucleus cuneiformis just ventral to the inferior colliculus and very sparsely to the lateral portion of the central gray matter. At the intercollicular level the degenerated fibers assemble in the thalamopetal bundle, a discrete collection of fibers situated at the dorsal tip of the medial lemniscus, immediately medial to the brachium of the inferior colliculus. In the Häggqvist-stained section of complete cervical (H4477, in case H3655 the rostral mesencephalon was not available) and thoracic lesions the degenerated fibers in the bundle are of varying diameter and are outnumbered by normal fibers of unknown origin. In the rostral midbrain the thalamopetal bundle becomes incorporated into the dorsal tip of the medial lemniscus. In Häggqvist-stained material no degenerated fibers can be traced beyond this level.

In the Nauta-stained sections the degenerated fibers are never limited to the thalamopetal bundle but cover a larger area. Degeneration is always present in the dorsal part of the medial lemniscus, the paralemniscal nucleus, located between the medial lemniscus and the medial geniculate body, and in the rostral pole of the cuneiform nucleus. In addition, degenerated fibers can be seen entering the deep layers (mainly in the stratum griseum intermedium) of the superior colliculus.

No degenerated fibers are found in the medial geniculate body itself. At pretectal levels the degeneration in and around the tip of the medial lemniscus appears to be minimal. A tremendous amount of preterminal degeneration in the lateral part of the ventral posterior nucleus of the thalamus is present (Fig. 2C, H5631). These spinothalamic terminations are characteristically arranged in clusters of terminals or "bursts" (Fig. 2C, a, b, c). In H5412 these bursts are not limited to the lateral part (Fig. 1B, b,c,d) but also extend into the adjoining medial part of the nucleus ventralis posterior (Fig. 1B, a). Dorsal to the nucleus of the centre médian, degeneration is also present in the internal medullary lamina and in the nucleus centralis lateralis. Degeneration in the centre médian seems to pass through, not terminate in this nucleus.

# 4
# Discussion on Spinal Ascending Systems

The course of the ascending degeneration following lesions of the spinal cord in the human brain stem had already been settled around the turn of the century, nineteenth to twentieth, that is, with the Marchi techniquer (Marchi and Algeri 1885) and essentially no new pathways have been added since. Excellent descriptions dating from this period are given in the papers of Quensel (1898), Thiele and Horsley (1901), and Collier and Buzzard (1903). The Häggqvist and the Marchi method both stain degenerated myelin after a fixation in potassium dichromate. The advantage of the Häggqvist method over the Marchi method, and for that matter also over the Nauta method, lies in the visualization of the fiber pattern of normal tracts, thus allowing a more complete study of the composition of complex fiber systems in which the spinal fibers participate, such as found in the restiform body.

After the introduction of selective silver impregnation of degenerating axons (Nauta and Gygax 1951; Nauta and Ryan 1952), it became clear that the images rendered by the stains for degenerated myelin were very incomplete. However, the application of the Nauta method to human material is often complicated by the presence of a large number of artifacts. These artifacts are due to the argyrophilic nature of the autolytic products in the non-perfused, often late and incompletely fixed human material. The artifacts often persist after the application of numerous modifications of the Nauta method, such as the ones of Albrecht and Fernstrom (1959) and Fink and Heimer (1967), and make a careful and critical study of each section necessary. When our results are compared to the silver impregnation studies of the spinal projection in the human brain stem of Mehler (1962, 1966) they appear to be in good accordance. Bowsher (1957, 1962) using the same method, generally reports more extensive projections, but his pictures also show a disturbingly high amount of dust-like artifacts.

Comparison to ascending systems in non-primates has largely been omitted in this paper. Only the rostral spinocerebellar tract, olivocerebellar tract, group "X", and the spino-olivary connections are related to non-primate results. The vindication of this is in the organization of the spinal cord and brain stem in man, which has unique features. Species differences can be demonstrated in the dorsal column nuclei (DCN), extensively studied in cat, rat, and raccoon (Snow and Wilson 1991), and in the spinomesencephalic tract in rat, cat, and monkey (Yezierski 1988) and man is not an exception (see part 5.1)

Ascending afferent pathways to the DCN can be subdivided into contingent or primary afferents and non-primary afferents. Primary afferents (and also the non-primary afferents in the rat) project more densely to the core than to the shell of these nuclei. Afferent fibers from cervical and thoracic segments terminate mainly rostrally in the internal cuneate nucleus. Fibers originating from segments below T6 terminate in corresponding regions of the gracile nucleus (see Snow and Wilson, 1991, for a review). In man a shell localization of the degenerating fibers in the gracile nucleus can be found, the core of this nucleus remaining free (H5412).

Moreover, an extension of the Nauta preterminal degeneration into the adjoining gray matter just above the central canal is reported for man (this article; indicated as Cajal's nucleus intermedius), and also into the supraspinal nucleus (Olzsewski and Baxter 1954). In case H5631 the caudal part of the gracile nucleus contains heavy Nauta degeneration, which is confirmed in case H5800, where a transverse lesion of T7 distinguishes sparse Häggqvist degeneration in the rostral part of the gracile nucleus (Fig. 3).

### 4.1
### Spinocerebellar Tracts, Precerebellar Nuclei and the Composition of Restiform Body

We maintain in this paper that the traditional distinction of dorsal and ventral spinocerebellar tracts is artificial. The tracts cannot be sharply delimited from each other and from other ascending fibers in the ventrolateral funiculus (Kohnstamm and Quensel 1909). In accordance with the observations of Sie Pek Giok (1956) and Smith (1957) in man we observed a shift of coarse fibers from the periphery of the ventrolateral funiculus into the area of the dorsal spinocerebellar tract at cervical and low bulbar levels. Part of the degenerated fibers interrupted by thoracic lesions moreover ascend in the lateral pyramidal tract and only join the dorsal spinocerebellar system at high cervical levels (see also Mott 1897). This may explain Collier and Buzzard's (1903) supposition that the contribution of the thoracic cord to the dorsal spinocerebellar tract is small but that an increasing number of fibers join it in the cervical cord.

The spinocerebellar tracts have been analyzed in laboratory animals with electrophysiological methods (see Oscarsson 1973 for a review) and retrograde transport techniques (Matsushita and Ikeda 1975, 1987; Matsushita and Tanami 1987; Matsusita et al. 1979, 1985; Snyder et al. 1978). The cervical cord gives rise to "rostral or cervical spinocerebellar tracts", which enter the cerebellum both through the restiform body and the superior cerebellar peduncle (Oscarsson and Uddenberg 1964, 1965; Petras and Cummings 1977), and to fibers originating from the central cervical nucleus (Wiksten 1975; Matshushita and Ikeda 1975; Cummings and Petras 1977; Petras and Cumming 1977; Snyder 1977), which is identical to Cajal's nucleus intermedius (group "a" of Meessen and Olzsewski 1949). The course of the spinocerebellar tracts was studied in the cat (Xu and Grant 1994). The dorsal spinocerebellar tract passes through the restiform body; the ventral spinocerebellar tract ascends through the superior cerebellar peduncle. The cervical ipsilateral spinocerebellar fibers pass through both, while contralateral cervical spinocerebellar fibers enter through the superior cerebellar peduncle. These rostral spinocerebellar tracts probably are also present in man, but cannot be distinguished on the basis of the level of the spinal lesion or the topography alone. In man the nucleus intermedius of Cajal receives fibers from the upper two cervical roots (H5554) and therefore contains degeneration after high cervical lesions of the cord. We did not observe a projection to this nucleus from lower levels of the cord as described by Mehler (1962).

The position of the dorsospinocerebellar, the reticulocerebellar, and the olivocerebellar tracts in the restiform body was studied in some detail. Our results generally confirm the observations in human myelogenetic material of Darkschewitsch and Freud (1886) and Bechterew (1896, 1899) and are basically similar to the situation existing in the cat (Busch 1961; see also Voogd et al. 1990). The origin of the external arcuate fibers, which join reticulocerebellar fibers arising from the lateral reticular nucleus, from the paramedian reticular nucleus, as advocated by Bechterew (1899) for man, could not be confirmed. The disappearance of the arcuate nucleus and the external arcuate fibers in cases of olivopontocerebellar atrophy could suggest an origin from the latter nucleus.

Olivocerebellar fibers in man are numerous (Dietrichs and Walberg 1989; Voogd et al. 1990, the present study). Most of the fascicles of olivocerebellar fibers traverse the spinal trigeminal tract or pass medial to it, and only a modest number of olivocerebellar fascicles is found lateral to the tract (see also Usunoff et al. 1997). Courville and Faraco-Cantin (1978) and Voogd and Bigaré (1980) called attention to the medial position of the fibers from the caudal parts of the accessory olives in the restiform body of the cat. Fibers from the rostral part of the inferior olive, especially those from the principal olive, pass through or medial to the spinal trigeminal tract, traverse the restiform body, and take up a dorsolateral position with respect to the spinocerebellar and reticulocerebellar components of the restiform body. The same situation seems to exist in man, but the laterally located olivocerebellar fibers are more numerous and the halo of olivocerebellar fibers surrounding the spinocerebellar and reticulocerebellar core of the restiform body is more complete (for a review see also Voogd et al. 1990).

Spinal projections to some precerebellar relay nuclei also exist in man. After thoracic cordotomies fibers terminate abundantly in the lateral half of the lateral reticular nucleus but are scarce in its medial part. This could be taken as a sign of a somatotopical projection, cervical fibers terminating in the medial part of the nucleus (Künzle 1973). However, in the Häggqvist-stained sections of complete cervical lesions (Nauta-stained material of cervical lesions was not available) degenerated fibers in the bundles of the medial part of the lateral reticular nucleus are extremely rare. Systems, which do terminate in the medial portion of this nucleus in man, include the rubrobulbospinal tract (Schoen 1970; Voogd et al. 1990) and the corticofugal system (Schoen 1969). No spinal fibers could be traced to the nucleus interfascicularis and the nucleus prepositus hypoglossi. However, in monkeys projection to the nucleus interfascicularis has been documented (Mehler et al. 1960). Braak (1970, 1971), using an aldehyde fuchsin method for lipofuchsin in nerve cells, considered the cell groups here assembled under the name "nuclei of the restiform body" (the nucleus marginalis dissiminatus, the promontorium of Ziehen (1934), and the repagulum cuneati) as subnuclei of the lateral reticular nucleus. Spinal projections to these nuclei are evident from our material, but were not mentioned by Mehler (1962, 1966). The presence of fibers from the spinal cord in the supratrigeminal region also was noticed by Collier and Buzzard (1903) in man and by Walker (1940) in the chimpanzee and considered by them as a col-

lateral projection of the dorsospinocerebellar tract, an opinion that is difficult to prove. The group "X" of Brodal and Pompeiano (1957), described in man (Sadjapour and Brodal 1968; Gerrits 1990; Paxinos et al. 1990), but designated as not being clearly present in man by Kaas (1990), also receives a projection from the spinal cord. Bowsher (1962) seems to localize the spinal projection to the group "X" slightly more ventrally and may have confused this nucleus with the rostral pole of the repagulum; and Bowsher also mentioned a spinosolitary connection. In fact the degeneration in the repagulum in our cases almost touches the lateral aspect of the solitary tract but never enters its nucleus. The group "Z" (Sadjapour and Brodal 1968) could not be identified in our material and no spinovestibular projections could be observed. The cerebellar projection of the nuclei of the restiform body was substantiated in cases of olivocerebellar atrophy, where they have disappeared, with the exception of the repagulum. The inclusion of the repagulum in the subnuclei of the lateral reticular nucleus by Braak (1971), therefore, is not justified. In Häggqvist-stained sections the repagulum can be seen to give origin to coarse internal arcuate fibers, which join the medial lemniscus (see under The Medial Lemniscus).

From our material it seems unlikely that dorsal column fibers enter the supratrigeminal area and terminate on the repagulum and the promontorium. Spinal projections reach these nuclei through the lateral funiculus and therefore should also be distinguished from dorsal column fibers from the dorsal horn cells, which in laboratory animals were found to terminate in the ventral and rostral parts of the dorsal column nuclei (Rustioni 1973, 1974, 1977; Rustioni and Kaufmann 1977). In this respect it should be noted that the repagulum is rudimentary in non-primates and seems to be well developed only in man and the anthropoids (Walker 1938a, b).

In the human brain stem fibers detach from the ventrolateral aspect of the pyramid at caudal bulbar levels and run steeply upward along the outer portion of the eminentia olivaris. After intruding into the outer portion of the ventrolateral funiculus they split into smaller bundles that proceed into the restiform body where they become lost. In Nauta-stained sections they accompany and terminate in the cell groups of Braak's nucleus marginalis disseminatus and in other cell groups surrounding the restiform body such as the lateral reticular nucleus, promontorium, repagulum, group "X", and pontobulbar body (unpublished observations). The small cells located at the surface of the dorsal spinocerebellar tract at high cervical levels also receive fibers from the pyramid and should be included in this category. In some brains the pyramidal component of the restiform body is excessively developed as the so-called circumolivary bundles (Schwank 1934; Schaffer 1938) that can be distinguished by the naked eye. In the ventrolateral funiculus the ascending fibers of the circumolivary bundles should not be confused with ectopically located bundles of pyramidal tract fibers that detach from the pyramid at higher levels and descend through the funiculus to enter the cervical cord (Barnes 1901).

## 4.2
## Spinoreticular and Spino-Olivary Projections

Although spinoreticular, spino-olivary, spinotectal, and spinothalamic fibers generally are assumed to be small, a possible contribution to these pathways of collaterals from the coarser fibers of the spinocerebellar tracts cannot be excluded. After injections of horseradish peroxidase into the ventroposterior thalamus (Albe Fessard et al. 1975; Carstens and Trevino 1978) and the medial reticular formation (Molenaar 1977), labeled cells in the spinal cord were usually located in a different position from the cells of origin of the spinocerebellar tracts. Moreover, in the electrophysiological investigations of Ekerot et al. (1979) in the cat, a collateral activation of the lateral reticular nucleus by the dorsal spinocerebellar tract was disproved. In the ventrolateral funiculus at the spinobulbar junction no separate spinoreticular or spinothalamic tracts can be distinguished. Fine fibers are present in the intermediate layer of the funiculus, but numerous fine and medium-sized fibers also are found in between the more superficially located spinocerebellar fibers, especially in oblique longitudinal sections.

Spinoreticular and spino-olivary projections generally correspond to the reports of previous authors. Spino-olivary fibers terminate in the lateral half of the dorsal accessory olive and ventrolaterally in the caudal pole of the ventromedial olive, just as in the cat (Brodal et al. 1950; Boesten and Voogd 1975). The spinoreticular projections roughly correspond to Mehler's descriptions and are most abundant in the caudal half of the medulla, to decrease in the rostral medulla and the pons where they are mainly restricted to the nucleus gigantocellularis, the nucleus paragigantocellularis, and the parabrachial nuclei. A contribution to the nucleus tegmenti pedunculopontinus pars compacta was also found by Bowsher (1962), but we could not confirm a number of his other terminal stations such as the basal pontine nuclei and the inferior colliculus. The termination of spinal fibers in the nucleus tegmenti pedunculopontinus, of which the efferent connections are unknown in man, is remarkable because it is the most caudal end station of fibers from the globus pallidus (Nauta and Mehler 1966). After lesions of the cord no degenerated fibers could be found in somatic motor nuclei such as the supraspinal nucleus and the nuclei of the hypoglossal, trigeminal, and facial nerves. Mehler et al. (1960) established a projection in man of spinal fibers to the facial motor nucleus and the supraspinal nuclei, but we noticed only degeneration in the latter nucleus in cases of section of the first two cervical dorsal roots.

The bilaterality of the spinoreticular connections, though generally accepted (Kerr 1973; Lippman and Kerr 1972), could not be confirmed in most of our material, because the cordotomies are usually made on both sides of the cord. In H5631, however, with a unilateral lesion, the spinoreticular projection did not extend to the side contralateral to the cordotomy.

## 4.3 Spinothalamic Projections

The literature on the spinothalamic tract was extensively reviewed by Bowsher (1957), Mehler (1962, 1966, 1974) and Kaas (1990; see also Zhang et al. 1990 and Kaas and Pons 1988). Spinothalamic fibers make up only a small fraction of the ventrolateral funiculus. In Mehler's estimate far less than one third of these fibers reach the thalamus, and in the fiber countings of Bowsher et al. (1960;12% of the 2–4-μm and 36% of the 4–7-μm fibers present at the C1 level reach the intercollicular level) the tremendous numbers of thin ascending fibers in the ventrolateral funiculus probably were underestimated. There are few anatomical data that support a somatotopical arrangement in the spinothalamic pathway. Foerster and Gagel (1932) arrived at this concept of such an arrangement by a careful evaluation of the disturbances in sensibility in a large number of anatomically verified cases of ventrolateral cordotomy. Their conclusion, that fibers from more rostral levels of the cord are located deep to those coming from more caudal levels later was corroborated by Walker (1940), Schwartz and O'Leary (1942), Glees (1951), and Glees and Bailey (1951). When our cases with midthoracic lesions are compared to those with complete cervical lesions, a dorsoventral rather than a mediolateral arrangement is found in the ventrolateral funiculus at low bulbar levels. The cervical fibers are located ventrally and do not degenerate after thoracic lesions. A similar dorsoventral lamination, described for the thalamopetal bundle by Glees and Bailey (1951), could not be confirmed in our material.

Not more than 7% of the fibers of the ascending thalamopetal bundle originate from the spinal cord (Verhaart and Sie Pek Giok 1957). The origin of the other fibers of this bundle, which do not degenerate in longstanding complete cervical lesions, is not known. Also in the case of a Wallenberg syndrome the majority of the fibers in the thalamopetal bundle is preserved. Moreover, the degeneration in Nauta-stained sections at rostral mesencephalic levels is never limited to the thalamopetal bundle but is also present in the neighboring reticular formation, in the deep layers of the superior colliculus, and in the dorsal tip of the medial lemniscus. Spinothalamic tract and thalamopetal bundle, therefore, are not equivalents, as stated by Glees and Bailey (1951). In the mesencephalon a few spinal fibers also terminate in the lateral part of the central gray. This projection which was also found in monkeys by Kerr and Lippman (1973), Mehler (1974), Mantyh (1982), Liu (1986), and Harmann et al. (1988) after spinal commissural lesions, may be of special importance in the regulation of pain sensation, because this part of the central gray was shown to contain opiate receptors in laboratory animals (Atweh and Kuhar 1977, Atweh et al.1978; see Beitz 1990). Before the Nauta era, the termination of spinal fibers in the ventral tier of thalamic nuclei was accurately described by Quensel (1898), Collier and Buzzard (1903), Goldstein (1910), Foerster and Gagel (1932), Walker (1940), Rasmussen and Peyton (1941, 1946), Schwartz and O'Leary (1941, 1942), Gardner and Cuneo (1945), and Glees and Bailey (1951). The sharply demarcated spinothalamic projection area as demonstrated with the Nauta method is larger

than could be demonstrated with the Marchi method and consists of clusters of terminals or "bursts" that are characteristic for spinothalamic projection in primates (Mehler 1962, 1966). In agreement with Mehler we did not find an evident termination in the nucleus of the centre médian (see also discussion in Apkarian and Hodge 1989), as did Bowsher (1957), but degeneration in the internal medullary lamina in the nucleus centralis lateralis is certainly present.

Species differences complicate the study of the spinothalamic tract. As an example, the presence in most mammals, including the lower primates, of the lateral cervical nucleus, which projects to the thalamus as the crossed cervicothalamic tract (Busch 1961), should be mentioned. Truex et al. (1965), in a comparative investigation, found this nucleus to be rudimentary in man and could distinguish it in only 2 of 16 human specimens. Edinger (1889), whose name is attached to the spinothalamic tract, indeed described a pain-mediating system in kittens and other animals that originates from the dorsal horn and ascends in the crossed medial lemniscus. Busch (1961) already noticed that Edinger's tract, judging from his pictures, actually takes its origin from the nucleus cervicalis lateralis. The cervicothalamic tract indeed is located in cat in the lateral part of the medial lemniscus. The spinothalamic tract, as we see it in man, only joins the medial lemniscus at the level of the thalamopetal bundle.

# 5
# The Medial Lemniscus

## 5.1
## Introduction

Recent literature contains controversial discussions on the origin, organization, and pathway of the human medial lemniscus. Several of these aspects also arise due to the application of MRI identification of brain stem lesions in patients. To mention a few:

- Laminar organization is described in the human medial lemniscus (see, e.g., Kim 2001; Cerrato et al. 2000; Lee et al. 2001).
- Fibers of the gustatory tract have been found to be related to the contralateral medial lemniscus in man (Hoshino et al. 1999; Uesaka et al. 1999).
- Lesions responsible for human brain stem cheiro-oral syndromes (opercular syndrome) are thought to involve the pontine medial lemniscus (Takezawa et al. 1990; Takamatsu and Takizawa 1991; Shintani et al. 2000).
- The main notion that the lateral cervical nucleus contributes to the medial lemniscus (e.g., Gilman 2002) can be debated, since most humans lacks such a clear lateral cervical nucleus as present in cats (see Truex et al. 1965).

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Several comparative results stress the inability to apply rat and cat results to the human. So both the clinical approach (1, 2, 3 above) and the comparative approach (4 above; see also Kosinski et al. 1988 for species differences in pontine projections of the medial lemniscus) indicate that a reappraisal of the medial lemniscus based on human material is a prerequisite in solving clinical uncertainties.

"Moreover functional considerations regarding the dorsal column pathways have been revised dramatically over the past few years. It now appears that the dorsal column pathways are not particularly important for vibration and joint sensation. Surgical lesions of the dorsal columns in humans can produce only minimal sensory deficits. There is evidence that the pathways are involved in highly complex discriminative tasks, such as two-point discrimination, judging the magnitude of cutaneous pressure and the ability to detect the speed and direction of moving stimuli" (Schoenen and Grant 1990).

The dorsal columns and their nuclei are also involved in visceral nociceptive relay systems as detected in recent research (Al-Chaer et al. 1996a, b).

The whole view on the function and organization of the dorsal column-lemniscus system is changing due to recent research. A reappraisal of this system in man, therefore, is a logic consequence of recent research in experimental animals.

This chapter will, among other results, show that the mediolateral arrangement in the medial lemniscus in animals (e.g., cat) is lost and replaced by a dorsoventral array in man. Moreover, the various components of the medial lemniscus in man differ from those of cat. Even the monkey medial lemniscus is more or less different from the human one.

Since the pathway itself is still under debate, this chapter starts with a description of the normal distribution of medial lemniscus fibers based on human Häggqvist series. One should also consult Usunoff et al. (1997) and Voogd et al. (1990).

## 5.2 The Normal Distribution and Localization of Medial Lemniscus Fibers

### 5.2.1 Short History

The white ribbon was originally noted by von Haller (1765), but described by Reil (1809). Therefore it is also known in older literature as the bundle (or ruban or Schleife) of Reil. A subdivision into a medial and a lateral portion was early distinguished. The lateral lemniscus was recognized to belong to the acoustic system. Within the lemniscus this secondary subdivision into medial (lmII) and lateral (lmI) parts was depicted by von Bechterew (1894; see Fig. 1413 B in von Bechterew in Voogd et al. 1990).

Ramon y Cajal (1911) described the difference between internal arcuate fibers and external arcuate fibers. Man contains a large component of internal arcuate fibers, while in the cat they are less developed. Discussing the "ruban de Reil médian" Cajal states: " Quant aux fibres sensitives ou arciformes internes si

développées chez l'homme (Fig. 281, E), elles font presque entièrement défaut chez le chat", confirming the difference between the medial lemniscus in man and other species. The medial lemniscus carried a series of names through early history. A general list of these synonyms can be found in Déjerine (1901).

Using the Marchi method the medial lemniscus was unraveled by Tschermak (1898) and Probst (1900) in cats and dogs. Rasmussen and Peyton gave an extensive description of the medial lemniscal pathway in man (1948) based on one case with a rhizotomy of the 4 upper cervical dorsal roots. However, these authors found no arguments for a lamination of the medial lemniscus.

### 5.2.2 Origin

The most caudal internal arcuate fibers (fibrae arcuatae internae), originating in the gracile nucleus and perhaps also in the caudal part of the internal cuneate nucleus, appear at a level just rostral to the pyramidal decussation. They are coarse and closely packed into small bundles, curving around the central gray matter and traversing the most dorsal portion of the medial longitudinal fascicle (FLM; see Fig. 7).

After decussating they bend rather sharply ventralward to constitute the most caudal part of the medial lemniscus, interposed between the ventral portion of the FLM and the dorsal margin of the pyramid (Fig. 7). Because they differ from the two other populations of internal arcuate fibers, they can be designated as the first type of internal arcuate fibers ($ia_1$), constituting the first component of the medial lemniscus ($ml_1$). Sagittal sections evidence that these $ia_1$ fibers run not only in a ventral direction toward their decussation, but simultaneously rostralward.

Slightly more rostrally a second type of internal arcuate fibers appears, contrasting with the $ia_1$ fibers by their smaller size (Figs. 8 and 9). They are called the $ia_2$ fibers, which give rise to the $ml_2$ component of the medial lemniscus, and seem to originate from the rostral portions of the internal cuneate nucleus (Fig. 9). They are less compactly bundled than the first type of internal arcuate fibers and take a considerably more lateral course through the tegmentum of the medulla oblongata (Fig. 8). They sweep in a ventral direction through the dorsal and ventral subdivisions of the nucleus centralis of the medulla oblongata, and even through the medial portions of the lateral funiculus nucleus to converge toward the dorsomedial tip of the principal olive (Fig. 10). They appear in sagittal sections to shift simultaneously somewhat rostrally. Just dorsomedial to the principal olive they bend sharply ventrally, and after traversing the medial accessory olive, decussate considerably more ventrally than the first type of internal arcuate fibers (Fig. 10). Immediately after decussation they move slightly dorsally and take a position dorsolaterally in the contralateral medial lemniscus. Already at a low magnification they can be recognized by their smaller size in the Häggqvist-stained sections, showing a slightly deeper blue than the $ml_1$ component.

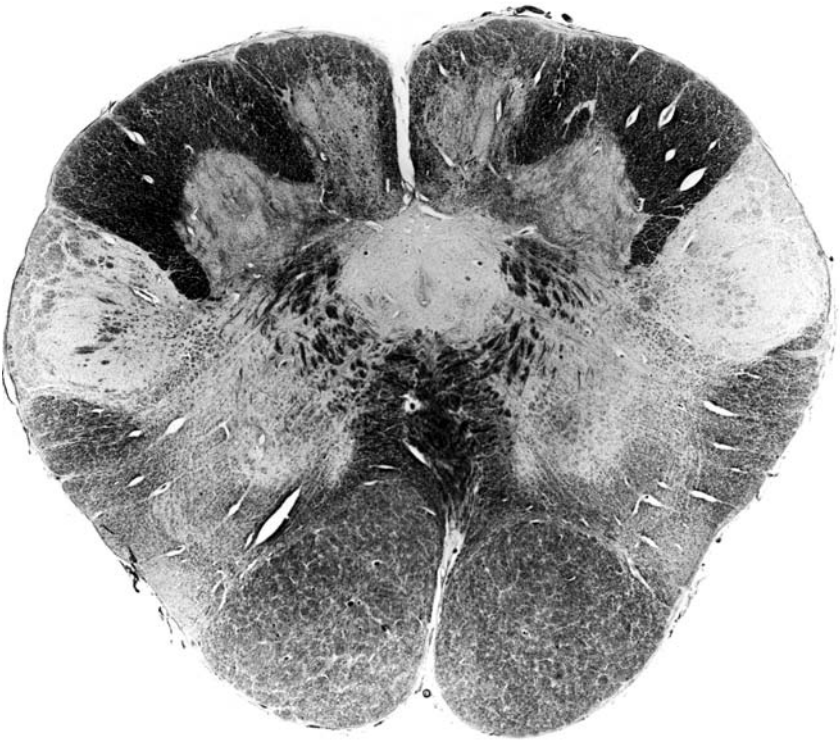


**Fig. 7** The fibrae arcuatae internae in series H5797. In this frozen Klüver section, the $ia_1$ compartment can be exclusively followed due to its compactness; it constitutes the most caudal part of the medial lemniscus (×16)

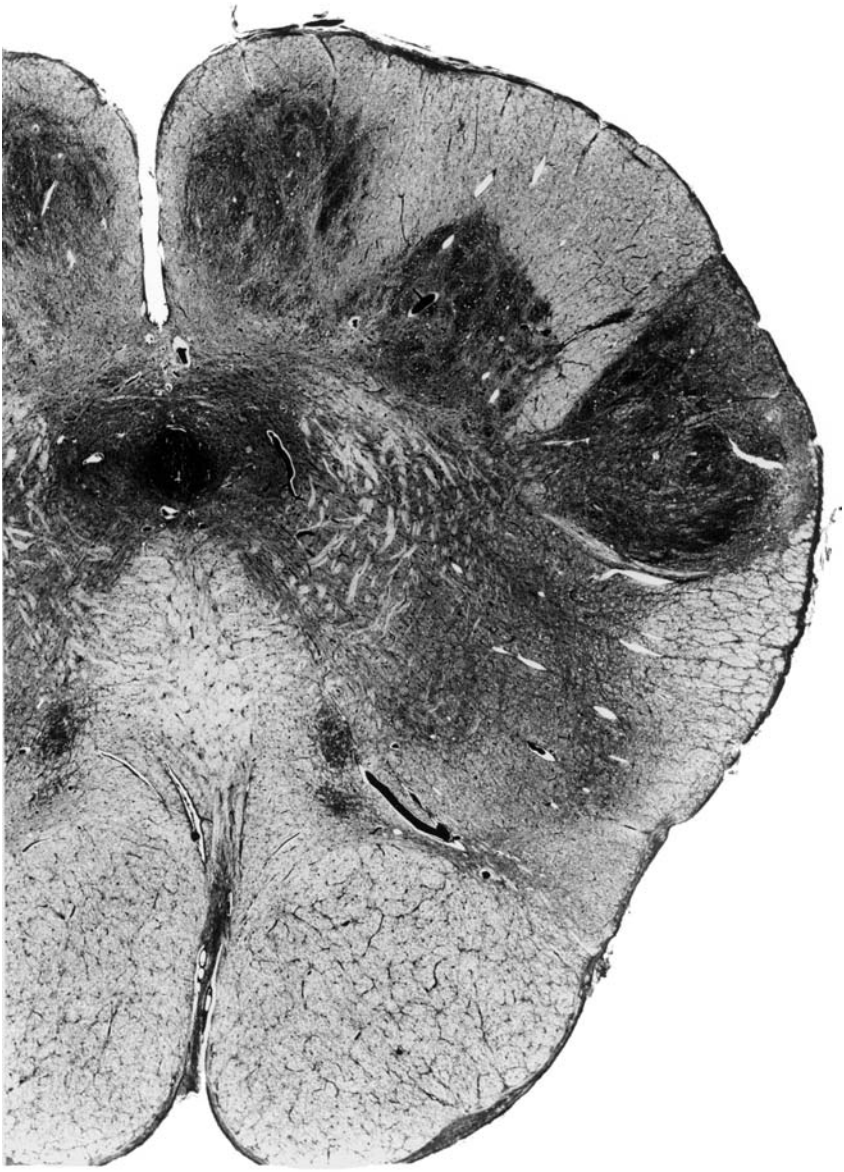


**Fig. 8** A more rostral Häggqvist section of series H5797. In this section the $ia_2$ fibers add as smaller bundles to the fibrae arcuatae internae and originate from the internal cuneate nucleus (×16)

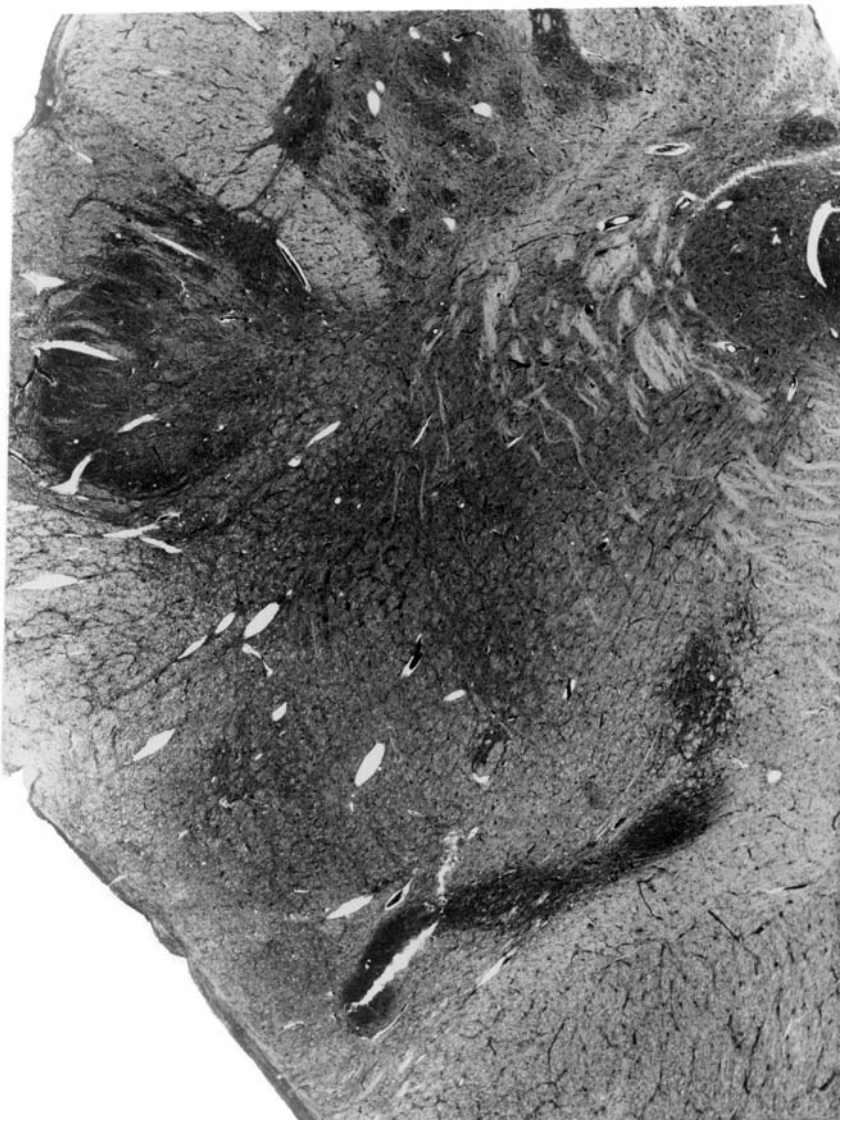


**Fig. 9** A frozen Häggqvist section of series H5631. This enlargement shows mainly $ia_1$ fibers from the gracile nucleus. The first $ia_2$ fibers more laterally join the fibrae arcuatae internae (×40)

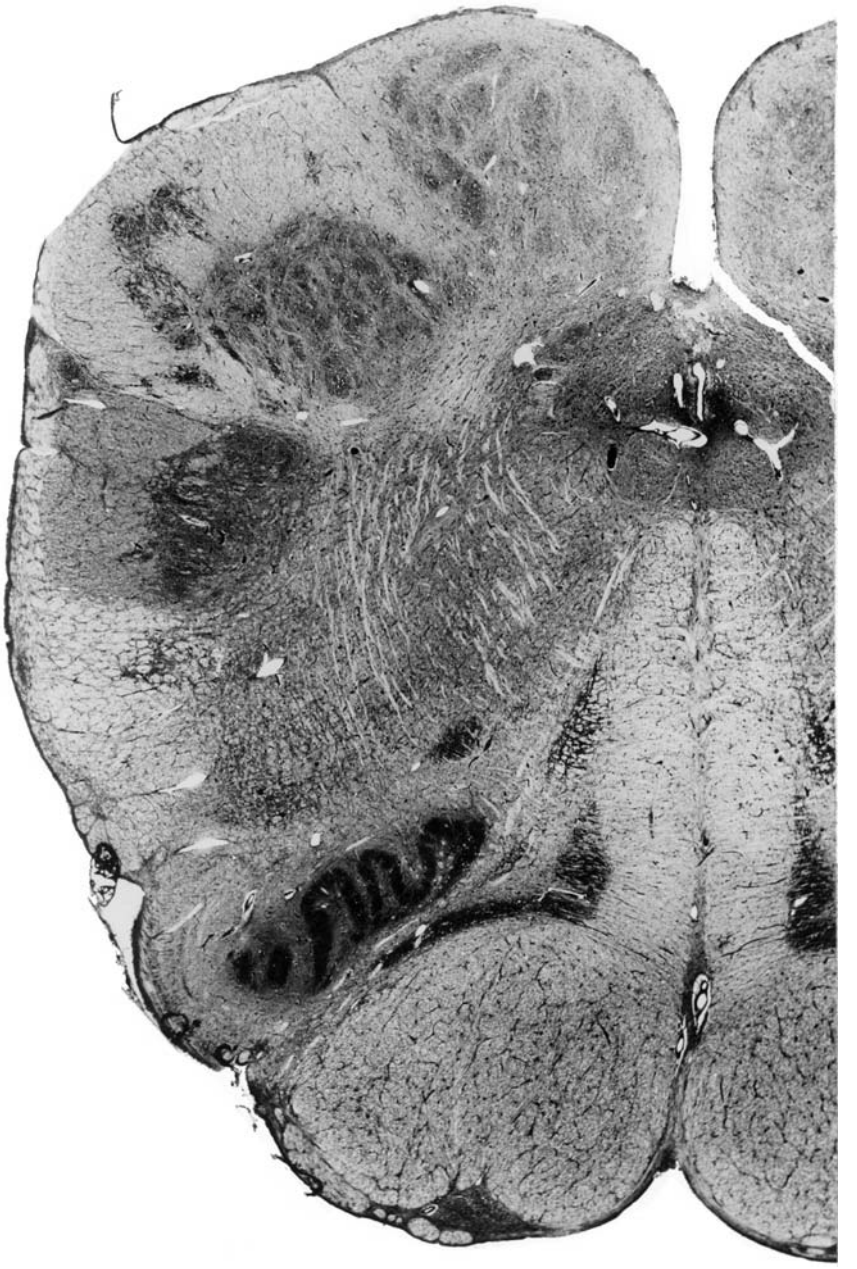


**Fig. 10** A further rostral Häggqvist section of series H5797. The $ia_1$ fibers diminish, while the $ia_2$ fibers extend their trajectory, passing through the caudal part of the dorsal, principal, and the top of the medial olive (×16)

The third type of internal arcuate fibers (indicated as $ia_3$) appears at a level just rostral to the obex, where the external cuneate nucleus has fully developed and the internal cuneate nucleus is shifting in a dorsomedial direction (Figs. 11 and 12). These $ia_3$ fibers are very coarse, even more so than the first type, and sprout in compact bundles from a distinct subnucleus, located immediately to the external cuneate nucleus and ventral to the rostral pole of the internal cuneate nucleus (Figs. 11 and 12). Within this subnucleus the $ia_3$ fibers form a conglomerate of coarse fibers among the cells before they leave it in ventromedial direction. Subsequently they curve in a S-shaped course through the dorsal portion of the reticular formation. They sometimes even pass along the dorsal margin of the solitary tract to decussate after having traversed the FLM. Immediately after decussating they bend sharply ventrally to take a position within the medial half of the medial lemniscus as the $ml_3$ component. Since the most ventral $ia_3$ – fibers traverse the dorsal accessory olive and the dorsomedial tip of the principle olive, and most dorsal $ia_3$ fibers to the dorsal part of the fascicle, it is obvious that their decussation covers a wide area. Their nucleus of origin is the so-called medial sub nucleus of the external cuneate nucleus.

These observations demonstrate:

- The coarse $ia_1$ fibers, originating mainly from the gracile nucleus and constituting the $ml_1$ component, decussate dorsally to take the most ventral position within the contralateral medial lemniscus.
- The smaller $ia_2$ fibers originating from the internal cuneate nucleus, run a smoother curved course through the lateral portions of the reticular formation and decussate more ventrally, and take a more dorsal position within the medial lemniscus as the $ml_2$ component.
- The third type, originating as the very coarse $ia_3$ fibers from the medial sub nucleus of the external cuneate nucleus, crosses in a wide dorsoventral area through the upper three-fourths of the raphe. They can be found in the medial, para-rapheal half of the medial lemniscus as its $ml_3$ component, easy to recognize by their large size.

The medial lemniscus is continuous with the FLM at caudal medullary levels. Nevertheless, even at low magnifications, a faint demarcation line between both systems can be distinguished, because the fibers of the $ml_2$ component (present in the dorsal part of the medial lemniscus) are considerably smaller than those of the FLM. From degeneration material, however, we do know that some mixing of both systems occurs. The borderline of the medial lemniscus with the medial reticular formation is very inconspicuous, because its fiber bundles fluently merge into those of the medial reticular fiber system

**Fig. 11** A Häggqvist section of series H6058. The principal inferior olive leaf has extended strongly. The gracile nucleus is nearly ended. The arcuate fibers are mainly $ia_2$ fibers. The repagulum begins. The $ia_3$ fibers appear as fine bundles just below the descending tract and nucleus V (×16)

**Fig. 12** This Häggqvist section of series shows the $ia_3$ fibers originating from the repagulum. They are situated above the olivo-cerebellar fibers and pass over and through the upper top of the principal inferior olive leaf (×16)

#### 5.2.2.1
#### Rostral Bulbar Levels

At rostral bulbar levels the continuity of the medial lemniscus and the FLM is no longer visible, but the three subdivisions of the lemniscus can readily be distinguished by their fiber patterns. The most conspicuous element is the $ml_2$–component, composed as it is of small, rather uniform fibers ranging in size in Häggqvist series from 2 to 3.5 μm. It can easily be distinguished in the dorsolateral quadrant of the lemniscus. The $ml_1$ component exhibits a more varied pattern of fairly coarse fibers, sizes ranging from 3 to 6 μm, located in the ventrolateral quadrant of the medial lemniscus. The $ml_3$ component stands out by its coarse fibers with diameters from 5 to 7 μm, occupying the whole para-rapheal area of the lemniscus and infiltrating other components.

The bulbar medial lemniscus is traversed by several other fiber systems. At first we encounter great numbers of olivocerebellar fibers, running in a horizontal plane in a lateromedial and, after crossing, mediolateral direction toward the restiform body (see also Voogd et al. 1990). Their presence often conceals the decussating $ml_2$ fibers, because both are of almost the same size.

Secondly, a great number of corticofugal fibers leave the dorsal margin of the pyramid and traverse the medial lemniscus either as dorsally directed, in transverse section obliquely cut bundles, or, more frequently, as small fields of pyramidal fibers running parallel to the lemniscal fibers. This occurs especially in the ventral half of the lemniscus. From silver-stained sections of pyramidal degeneration cases it is known that the medial lemniscus is also traversed by fibers from the contralateral pyramid, running in a dorsolateral direction on their way to the reticular formation. They cannot be distinguished in normal material because they are not grouped in bundles. The aberrant pyramidal tract (APT) in the medial lemniscus in the human brain stem (Yamashita and Yamamoto 2001) is herewith explained as homolateral pyramidal bundles grouped parallel to the medial lemniscus.

Very remarkable is the presence within the bulbar medial lemniscus, especially in its rostral half, of small clusters or streaks of gray matter composed of small cells resembling those of the arcuate nuclei and easily distinguishable from larger cells of the medial accessory olive. They are mainly located along the ventrolateral margin of the lemniscus. Olszewski and Baxter (1954) indicate one of them, found at the borderline between the pyramid and the medial lemniscus, as nucleus conterminalis. These patches of intralemniscal gray matter receive an important cortical projection.

#### 5.2.2.2
#### Level of the Facial Nucleus

While at bulbar levels a vertically directed structure, at the level of the facial nerve nucleus the medial lemniscus gradually assumes a more or less elliptical

shape, and in the pons becomes a horizontally directed area of white matter. At this facial nucleus level the coarse-fibred $ml_3$ component can be recognized in the medial part of the lemniscus, but more laterally its fibers spread among the other components and can no longer be distinguished separately. In the dorsolateral part of the medial lemniscus the rather uniform fiber pattern of the $ml_2$ component is distinct. It touches the central tegmental tract, from which it can be distinguished because the fibers of the latter are slightly smaller and still more uniform in size. The demarcation from the lemniscus lateralis also offers no problem for the same reason.

#### 5.2.2.3 Level of the Motor Trigeminal Nucleus

At the level of the motor trigeminal nucleus the medial lemniscus covers the ventromedial margin of the tegmentum pontis and shows a flattened, horizontal structure, in whose medial extent the coarse $ml_3$ fibers constitute the predominant component. They are grouped into small bundles, spreading amongst the cells of the processus medialis griseum pontis, which breaks up this medial portion of the lemniscus into small fascicles. Immediately dorsal to this nucleus, the descending branch of the brachium conjuctivum is seen with some coarse lemniscal ($ml_3$) fibers infiltrating the otherwise monotonous field of smaller fibers. In the lateral half of the medial lemniscus an intensive intermingling of the $ml_3$ with the other two components occurs. Yet, although it proves to be impossible to locate $ml_1$ and $ml_2$ as definitely at high bulbar levels, the dorsal quarter seems to contain more delicate fibers ($ml_2$) than the ventrolateral part of this half.

Corticofugal fibers (H5671, Fig. 13, sections 3 and 28; see also Usunoff et al. 1997, Voogd et al. 1990, for an extensive description) similarly can be seen in great numbers to pass through the pontine medial lemniscus at the level of superior colliculus. At caudal pontine levels they constitute dorsally directed bundles, coursing perpendicular to the lemniscal fibers. More rostrally they are found within the areae nebulosae forming islands of degeneration at the medial ventral edge of the medial lemniscus. The two types of fibers in the pontine medial lemniscus can be discerned and they give it its characteristic aspect at this level. Moreover, in the caudal pons a bundle can be traced of degenerated corticofugal fibers (fibres aberrantes bulboprotuberantiels de Jumentié; see Winkler 1920). These fibers turn rostrally and cross the medial lemniscus medially at the level of the facial nucleus (see arrow in Fig. 13, section 3 and 28). Disruption of these corticofugal fibers at pontine levels due to a lesion in the medial lemniscus must be responsible for the cheiro-oral deficiencies in man (Usunoff et al. 1997), since cortical steering of cheiro-oral brain stem nuclei is disrupted (see Shintani et al. 2000; Takamatsu et al. 1991; Takezawa et al. 1990).

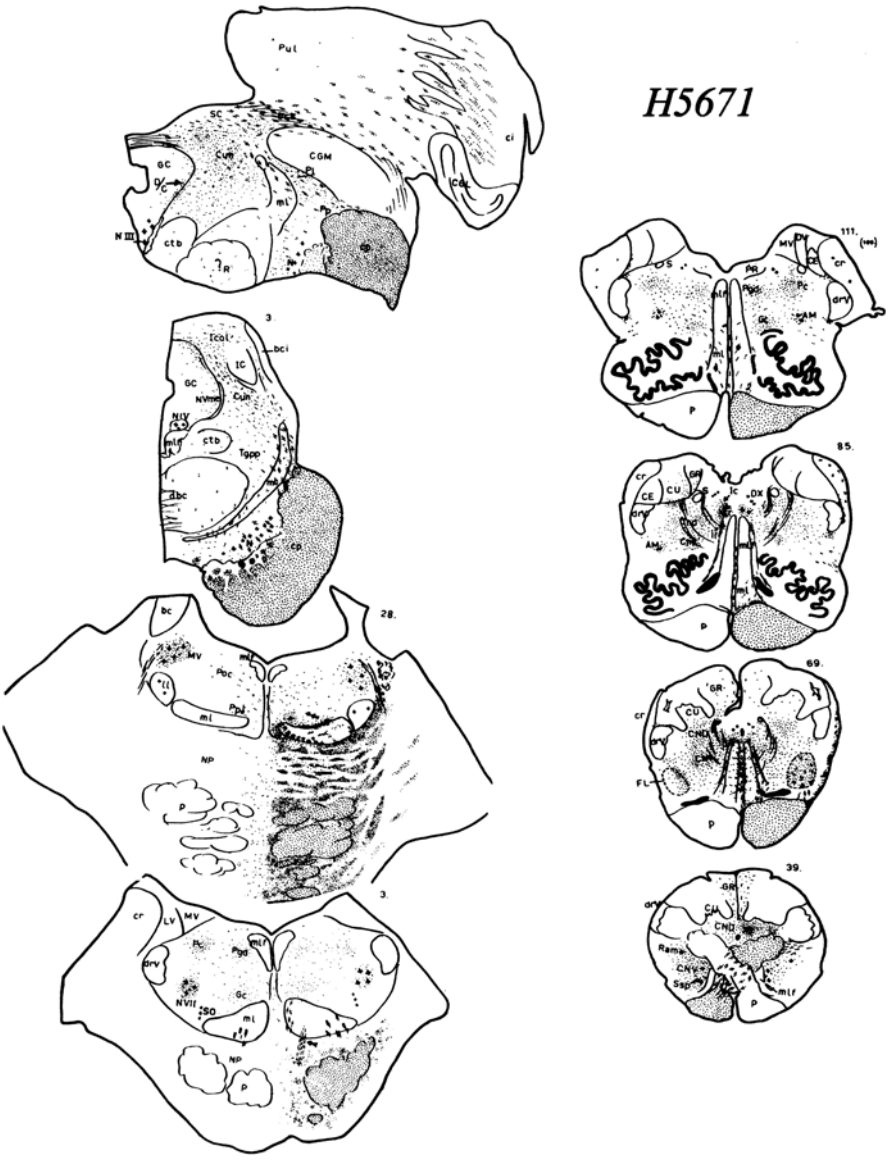



**Fig. 13** *Stippled* diagram of the degeneration in series H5671. Note *arrows* in sections *3* and *28* (see text)

#### 5.2.2.4
#### Level of the Rostral Pons

Rostrally in the pons, a flat elliptic area of small fibers comes to lie at the dorsal margin of the medial lemniscus. This area, representing its trigeminal princeps nucleus component ($ml_p$ component) gradually enlarges rostrally, but caudalward it rapidly loses all its fibers. These fibers leave in a medial direction, and are, therefore, longitudinally cut in transverse sections. They traverse the descending branch of the brachium conjuctivum, decussate and, subsequently converging slightly, pass along and sometimes through the ventral margin of the central tegmental tract. They arrive in the tegmental region just ventral to the motor trigeminal nucleus, where they somewhat diverge and can no longer be discerned. This invisibility is due to their once more changing direction in this area, from mediolateral to rostrocaudal. In horizontal sections they are seen to converge toward the ventrocaudal pole of the principal trigeminal nucleus, which they enter after traversing the rootlets of the trigeminal nerve. In transverse sections they are localized medial to the radix motoria of the trigeminal nerve, interposed between the trigeminal motor nucleus and the ventral spinocerebellar tract dorsally, and the lateral lemniscus ventrally (see also Usunoff et al. 1997). They are conspicuous when traversing the trigeminal rootlets and when their fine fibers enter the ventral half of the princeps sensory trigeminal nucleus.

Rostralward this $ml_p$ area gradually enlarges and covers the middle third of the medial lemniscus. This area is densely packed with uniformly sized fibers with a diameter of 2 μm in Häggqvist series. Even more rostrally, infiltration of their area by other elements is noted, especially the $ml_3$ component fibers, caused by change in position and shape of the medial lemniscus at the pontomesencephalic junction.

The decussating $ml_p$ component occupies a large elliptic area rostral and ventral to the trigeminal nuclear complex, caudal and ventral to the nucleus centralis superior, caudal to the decussation of the brachium conjunctivum, and medial to the descending branch of the brachium conjunctivum. They are most marked in the paramedian area and lost more laterally among the other structures.

#### 5.2.2.5
#### Caudal Mesencephalic Levels

At caudal mesencephalic levels the medial lemniscus is gradually pushed into the lateral parts of the tegmentum by the enlarging decussated brachium conjunctivum. It acquires the shape of a horn with its base directed medially. It borders the lateral margin of the brachium conjunctivum, while its apex is directed laterally and dorsally. In the extreme dorsomedial corner of the lemniscus the small fibers of the $ml_p$ component intermingle with a great number of others, mostly coarse fibers of the $ml_3$ component. This intermingling increases rostrally. Although the coarse fibers predominate in its medial half and the finer fibers seem to prevail in its lateral extent, a clear subdivision of the main components has disappeared.

#### 5.2.2.6
#### Rostral Mesencephalic Levels

At rostral mesencephalic levels the lateral extremity of the medial lemniscus extends more dorsally into the small area between the brachium of the inferior colliculus and the so-called thalamopetal bundle, finally to fuse with this latter bundle. Striking is the reticulate aspect of the medial lemniscus all along its course through the midbrain; this is caused by great quantities of delicate cortical fibers, splitting the lemniscus up into numerous bundles. Still more rostrally, its club-shaped appearance still containing the thalamopetal bundle, the lemniscus borders the medial geniculate body. At the level of the posterior commissure the vertical limb of the medial lemniscus shortens and, bending medially, approaches the dorsal margin of its horizontal limb. Soon they fuse into a more or less triangular area, hardly to separate from the surroundings. From here on it proves impossible to follow its constituents separately by their fiber composition.

## 5.3
## Degeneration Studies from Pathological Material

In this section an attempt will be made to present conclusive evidence from cases in which small, mostly vascular lesions have damaged part of either the medial lemniscus or the internal arcuate fibers.

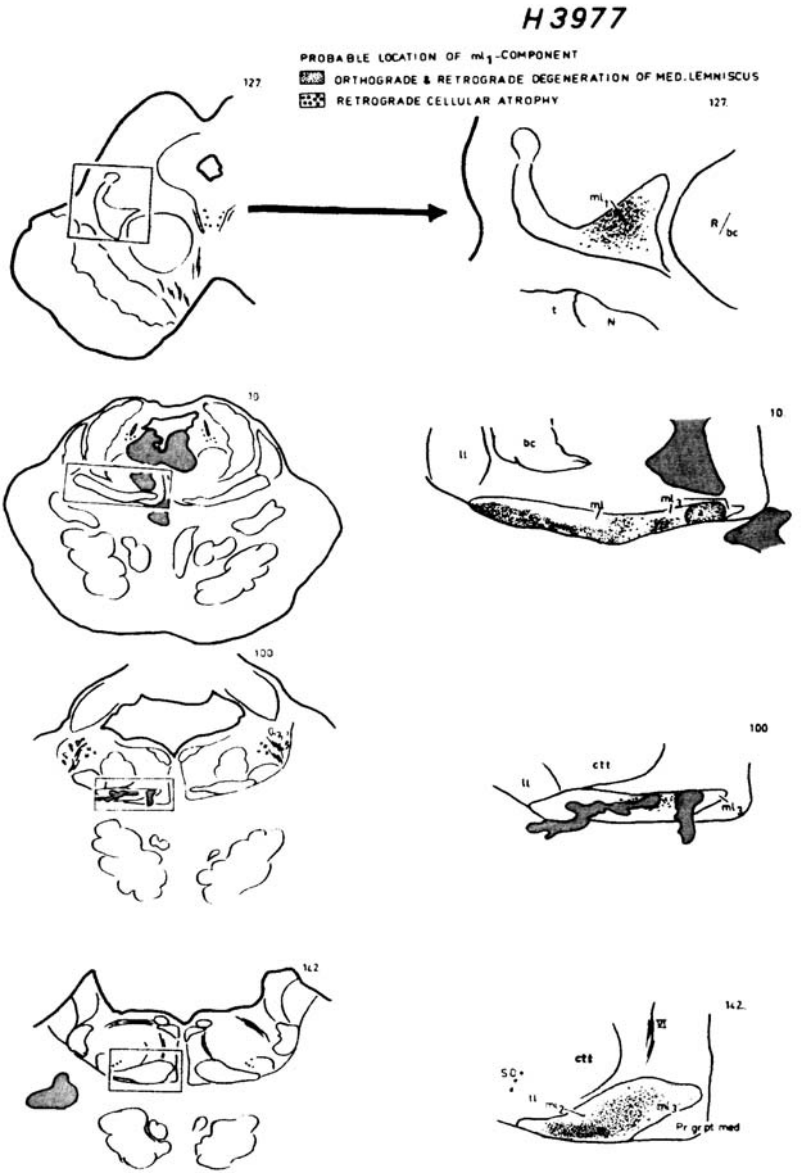
### 5.3.1
### H3977 $ml_1$ and $ml_p$ Components of the Medial Lemniscus

This case with a 4-month survival time showed degenerated lemnicus fibers distinctly, since the lemniscal fibers degenerate retrogradely in a relatively short time. The medial lemniscus at the level of the motor and princeps sensory trigeminal nuclei contains a circumscribed lesion that predominately affects its ventral half, with a small extension into its dorsal part. Just medial to it a second, smaller lesion is present (Fig. 14)

### 5.3.2
### H3977 $ml_1$

At the level of the abducens nucleus the degeneration in the medial lemniscus is clearly present in its ventral part, tapering out into its central and dorsal portions, partially intermingling with some degenerated $ml_3$ fibers (caused by the medial of the two lesions). At rostral bulbar levels the $ml_1$ component is degenerated in its

**Fig. 14A, B** The location of the $ml_1$ compartment in the medial lemniscus. Drawings made of sections of H3977**.** Both orthograde and retrograde degeneration and retrograde cellular atrophy is indicated


H 3977
PROBABLE LOCATION OF ml1-COMPONENT
ORTHOGRADE & RETROGRADE DEGENERATION OF MED. LEMNISCUS
RETROGRADE CELLULAR ATROPHY
127
127
ml1
R/bc
t
N
10
10
ll
bc
ml
ml1
100
100
ctt
ll
ml1
142
142
VI
ctt
SO
ll
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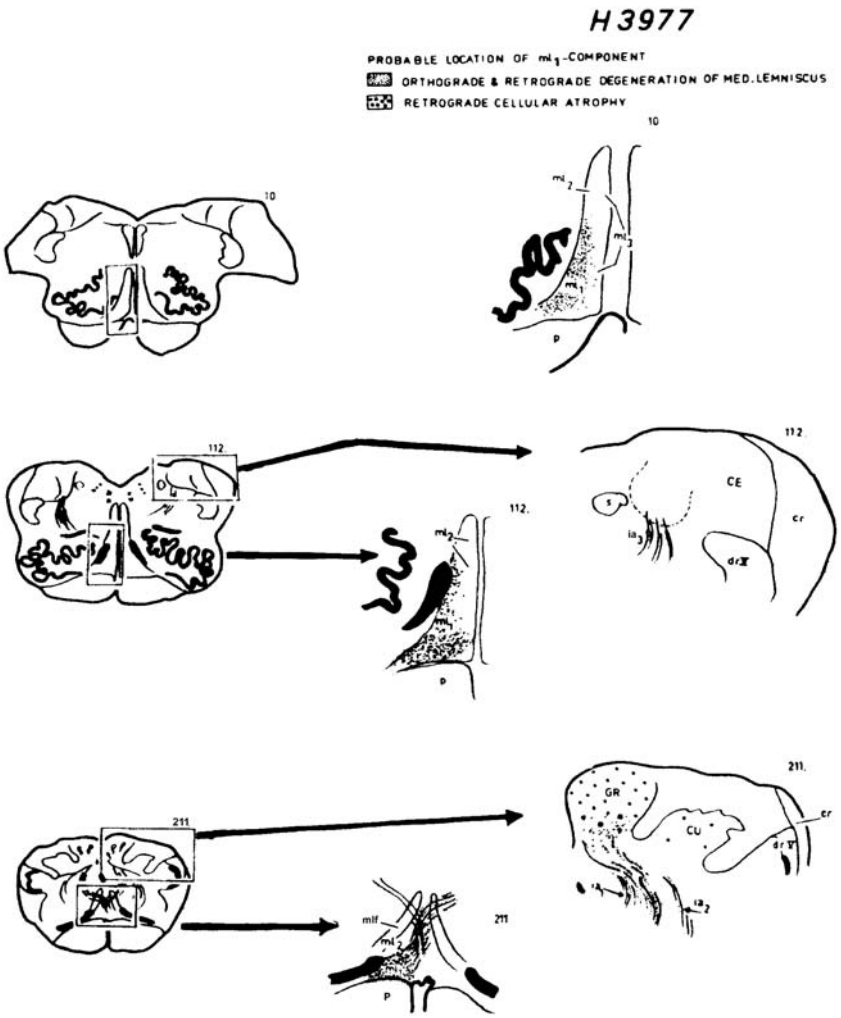
Pr gr pt med


H 3977
PROBABLE LOCATION OF ml1-COMPONENT
ORTHOGRADE & RETROGRADE DEGENERATION OF MED. LEMNISCUS
RETROGRADE CELLULAR ATROPHY
10
112
211
CE
GR
CU
cr
p

ventrolateral quadrant. The delicate $ml_2$ fibers dorsal to $ml_1$ are obviously intact. However, its medial demarcation towards the $ml_3$ component is not sharp, due to a very modest degeneration in the latter (Fig. 14).

At the level of the dorsal column nuclei, the coarse $ia_3$ fibers arising from the external cuneate subnucleus, producing the $ml_3$ component, disappear. The degenerated area gradually shifts more medially. Similar to findings in the normal material, this series proves that the $ml_1$ component rostrally is pushed laterally by the developing $ml_3$ component. Finally, at the level of the decussatio lemniscorum, the intact $ml_2$ area can easily be distinguished from the degenerating $ml_1$ fibers, which course in great numbers alongside the $ia_1$ fibers of the opposite side toward the DCN. It could again be maintained that, in this case, the $ia_3$ and the $ia_2$ fibers contain only very modest degeneration. The bulk of the degenerated fibers accompanying the $ia_1$ fibers reach the gracile nucleus, which together with the caudal part of the internal cuneate nucleus, exhibits a considerable cell loss (Fig. 14). This loss is less pronounced in the more rostral portions of the internal cuneate nucleus and is absent in the external cuneate complex. It is therefore justified to suppose that the pontine lesion affected mainly the $ml_1$ component and that this component, at least at rostral levels, occupies the ventral half of the medial lemniscus. The $ml_1$ component apparently maintains this ventral position throughout pons and medulla and originates as the $ia_1$ fibers from the gracile nucleus as well as from the caudal half of the internal cuneate nucleus. Rostralward it takes a position in the medial half of the mesencephalic lemniscus, more exactly in its dorsal and central portions, leaving free the most dorsomedial corner of the mesencephalic lemniscus and its medial border with the red nucleus.

### 5.3.3
### H3977 $ml_p$

This case also gives valuable information about the $ml_p$ component. The diagram in Fig. 14 shows the area of the decussating $ml_p$ fibers, just caudal to the decussation of the brachium conjectivum, to be damaged by a paramedian lesion. This lesion interrupts both the crossed and the uncrossed fibers. Consequently this $ml_p$ component, due to retrograde atrophy, lost most of its tiny fibers; the small streets splitting up the trigeminal rootlets are empty. This dearth of fibers coincides with a considerable cell loss in the main sensory trigeminal nucleus. In only its most dorsal portion are a few neurons preserved, these just ventral to the area where, more rostrally, the trigemino-thalamic tract appears. Diffusely spread bilaterally over the atrophic area are found a great number of fine degenerated axons. They are absent in the preserved part of the nucleus. This suggests that the $ml_p$ component arises in the atrophic part of the nucleus sensorius princeps n. trigemini, excepting its dorsal cap.

### 5.3.4
### H3382: The $ml_2$ Component

The series H3382 has been described in the thesis of Sie Pek Giok (1956) as his case XXXII, with regard to the position of the bulbar lemniscus in relation to the predorsal and medial FLM.

A syrinx exclusively interrupts the second type of internal arcuate fibers ($ia_2$) at their origin from the dorsal funiculus nuclei. The first and third type of internal arcuate fibers ($ia_1$ and $ia_3$ fibers) are intact. The characteristic appearance of the $ia_2$ fibers, sweeping broadly through the lateral tegmental area, is lacking completely. The opposite medial lemniscus is similar in that at this level it contains only the $ml_1$ component. At the caudal pole of the juxtarestiform body, however, the contralateral medial lemniscus conspicuously lacks its dorsolateral half, when compared to the homolateral one. This confirms the position of the other $ml_2$ component as described in normal material.

At caudal pontine levels this situation is unchanged, but more rostrally the lack of the $ml_2$ component becomes concealed by the intermingling of the ml components. At the level of the red nucleus the atrophy involves the whole medial lemniscus, although it seems greatest in its dorsal part at the fusion with the thalamopetal bundle.

### 5.3.5
### H5747: The $ml_2$ Component

This series contains a small ischemic lesion that only destroyed a part of the $ml_2$ component at rostral bulbar levels (see Fig. 16) The Nauta staining shows modest $ml_2$ degeneration in the dorsolateral part of the lemniscus at a caudal and in the dorsal part of the middle third of the rostral pontine level. This in general confirms the results of series H3382

### 5.3.6
### The $ml_3$ Component: H5517, H5579, H7251, and H5017

These series have been extensively described and documented in Usunoff et al. 1997. Here we give the diagram of series H5517 for the picturing of the $ml_3$ component (see Fig. 15). The ischemic lesion interrupts the very coarse third type of internal arcuate fibers ($ia_3$) originating from the medial subnucleus of the external cuneate nucleus. Due to the 9-month survival time the degenerating $ia_3$ fibers can clearly be seen traversing the medial reticular formation, the dorsal accessory olive, and the FLM, as well as the homolateral medial lemnicus. After decussation they bend sharply ventrally to take their position at the para-rapheal margin of the opposite lemniscus. In this series there was also degeneration of the FLM due to a recent lesion at the level of the abducens nucleus. However. the chronic degeneration stands out clearly. At caudal pontine levels the $ml_3$ degeneration is localized in the medial half, but at rostral pontine levels it not only fills the medial

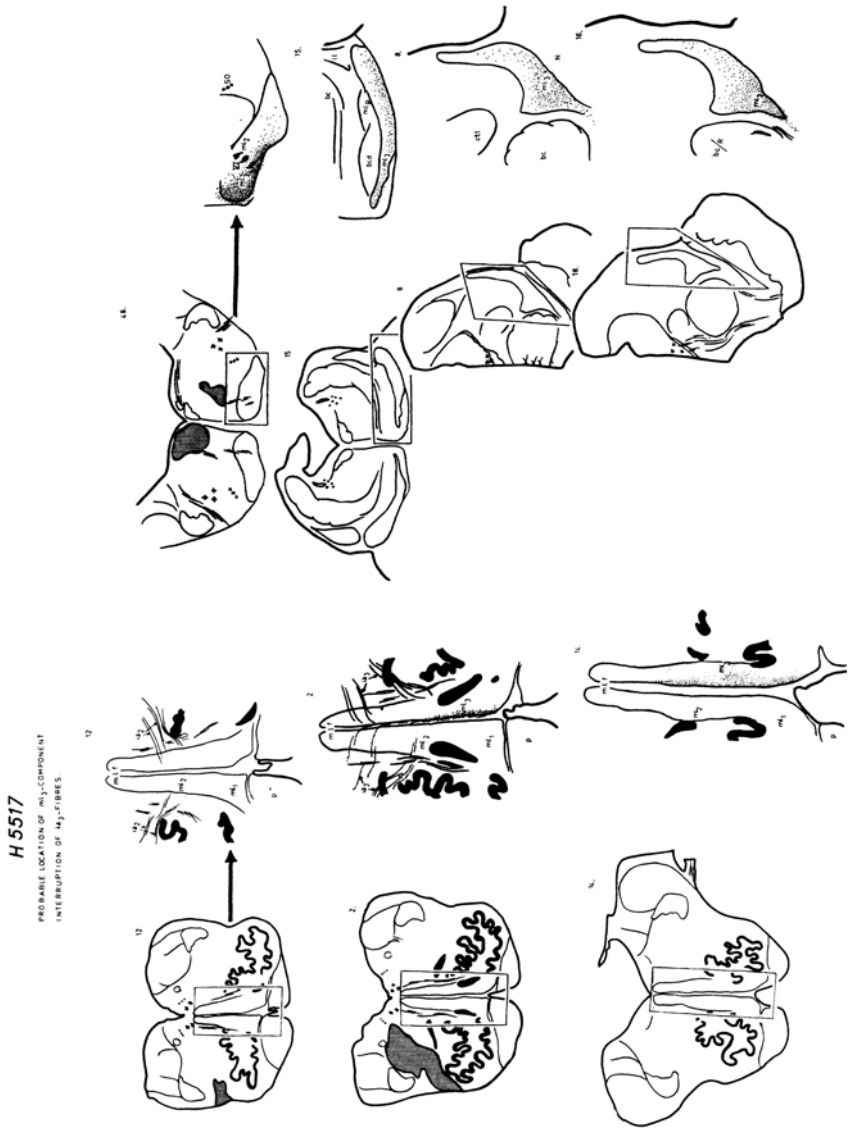



**Fig. 15** The location of the $ml_3$ component is shown by the interruption of the $ia_3$ fibers in series H5517

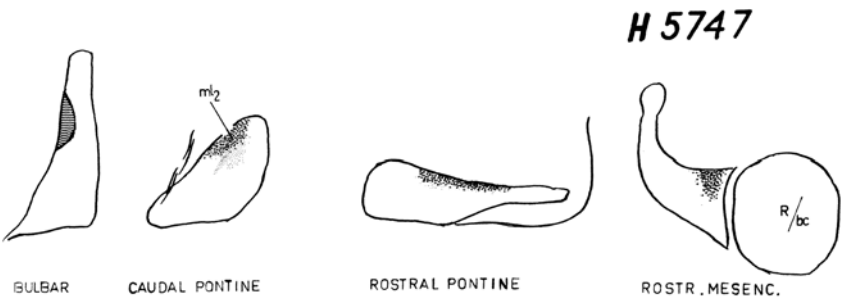



**Fig. 16** The $ml_2$ component and the lesion are shown in images of the medial lemniscus in series H5747

extent, but laterally it intermingles with the other lemniscal components, mainly in the ventral half. Striking is the presence of degenerated fibers in small bundles interspersed between the processus medialis griseum pontis. At mesencephalic levels the $ml_3$ degeneration occupies the medial, central and ventral portions of the horn-shaped medial lemniscus (Fig. 15).

Remarkably, even at high mesencephalic levels a slender elongation of degenerated $ml_3$ fibers from the ventromedial corner of the lemniscus curves like a finger around the ventral margin of the red nucleus. In the dorsomedial corner where the $ml_p$ component is located a few degenerated fibers can likewise be detected.

A similar picture is visible in H5579 (see Usunoff et al. 1997) where the $ia_3$ fibers are severed by a softening. The degenerated $ml_3$ fibers clearly take their position in the para-rapheal part of the bulbar lemniscus (see Fig. 17 of series H7251), although they, to some degree, also intermingle with intact fibers in the lateral half. Unfortunately, the sections of pontine and mesencephalic levels were not available for examination.

That the bulk of the $ml_3$ fibers at the rostral pontine level still keeps its original position in the medial half of the medial lemniscus is demonstrated by series H5017 (see Usunoff et al. 1997) with a longstanding lesion in the lateral half of the medial lemniscus at the transition of the pons to the midbrain. Intensive degeneration was present in both the $ml_1$ and the $ml_2$ components in combination with gracile and internal cuneate nuclei atrophy. The $ml_3$ component, the $ia_3$, and the ventromedial portion of the internal cuneate nucleus, however, remained almost intact, confirming the predominant site of the $ml_3$ component in the medial half of the medial lemniscus in this part of the brain stem.

### 5.3.7
### Termination of Medial Lemniscus H5412

The Nauta-Gygax sections of series H5412 show a gradual decrease in the number of degenerating spinal fibers. An unexpectedly large amount of preterminal degeneration is encountered in the VPL, though less apparent in the VPM nucleus of the thalamus (Fig. 1B). A small amount of preterminal degeneration is also present

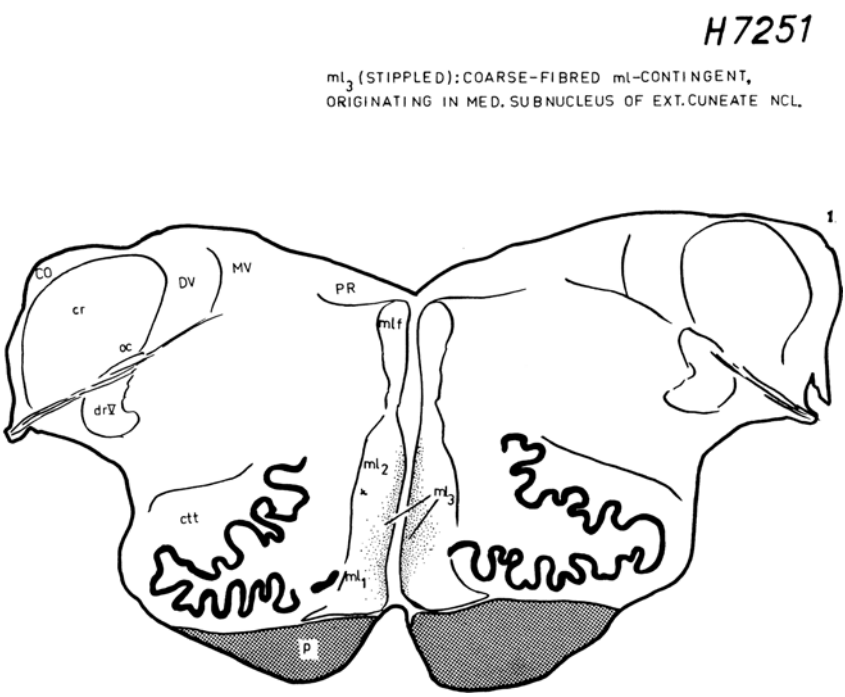



**Fig. 17** The distribution of the $ml_3$ component, originating from the repagulum or medial subnucleus of the external cuneate nucleus, is demonstrated at the inferior olive level

in the intralaminar nuclei, more precisely in the nucleus centralis lateralis, dorsal to the centre médian nucleus of Luys.

### 5.3.8
### Somatotopy in the Cuneate Nuclei: H5151, H5554, H7228, H4477

Extensive studies have been carried out on the somatotopy in the dorsal funiculi (see, e.g., Peerbolte 1932; Smith and Deacon 1984). These results, whether collected by the Marchi method or by using modern tracer studies, are part of the debate on the topography of primary afferent fibers in man. In this part, the projections of the cervical roots on the dorsal funiculus nuclei are exemplified.

The diagram (Fig. 18) depicts the results of three cases. In the first one (H5554; see Usunoff et al. 1997) the upper two cervical roots were sectioned. The ascending degeneration in the fasciculus cuneatus is present in the most ventral part, bordering the spinal trigeminal tract and its nucleus, which due to a metastasis destroyed the trigeminal nerve and also shows degeneration. The upper two cervical roots prove in Nauta sections to project to the most ventral part of the external cuneate nucleus, its so-called medial subnucleus included. The trigeminal degeneration on its way toward the solitary tract nucleus seems to pass along the ventral side of this nucleus (see also Usunoff et al. 1997), but evident termination is not found in

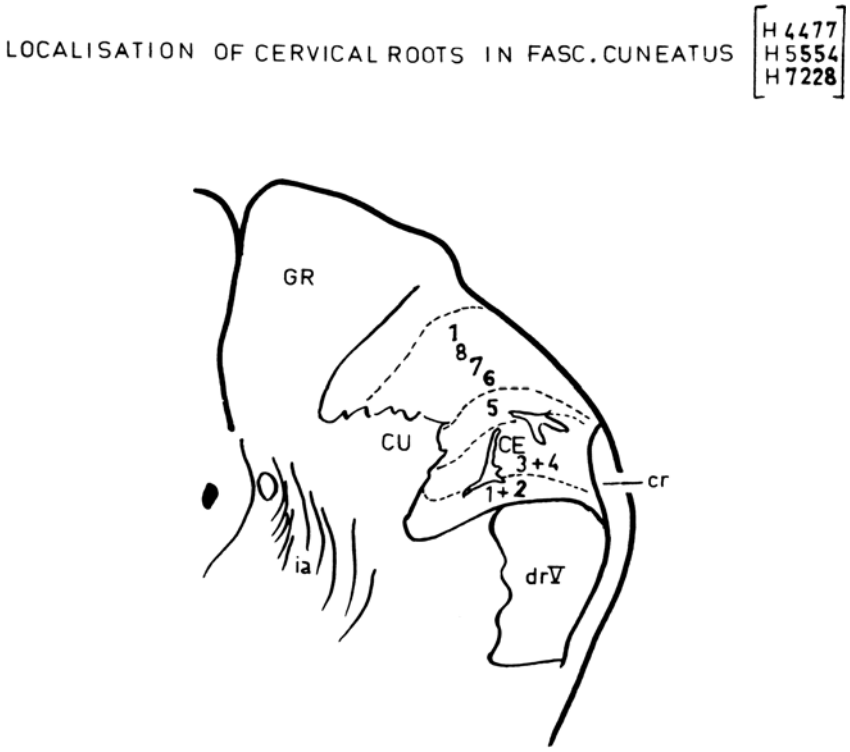



**Fig. 18** Localization of the degeneration of the cervical roots in the cuneate fascicle and the cuneate nuclei. H7228 rhizotomy of C6–8 and T1, H5554 rhizotomy C1 and C2, H4477 cordotomy C5

it. The same observation is made in H5151 (see Usunoff et al. 1997) with spinal trigeminal tract degeneration. This medial subnucleus, therefore, receives afferents from at least the two upper cervical roots, but none from the spinal trigeminal tract. That this subnucleus is not to be considered as a part of the external cuneate nucleus proper is evidenced by longstanding cerebellar lesions, which causes retrograde atrophy of the external cuneate nucleus along the restiform body, this medial subnucleus remaining unchanged (see also Voogd et al. 1990).

In the second case (H7228), in which the roots C6–8 and T1 were severed, the degeneration is present in the dorsal part of the fasciculus cuneatus (bordering the dorsal margin of the internal cuneate nucleus) and shows a remarkable ventrolateral prolongation along the periphery of the cord. The projections to the medial subnucleus are, due to a failure of the Nauta technique, unclear.

The same distribution of degeneration holds for the third case (H4477) in which a complete transverse lesion at C5 lasted 4 months. The Häggqvist stained sections showed how the intact root fibers of the upper four cervical segments assemble in the ventral half of the cuneate fascicle.

### 5.3.9
### The Medial Subnucleus of the Internal Cuneate Nucleus

The medial subnucleus produces the $ia_3$ fibers. In a series (H6995) with a cerebellar lesion the restiform body contains atrophy, as does the external cuneate nucleus. However, the medial subnucleus does not show atrophy. In series H5554 (see Usunoff et al. 1997), with a rhizotomy of C1 and C2 and a tractotomy of the trigeminal root no clear degeneration was found in this subnucleus. In series H5631 (see Voogd et al. 1990) the medial subnucleus was seen to receive spinal degenerated fibers from a bilateral anterolateral cordotomy at T2, as is the case in series 7085 after a cordotomy at T5 (see Fig. 6) The fibers pass via the supratrigeminal nucleus, along the dorsal edge of the spinal tract of the trigeminal nerve into the medial subnucleus.

## 6
## Discussion on the Medial Lemniscus

Although a great number of publications have been dedicated to the medial lemniscus, restricted attention has been paid to the human medial lemniscus, except for the papers by Rasmussen and Peyton (1948) and the thesis of Sie Pek Giok (1957). Edinger's (1885) investigations leading to the conception of a crossed spinothalamic pathway, mediating pain and temperature, originally was set up to refute the previously held assumption that the posterior funiculus fibers are destined for the contralateral restiform body after traversing the inferior olivary complex. Edinger (1885) demonstrated the fibers so destined to be in fact internal arcuate fibers ascending rostralward in the crossed medial lemniscus. There is nowadays-total consensus that the majority of the fibers of the medial lemniscus originate in the contralateral dorsal column nuclei. Controversial, however, is still the existence of a certain lamellation of its constituents.

### 6.1
### Dorsal Column Nuclei Components

Walker (1938) in his study on the thalamic afferents in the chimpanzee made a lesion of the right internal cuneate nucleus and the left gracile nucleus. The resulting Marchi degeneration in the bulbar medial lemniscus was laminated in such a manner that the efferents from internal cuneate nucleus were localized in the dorsal portion of the medial lemniscus. Although Walker (1938) mentions an intermingling of the lemniscal constituents in the pons, he believed this lamellation was retained to some degree even in the mid brain.

Matzke (1951) mostly denies such a lamination, although the manner of decussation from the dorsal funiculus nuclei as described is supported in his monograph. Moreover, he seems to give some indication of a $ml_2$ component, when he writes: "However, in the lower pons scattered degeneration dorsal to the main body of

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the medial lemniscus is noted only when the cuneate nucleus is involved." Still the majority of the advocates of a certain lamination within the medial lemniscus agree on the localization of the gracile component ventrally in the bulbar lemniscus and the cuneate component dorsally. More rostrally in the brain stem the lemniscus as a whole shifts in such a manner that the gracile component occupies its medial and the cuneate component its lateral half (von Bechterew 1895; Ferrier and Turner 1895; van Gehuchten 1903; Dejerine 1910; Winkler 1917; Ferraro and Barrera 1936).

In the cat (Busch 1961; Verhaart's atlas 1964) $ml_1$ is located laterally and $ml_2$ medially, but $ml_3$ is lacking. The $ml_c$ component is very distinct in the cat, but absent in man, since the nucleus cervicalis lateralis is not developed. The situation in Macaca is more or less similar, although Ferraro and Barrera (1936) mention, that in the monkey the $ml_1$ component is found ventrolateral and $ml_2$ dorsomedial in the medial lemniscus. This corresponds with the findings described herein, although Ferraro and Barrera did not mention explicitly an $ml_3$ component. From the Häggqvist Macaca series we can conclude that the $ml_3$ component is not as distinct as in man. The medial subnucleus of the internal cuneate nucleus in the monkey is well developed, but the internal arcuate fibers sprouting from it are more medium sized than in man.

The most evident difference from cat and monkey is the presence in man of $ml_3$ at high bulbar levels, located para-rapheal. This third component of the medial lemniscus in man is in most instances not recognized except in De Graaf's (1967) thesis. The statements of Rasmussen and Peyton (1948) that the medial lemniscus extends over a larger surface, intruding into the FLM, than usually indicated in textbooks, could not be confirmed by our studies.

Apparently some kind of lamination does exist in the human medial lemniscus: originally gracile fibers ventral and internal cuneate fibers dorsal. This topography changes if the third component is added, to take its position in the medial, para-rapheal part of the medial lemniscus. The other two components are shifted laterally. This dorsoventral somatotopy is maintained at pontine levels and is lost in the midbrain due to intermingling of these components.

## 6.2 The Trigeminal Component

The trigeminal component of the medial lemniscus in man is well developed. Immediately after its rostral pontine decussation, this trigeminal component can be detected as a newly added area of uniformly sized small fibers in the dorsal part of the lemniscus. At the caudal mesencephalic level it occupies mainly the dorsomedial angle of this tract, but more rostrally the fibers are lost sight of due to an intensive intermingling, mainly with the $ml_3$ component in normal material. In retrograde degeneration (H3977) the fibers can be traced into the contralateral princeps trigeminal nucleus. This series also gives strong evidence that this trigeminal component originates in the main sensory trigeminal nucleus,

except for its utmost dorsal portion, as substantiated by Carpenter (1957). This dorsomedial part does not project via the medial lemniscus but via the homolateral dorsal trigeminothalamic tract of Wallenberg (see also Usunoff et al. 1997).

The divergence of the opinions about the projection of the main sensory trigeminal nucleus via the contralateral medial lemniscus should be partly attributed to differences in the species studied:

- Rat and cat with a large trigeminal lemniscus, but an inconspicuous dorsal trigeminothalamic projection
- Perisso- and artiodactyla with the reverse situation

It therefore is important to discern, in the principal trigeminal nucleus, a dorsomedial and a ventrolateral division giving rise to the lateral dorsal trigeminothalamic tract of Wallenberg and the trigeminal lemniscus, respectively. (For an extensive discussion on trigeminothalamocortical connections see Usunoff et al. 1997.)

### 6.3
### The Cervicothalamic Component

In man no definite nucleus cervicalis lateralis can be established. At most, a very few scattered cells can be detected in the dorsolateral funiculus of the upper cervical spinal cord. This explains the absence of a cervicothalamic component in the medial lemniscus of man, as described in cat (Busch 1957) and rabbit (Matricali 1961).

The lateral cervical nucleus appears to relay touch pressure and vibration information, largely from hairy skin, to the contralateral thalamus, inferior olive and midbrain. In humans the lateral cervical nucleus may be a rudimentary structure because it is well defined only in some individuals (Truex et al. 1965). In such humans, the nucleus contains up to 4,000 neurons, while nearly double that number may exist in cats (Boivie 1983).

Remarkable, however, is that while in the cat's midbrain the $ml_c$ fibers are located in the dorsolateral extremity of the medial lemniscus, touching the central acoustic tract, in man this central acoustic tract is replaced by the so-called "thalamopetal" bundle, which is known to contain, among others, the remaining fibers of the spinothalamic tract. So in man a slight dorsalward shift is present.

The material presented herein does not allow conclusions on the termination of the medial lemniscal fibers in the inferior colliculus and other nuclei of the brain stem, due to the use of mainly Häggqvist sections. The same holds for the termination at thalamic levels.

### 6.4
### Internal and External Cuneate Afferent Projection Areas

The functional and topographical organization of tactile input from the hand into the internal cuneate nucleus in man is unknown, but speculated upon (see Florence

et al. 1989). Using physiological methods in monkeys (Xu and Wall 1999) the tactile response over the internal cuneate nucleus has been studied, but a topographical division is not evident. Such a functional topographical organization within the DCN is masked by the scrambling of fibers (Pubol et al. 1965), which contrasts sharply to the detailed somatotopic organization in the dorsal columns (Walker and Weaver, Macaca, 1942). The study of Smith and Deacon (1984) shows the afferent projection areas in man from the cervical spinal nerves in the internal cuneate nucleus in man. The distribution is clearly perpendicular to the pial surface and is laminated in structure. The laminar distribution in the posterior columns as debated by Smith, (1957; Smith and Deacon 1984) in man versus Peerbolte (1932) in cat can be traced back to the results of Kahler-Pick (see, e.g., Mott 1895; Russell 1898) versus Bok (1928). The Kahler-Pick arrangement in the posterior columns accepts lamina or flat ribbons perpendicular to the pial surface. On embryological investigations, Bok (1928) suggested a bowing of the lamina around the paramedial septum. The projection areas in the cuneate nuclei are, according to the position of the cervical spinal nerve, those of primary afferents, as described by Smith and Deacon (1984). However, this lamination in man turns from T1 medial to the internal cuneate nucleus toward C1 and C2 laterally into the external cuneate nucleus. This topography, however, is clearly different from the one described in Walker and Weaver (1942) for *Macaca mulatta*. In Macaca: "The fibers originating in the caudal segments and situated in more medial portion of the cuneate fascicle terminate in the medial part of *both* the nuclei cuneatus proprius (internal) and cuneatus externus, .... The fibers of the fasciculus cuneatus that originate from upper cervical posterior roots terminate in the lateral part of the main (internal) and external cuneate nuclei." (Walker and Weaver 1942). A bifurcation of each segmental cervical posterior root endings is proposed. One series of axons or branches somatotopically ends in the internal cuneate nucleus, the other in the external cuneate nucleus. This repetition of somatotopy in the internal and external cuneate nucleus for the cervical fibers is not supported by our results in man, and also not by Pubol et al. 1965 (see their Fig. 14) and Cliffer and Willis (1994). The latter authors describe that after *Phaseolus vulgaris* injections into the cervical spinal cord, a projection of postsynaptic fibers was demonstrated in the pars rotunda and the external cuneate nucleus of monkeys, supporting our initial results.

The external cuneate nucleus is generally considered to project to the cerebellum. However, the external cuneate nucleus also projects to the thalamus in rats and monkeys, but not in cats ( Albe-Fessard et al. 1974, 1975; Boivie et al. 1975; Fukushima and Kerr 1979; Boivie and Boman 1981; Massopust et al. 1985; Mantle-St John and Tracey 1987; Cliffer and Giesler 1989). "Presumably, neurons of the lateral cuneate nucleus that have a thalamic projection belong to the somatosensory system" (Willis and Coggeshall 1991).

At least in various species, including monkeys, the external cuneate nucleus cannot be considered to project exclusively to the cerebellum, and the residing thalamic projection neurons relay somatosensory information. Our findings point

to a rather large relay system from the lateral cuneate nucleus toward the thalamus in Man.

Till now the sensory somatotopic representation of the afferent projections into the dorsal column nuclei has only been verified in species other than man. Walker and Weaver (1942) showed projection areas for C7 and C3, but could not demonstrate a laminated somatotopical arrangement in the dorsal column nuclei. In the first part of this monograph we described a termination of the afferents in the periphery of the cell clusters, the so-called shell localization (Snow and Wilson, 1991) without any somatotopy in the gracile nucleus. For the cuneate nuclei, however, a laminar somatotopy emerged from the lesions H4477, H5554, and H7228. The endings of C7 and C8 are located just over the pars rotunda of the internal cuneate nucleus, which is in accordance with the digit projections as elaborated by Florence et al. (1989) in monkeys.

### 6.5
### The Medial Subnucleus of the Internal Cuneate Nucleus: The Repagulum

The terminology of (sub)nuclei around the cuneate nuclei and the paratrigeminal region is confusing (broadly discussed in Usunoff et al. 1997). The position, extension and the appearance of the neurons in several stainings undoubtedly infers that the medial subnucleus of the internal cuneate nucleus is identical with the repagulum cuneati of Braak (1971), also known as the medial pericuneate nucleus of Paxinos and Huang (1955). Therefore, the $ai_3$ fibers originate from the repagulum or medial pericuneate nucleus and produce the $ml_3$ compartment.

### 6.6
### The Dorsal Column Nuclei and Nociception

Electrophysiological studies addressed for the first time the role of the dorsal columns in mediating visceral pain (Amassian, 1952). More recently, Berkley et al (1993) and Berkley and Hubscher (1995) have shown that the nucleus gracilis neurons can be activated by distension of vagina, uterus, and colon; and the half of the nucleus gracilis cells that respond to cutaneous stimulation are also activated by uterine or vaginal distension. Apkarian et al. (1995) even suggested that the DCN may be more important for visceral pain than is the spinothalamic tract. Willis and his colleagues published a comprehensive series of papers that unanimously demonstrate the profound involvement of the DCN in the transmission of visceral pain via the dorsal columns and medial lemniscus (Al-Chaer et al. 1996 a, b; 1997, 1998; Nauta et al. 2000; Wang and Westlund 2001; Palecek et al. 2002, 2003).

These nociceptive inputs reach the DCN via two routes:

- Monosynaptic input from primary afferent cells in the spinal ganglia
- A pathway consisting of two neurons: primary afferent neuron and a neuron in the spinal cord gray matter.

The "classic" monosynaptic nociceptive input was described repeatedly (Kuo and De Groat 1985; Conti et al. 1990; Patterson et al. 1989; Willis and Coggeshall 1991, 2003). According to Conti et al. (1990) the nociceptive input to the DCN may be mediated, though to a very limited extent by way of small substance –P containing primary afferent neurons.

Far more important is the second route, via the so-called " postsynaptic fibers", traveling in the dorsal columns. By this bisynaptic pathway the central process of the primary afferent neuron terminates upon a second-order projection neuron, located in the gray matter of the spinal cord. The axons of these neurons, the postsynaptic fibers, reach the DCN (Petit 1972; Rustioni 1977; Rustioni and Kaufman 1977; Rustioni et al. 1979; Cliffer and Willis 1994; Hirsch berg et al. 1996).

Rustioni 's group (Rustioni 1977; Rustioni et al. 1979) investigated the cells of origin of postsynaptic fibers in monkeys. They found that the fibers originate mainly from the ipsilateral dorsal horn, particularly from its medial part at upper cervical levels and from a band of gray matter throughout the spinal cord, largely corresponding to lamina IV and adjacent laminae. In the cat (Rustioni and Kaufman 1977) the cells of origin are numerous in the upper cervical, brachial, and lumbosacral spinal cord, but sparse in thoracic segments. The cells of origin are mainly in lamina IV. Hirschberg et al. (1996) reported a population of cells of origin in lamina X at the sacral level of the rat spinal cord.

In our study we have hardly been able to distinguish primary and secondary afferents in the DCN. However, those lesions that exclusively involve the spinal nerves or their ganglia should exclusively show the primary afferents in Nauta degeneration sections. This does not hold for the laminated structure in the internal and external cuneate nuclei, since our projection compares to the postsynaptic dorsal column projections in monkeys (Cliffer and Willis 1994), and we cannot show a selective projection on the pars rotunda for the primary afferents from the hand digits (Florence et al. 1989).

We cannot make any statement on the visceral nociceptive connections of the dorsal columns and their projections into the dorsal column nuclei, since exclusive lesions in the cervical gray matter are not present in our material.

## 7 Conclusion

This monograph demonstrates the unique position of the dorsal columns in man. Humans differ in the amount of internal arcuate fibers (Cajal 1911) and in the topography of the termination in gracile and cuneate nuclei (this monograph) from other experimental animals. For the gracile nucleus a so-called shell-like termination pattern is dominant, while for both cuneate nuclei a laminated termination pattern was found. The fibers originating from the dorsal column nuclei can be discerned both with classical staining and with degeneration in three components. These demonstrate a dorsoventral organization in the medial lemniscus in man

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instead of mediolateral organization as present in experimental animals. In literature the so-called $ia_3$ component of the medial lemniscus is neglected. Moreover, it was observed that the repagulum contributed to the medial lemniscus with $ia_3$ fibers.

Our series did not contain sections with the whole lemniscus exclusively degenerated that could be followed into the thalamus. However, since the external cuneate nucleus exclusively contained high cervical root termination, an extensive projection from this nucleus toward the thalamus can be expected in future human research.

The dorsal column fibers do not reach the repagulum, but do reach nuclei present in the central gray, just above the central canal (Cajal's nucleus intermedius and the supraspinal nucleus). These new findings, together with the absence of a nucleus cervicalis lateralis in man (Truex et al. 1965), mean that the organization of the transitional area from spinal cord to the brain stem is different in man compared to experimental animals.

The nuclei of the restiform body (Braak 1970, 1971), including the repagulum, which is nearly nonexistent in non-primates (Walker 1938a, b), do receive termination from spinal projections, but seemingly not from the dorsal columns. The results for the nuclei of the restiform body are new for man (this monograph) and stress the differences for the transitional area between spinal cord and brain stem.

The spinothalamic pathway was thought to contain a mediolateral organization (Walker 1940; Schwartz and O'Leary 1942; Glees 1951; Glees and Bailey 1951). The observations presented in this monograph support a dorsoventral organization at low bulbar levels. Based on the projections of the thalamopetal bundle and the spinothalamic pathway endings in the human, these tracts are not equivalents as stated by Glees and Bailey (1951).

The cervicothalamic tract is absent in man. In cats this tract joins the medial lemniscus laterally. In man the spinothalamic tract joins the medial lemniscus at the level of the thalamopetal bundle.

## Appendix: Description of the Pathology Cases Used in this Study

The pathology cases that follow were mentioned in this paper. The serial sections and the clinical and pathology notes on them are kept at the Department of Physiology, University of Leiden.

**H3382** A 50-year-old man presented with paraplegia, starting in the left leg and later involving the right leg. Hypesthesia at T12 and L1 and hypesthesia and hyperalgesia was found in both legs. The patient died suddenly, dyspneic, cyanotic, and in shock. Diagnosis was tumor medulla spinalis at the level of L1. Thrombosis in the left femoral vein was found at autopsy, together with multiple lung embolisms. Syringomyelia was found in the upper lumbar segments. The amount of gray substance was reduced in the spinal cord, and a flat spinal cord was noted at all thoracic levels. In the medulla a gliotic fissure was seen throughout the level of the

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caudal half of the nucleus N.XII. It extended from the medial side of the descending branch of N.V to the dorsal side of the nucleus N. XII.

**H3655** A 66-year-old man suffered from psychotic dementia. Compressio medullae was caused by fracture of the dens of C1 after a fall, resulting in a total cordotomy. The patient died 6 months later of respiratory insufficiency. The cerebrum showed no distortions. Paraffin Häggqvist transverse sections were made.

**H3977** A 46-year-old man suffered from basilar thrombosis, dysarthria, strabismus divergens, tetraplegia, and had a strong lues reaction. After 3.5 months of lues treatment the patient died cachectically. His brain weighted 1,140 g and showed pons softening. The spinal cord was small.

**H4477** A 17-year-old boy suffered a cordotomy from diving. Tetraplegia and subluxation of C6 was found clinically. The patient died 4 months later. A total cordotomy was found at the C4/5 level. After transverse sectioning and Häggqvist staining. the lesion was found to extend up to C2.

**H4685** A 60-year-old woman lived for 13 years after being operated on for a rectal carcinoma, at which time a total cordotomy was carried out at T2/3 for intractable pain. Six weeks later she died of septic phenomena. Nauta staining of the medulla oblongata was unsuccessful. Häggqvist staining was carried out on the other parts and the medulla.

**H5017** A 58-year-old man was in coma following severe head trauma (transport accident) and died 4 months later without regaining consciousness. The autopsy revealed brain stem and cerebellar lesions. The lesions in the brain stem comprised the lateral half of the pontine tegmentum rostral to the trigeminal nerve entrance on both sides. On the left the lesion also involved a lateral portion of the midbrain tegmentum. On this side the rostral pole of the trigeminal motor nucleus and the lateral border of the medial lemniscus were damaged. There was softening of the anterior cerebellar lobe.

**H5151** A 51-year-old man was hospitalized with the clinical signs of an acute pontine lesion, probably of vascular origin. After 8 days the patient died and at the autopsy a thrombosis of the basilar artery was found. The right half of the pons was softened in its lateral part, and there was softening of the right cerebellar hemisphere and the right occipital pole.

**H5379** Due to a car accident this 32-year-old man incurred a total cordotomy at T5. Ten months after the accident the patient died from respiratory complications. Transverse paraffin Häggqvist sections were made.

**H5412** Male patient, 37 years old, suffered from a larynx carcinoma with metastasis in vertebra T12. Due to intractable pain a cordotomy was carried out at the levels T2, T3, and T4. At T2 andT4 a right anterolateral quadrant and at T3 a left anterolateral quadrant incision was made. Four weeks after the operation the patient succumbed suddenly from a lung embolus.

**H5517** A female, 65 years old, died 9 months after developing Wallenberg's syndrome. Clinical data are not available. Autopsy revealed an old malacia in the cerebral hemisphere and some recent infarcts in the pontine tegmentum. The Wallenberg syndrome was due to a large lesion in the medulla comprising the lateral part of the reticular formation, the anterolateral funiculus, and the spinal tract of the trigeminal nerve. The nucleus of the spinal tract was spared. A more recent softening was present in the caudal pontine tegmentum comprising both medial longitudinal fasciculi with the abducens nerve nuclei and the genu of facial nerve. The brain stem was embedded in paraffin and stained by the Häggqvist method.

**H5554** Male patient, age 54, suffered severe trigeminal neuralgia caused by thyroid carcinoma metastases infiltrating the base of the skull. As a palliative measure for intractable pain the patient underwent a unilateral tractotomy N.V at a level just caudal to the obex, over a distance of 3 mm, at a depth of 2.5 mm, and dorsal rhizotomies at C1 and C2. Three weeks after the operation the patient died from operative complications.

**H5579** In this patient, age unrecorded, a Wallenberg's syndrome developed 6 weeks before death. The autopsy revealed a lesion at the left side of the medullary tegmentum, destroying the anterolateral funiculus, the spinal trigeminal tract, and the external cuneate nucleus. There was a softening in the medial pontine tegmentum on the right side, partially damaging the corticofugal longitudinal pontine fascicles, the descending limb of brachium conjunctivum, and the predorsal bundle. Finally, on the left side there was a lesion of the middle cerebellar peduncle encroaching upon the trigeminal nerve roots.

**H5631** A 66-year-old man received bilateral cordotomies at T2 for intractable pain. He died 4 weeks after the operation. A recent compression of the cord was found at autopsy. The cord and the brain stem were sectioned transversely and stained according to the methods of Häggqvist and Nauta.

**H5671** A 56-year-old woman, struck by a cerebrovascular accident, died after 6 weeks from complications. There was softening in the superior and middle temporal gyri, in the lower part of the precentral gyrus, in the inferior frontal gyrus, and in the insula. Medially the softening extended into the lentiform nucleus and corona radiata (for an extensive description see Schoen 1969 and Voogd et al. 1990).

**H5747** A 67-year-old man died 6 weeks after an operation for otitis media. Autopsy revealed a well-encapsulated otogeneous brain abscess situated in the center of the temporal lobe, interrupting the connections of the inferior and middle temporal gyri. A small infarct was located in the superior temporal gyrus. In addition, small lesions in the brain stem interrupted the medial tegmental tract in the medial longitudinal fascicle at the level of the vestibular nuclei, and a lesion in the caudal bulbus was present in the contralateral lemniscus at the same level.

**H5800** This 69-year-old man developed an X-ray myelopathy resulting in a nearly total cordotomy at T7. A small part of the anterolateral funiculus was not involved. The patient died 1 year later from a secondary plano-cellular carcinoma of the right upper part of the lung. The spinal cord lesions established themselves over a period of 9 months. Transverse paraffin Häggqvist sections were made.

**H6688** This case concerns a female patient, 71 years old. Six years before her death a hemicordotomy of the anterolateral quadrant at T4 was made by two cuts with a distance of 22 mm for intractable pain. The medulla oblongata was stained for Nauta and frozen Häggqvist. Nauta staining was dissatisfactory. The pons and spinal cord were Häggqvist stained. The gracile funiculus contained degeneration at its dorsomedial side. The mesencephalon did not embed and stain.

**H6995** This male patient, age unrecorded, had a pseudobulbar syndrome with left side paralysis. The patient survived 1 month after a hemorrhagia cerebri. After autopsy this Wallenberg syndrome also showed an old cystic softening in the putamen and a left-sided infarct in capsula and putamen. There were left-sided softenings of the cerebellum and pons. The medulla oblongata was smaller on the left.

**H7085** A 55-year-old female underwent an uterectomy for sarcoma botryoides. One year later severe pain developed on the left side of the body. Metastases were found in the left leg. A laminectomy at T4–T5 was carried out followed by a right sided cordotomy. Three weeks later the patient died. The normal brain stem and the lesioned spinal cord were transversally sectioned and stained for Häggqvist and Nauta.

**H7228** A 68-year-old male underwent a rhizotomy of the dorsal roots C6, C7, C8, and T1 three weeks before death for intractable pain due to metastatic tumors. The tumors compressed the lower cervical cord, which gave rise to ascending degeneration in the ventrolateral and the dorsal funiculi bilaterally. Only demyelinization in the cuneate funiculus was studied, using the Klüver method.

**H7251** A 42-year-old man had suffered a left sided hemiplegia for 2 years due to a right-sided middle cerebral artery thrombosis. Twenty days after an acute coma due to a left-sided carotid thrombosis he died. The series shows pyramidal atrophy.

**H7980** A 60-year-old man died in a nursing home where he had been hospitalized for several years because of an olivopontocerebellar syndrome. Severe cerebellar ataxia and progressive spastic paraplegia were clinical symptoms. He died suddenly of a pulmonary embolism 7 years after the onset of the disease.

# References


Albe-Fessard D, Levante A, Lamour Y (1974) Origin of spinothalamic tract in monkeys. Brain Res., 65:503–509

Albe-Fessard D, Boivie J, Grant G, Levante A (1975) Labelling of cells in the medulla oblongata and the spinal cord of the monkey after injections of horseradish peroxidase in the thalamus Neurosci Lett 1:75–80

Albrecht,MH, Fernstrom RC (1959) A modified Nauta-Gygax method for human brain and spinal cord. Stain Technol:91–94

Al-Chaer ED, Lawand NB, Westlund KN, Willis WD (1996a) Visceral nociceptive input into the ventral posterolateral nucleus of the thalamus: A new function for the dorsal column pathway. J Neurophysiol 76:2661–2674

Al-Chaer ED, Lawand NB, Westlund KN, Willis WD (1996b )Pelvic viscera input into the nucleus gracilis is largely mediated by the postsynaptic dorsal column pathway. J Neurophysiol 76:2675–2690

Al-Chaer ED, Westlund KN, Willis WD (1997)Nucleus gracilis: an integrator for visceral and somatic information. J.Neurophysiol 78:521–527

Al-Chaer ED, Feng Y, Willis WD (1998)A role for the dorsal column in nociceptive visceral input into the thalamus of primates. J.Neurophysiol 79:3143–3150

Amassian VE (1952) Interaction in the somato-visceral projection system. Res Publ Assoc Res Nerv Ment Dis 30:371–402

Apkarian AV, Brüggemann J, Shi T, Airapetian LR (1995) A thalamic model for true and referred visceral pain. In: Gebhart GF (ed) Visceral pain IASP Seattle pp. 217–259

Apkarian AV, Hodge CJ (1989) Primate spinothalamic pathways: III. Thalamic terminations of the dorsolateral and ventral spinothalamic pathways. J. Comp. Neurol. 288:493–511

Atweh SF, Kuhar Ml (1977) Autoradiographic localization of opiate receptors in rat brain: II. The brainstem. Brain Res. 129:1-12

Atweh SF, Bid SJ, Kuhar MJ (1978) Histochemical localization of opiate receptors and opioid peptides. Fed. Proc. 37:153–157

Barnes S (1901) Degenerations in hemiplegia: With special reference to a ventrolateral pyramidal tract, the accessory fillet and Pick's bundle. Brain 24:463–502

Bechterew von W (1894) Die Leitungsbahnen im Gehirn und Rueckenmark. Verlag E. Besold (A. Georgi) Leipzig

Bechterew W (1896, 1899) Die Leitungsbahnen im Gehirn und Rückenmark. St. Petersburg

Beitz AJ (1990) Central gray in the human nervous system. In: The human nervous system. ed: G. Paxinos, Acad. Press, San Diego. pp 307–320

Berkley KJ, Hubscher CH (1995) Are there separate central nervous system pathways for touch and pain? Nature Med 1:766–773

Berkley KJ, Hubscher CH, Wall PD (1993) Neuronal response to stimulation of the cervix, uterus, colon, and skin in the rat spinal cord. J.Neurophysiol 63:545–556

Beusekom, G.T. van (1955) Fibre analysis of the anterior and lateral funiculi of the cord in the cat. Thesis, Leiden

Boesten AJP, Voogd J (1975) Projections of the dorsal column nuclei and the spinal cord on the inferior olive in the cat. J. Comp. Neurol. 161:215–238

Bok (1928) Das Rueckenmark. V. Moellendorff's Handbuch d. mikrosk. Anat. d. Menschen Bd IV, Teil I, 478

Boivie J (1983) Anatomic and physiologic features of the spino-cervico-thalamic pathways. In: Macchi G, Rustioni A, Spreafico R (eds) Somatosensory integration in the thalamus. Elsevier, Amsterdam pp. 63–106

Boivie J, Boman K (1981) Termination of separate (proprioceptive?) cuneothalamic tract from external cuneate nucleus in monkey. Brain Res 224:235–246

Boivie J, Grant G, Albe-Fessard D, Levante A (1975) Evidence for a projection to the thalamus from external cuneate nucleus in the monkey. Neurosci Lett 1:308

Bowsher D (1957) Termination of the central pain pathway in man: The conscious appreciation of pain. Brain 80:606–622

Bowsher D (1962) The topographical projection of fibers from the anterolateral quadrant of the spinal cord to the subdiencephalic brain stem in man. Psychiat Neurol 143:75–99

Braak H (1970) Ueber die Kerngebiete des Menschlichen Hirnstammes. I. Oliva inferior, Nucleus conterminalis und Nucleus vermiformis corporis restiformis. Z. Zellf. 105:443–456

Braak H (1971) Ueber die Kerngebiete des Menschlichen Hirnstammes. IV. Der Nucleus reticularis lateralis und seine Satelliten. Z. Zellforsch 122, 145–159

Brodal A Pompeiano 0 (1957) The vestibular nuclei in the cat. J. Anat. 91:438–454

Brodal A, Walberg F, Blackstad T (1950) Termination of spinal afferents to inferior olive in cat. J. Neurophysiol. 13:431–454

Busch HFM (1961) An anatomical analysis of the white matter in the brain stem of the cat. Thesis, Leiden

Carpenter MB (1957) The dorsal trigeminal tract in the Rhesus monkey. J. Anatomy 91:82–90

Carstens E, Trevino, DL (1978) Laminal origins of spinothalamic projections in the cat as determined by retrograde transport of horseradish peroxidase. J. Comp. Neurol. 182:151–166

Cerrato P, Imperiale D, Bergui M, Giraudo M, Baima C et al. (2000) Restricted dissociated sensory loss in a patient with a lateral medullary syndrome: A clinical- MRI study. Stroke 31:3064 – 3068

Cliffer KD, Giesler GJ (1989) Postsynaptic dorsal column pathway of the rat. III Distribution of ascending afferent fibers J.Neurosci 9:3146–3168

Cliffer KD, Willis WD (1994) Distribution of the postsynaptic dorsal column projection in the cuneate nucleus of monkeys. J.Comp Neurol 345:84–93

Collier J, Buzzard EF (1903) The degeneration resulting from lesions of posterior nerve roots and from transverse lesions of the spinal cord in man. A study of twenty cases. Brain 26:559–591

Conti F, DeBiasi S, Giuffrida R, Rustioni A (1990) Substance P-containing projections in the dorsal columns of rats and cats. Neuroscience 34:607–621

Courville J, Faraco-Cantin F (1978) On the origin of the climbing fibers of the cerebellum. An experimental study in the cat with an autoradiographic tracing method. Neurosc. 3, 797–809

Cummings JF, Petras JM (1977) Origin of spinocerebellar pathways I. Nucleus cervicalis centralis of cranial cervical spinal cord. J. Comp. Neurol. 173:655–691

Darkschewitsch L, Freud S (1886) Ueber die Beziehung des Strickkörpers zum Hinterstrang und Hinterstrangkern nebst Bemerkungen ueber zwei Felden der Oblongata. Neurol. Zentralbl. S: 121–129

Dejerine J (1901) Anatomie des centres nerveux. J.Rueff. Paris 2:569–571

Dejerine J (1910) Sémiologie des affections du système nerveux. Paris

Dietrichs E, Walberg F (1989) Direct bidirectional connections between the inferior olive and the cerebellar nuclei. Exp. Brain Res. Series 17:61–81

Edinger L (1885) Zur Kenntnis des Verlaufs der Hinterstreangfasern in der Medulla oblongata und im Kleinhirnschenkel. Neurol Zentralblatt 4:73–76

Edinger L (1889) Ueber die Fortsetzung der Hinteren Rückenmarkswurzeln zum Gehirn. Anat. Anz. 4:121–128

Ekerot CF, Larson B, Oscarsson 0 (1979) Information carried by the spinocerebellar paths. Progr. Brain Res. 50:79–90

Feirabend HKP, Chouffoer H, Ploeger S, Holsheimer J, van Gool JD (2002) Morphometry of human superficial dorsal and dorsolateral column fibers: significance to spinal cord stimulation. Brain 125:1137–1149

Ferraro A, Barrera SE (1936) Lamination of the medial lemniscus in Macacus rhesus. J. Comp. Neurol 64:313–324

Ferrier D, Turner W (1895) A record of experiments illustrative of the symptomatology and degenerations following lesions of the cerebellum and its peduncles and related structures in monkey. Phil. Trans. B 185:719–779

Fink RP, Heimer L (1967) Two methods for selective silver impregnation of degenerating axons and their synaptic endings in the central nervous system. Brain Res. 4**:** 369–374

Florence SL, Wall JT, Kaas JH (1989) Somatotopic organization of inputs from the hand to the spinal gray and cuneate nucleus of monkeys with observations on cuneate nucleus of humans. J.Comp.Neurol 286:48–70

Foerester O, Gagel 0 (1932) Die Vorderseiten-strangdurchschneidung beim Menschen. Zeitschr. ges. Neurol. Psychiat. 138:1-92

Fukushima K, Kerr FWL (1979) Organization of trigeminothalamic tracts and other thalamic afferent systems of the brainstem in the rat: presence of gelatinosa neurons with thalamic connections. J.Comp Neurol. 183:169–184

Gardner E, Cuneo HM (1945) Lateral spinothalamic tract and associated tracts in man. Arch. Neurol. Psychiat. (Chicago) 53:423–430

Gehuchten van A (1903) La voie centrale des noyeaux des cordons posterieurs ou voie centrale medullo-thalamique. Le Nevraxe 4:3-44

Gerrits NM (1990) Vestibular Nuclear Complex. In: The human nervous system ed. G. Paxinos, Acad. Press. San Diego. pp. 863–888

Gilman S (2002) Joint position sense and vibration sense: anatomical organization and assessment. J. Neurol Neurosurg Psych. 73:473–477

Glees P (1951) The course and relations of the spinothalamic tract in man. Acta Psych. Neurol. Scand. 74, 199–206

Glees P, Bailey RA (1951) Schichtung und Fasergrösse des Tractus spinothalamicus des Menschen. Monatschr. Psychiat Neurol. 122, 129–141

Goedhart ZD, Francaviglia N, Feirabend HKP, Voogd J (1984) Technical pitfalls in median commissural myelotomy for malignant sacral pain. Appl. Neurophysiol. 47:216–222

Goldstein, K. von (1910) Ueber die aufsteigende Degeneration nach Querschnittsunterbrechung des Rueckenmarks Tractus Spinocerebellaris posterior, Tractus Spino-olivaris, Tractus Spinothalamicus. Neurol. Centralblatt 20:898–91 1

Graaf de AS (1967) Anatomical aspects of the Cetacean brain stem. Van Gorcum & Co, Assen

Häggqvist G (1936) Analyse der Faserverteilung in einem Rückenmarkquerschnitt (Th 3). Zeitschr. f. mikrosc.-anat. Forschung 39:1-34

Haller von A (1765) Elementa physiologiae corporis humani, 4:175

Hamani C, Saint Cyr JA, Fraser J, Kaplitt M, Lozano AM (2003) The subthalamic nucleus in the context of movement disorders. Brain 127:4-20

Harmann PA, Carlton SM, Willis WD (1988) Collaterals of spinothalamic tract cells to the periaqueductal gray: a fluorescent double-labeling study in the rat. Brain Res. 441:87–97

Hirschberg RM, Al-Chaer ED, Lawand NB, Westlund KN, Willis WD (1996) Is there a pathway in the posterior funiculus that signals visceral pain. Pain 67:291–305

Hoffmann CFE, Thomeer RTWM, Marani E (1993) Reimplantation of ventral rootlets into the cervical spinal cord after their avulsion: an anterior surgical approach. Clin. Neurol. Neurosurg. 95: S112-S118

Hoffmann CFE, Van Dijk JG, Thomeer RTWM, Marani E (1996) Functional reinnervation of avulsed ventral rootlets after their reimplantation in the cervical spinal cord of the cat. J. Neurosurg. 84:234–243

Holtzer C.A.J, (2003) Experimental avulsion of motor rootlets. Thesis, Leiden

Hoshino S, Hayashi A, Tamaoka A, Shin' ichi Shoji (1999) Bilateral gustatory disturbance by a unilateral pontine lesion. Neurology 53:1158–1159

Kaas JH (1990) Somato-sensory systems. In: The human nervous system Ed: G. Praxinos, Acad. Press, San Diego. pp. 813–844

Kaas JH, Pons TP (1988) The somatosensory system of primates. In: Comparative Primate Biology 4:421–468. Alan R Liss Inc

Kerr FWL (1975) Ventral spinothalamic tract and other ascending systems of ventral funiculus of spinal cord. J. Comp. Neurol. 159:335–356

Kerr FWL, Lippman H (1973) Ascending degeneration following antero-lateral cordotomy and midline myelotomy in primates. Anat. Rec. 175:356–367

Kim JS (2001) Restricted dissociated sensory loss in lateral medullary infarction. Stroke 32:1696–1697

Kosinski RJ, Lee HS, Mihailoff GA (1988) A double retrograde fluorescent tracing analysis of dorsal column nuclear projections to the basilar pontine nuclei, thalamus and superior colliculus in the rat. Neurosci Letters 85:40–46

Kohnstamm O, Quensel F (1909) Centrum receptorium der formatio reticularis und gekreuzt aufsteigende Bahn. Dtsch. Zeitschr. Nervenheilk. 36:182–188

Künzle H (1973) The topographic organization of spinal afferents to the lateral reticular nucleus of the cat. J. Comp. Neurol. 149:103–166

Kuo DC, De Groat WC (1985) Primary afferent projections of the major splanchnic nerve to spinal cord and gracile nucleus of the cat J.Comp Neurol 231:421–434

Lee S-H, Kim D-E, Song E-C, Roh, J-K (2001) Sensory dermatomal representation in the medial lemniscus. Arch Neurol 58:649–654

Lippman UH, Kerr FWL (1972) Light and electron microscopic study of crossed ascending pathways in the anterolateral funiculus in monkey. Brain Res. 40:496–499

Liu RPC (1986) Spinal neuronal collaterals to the intralaminar thalamic nuclei and periaqueductal gray. Brain Res. 365:145–150

Manola L, Roelofsen BH, Holsheimer J, Marani E, Geelen J (2005) Modelling motor cortex stimulation for chronic pain control: electrical potential field, activating functions and responses of simple nerve models. Med Biol Eng Comput 43:335–343

Mantle St-John LA, Tracey DJ (1987) Somatosensory nuclei in the brainstem of the rat: independent projections to the thalamus and cerebellum. J.Comp Neurol 255:259–271

Mantyh PW (1982) The ascending input to the midbrain periaqueductal gray of the primate. J. Comp.Neurol. 211:50–64

Marchi V, Alghieri G (1885) Sulle degenerazione discendenti consecutive a lesioni sperimentale in diverse zone della corteccia cerebrale. Riv. Sper. Freniatr. Med. Leg. Alienazioni Ment. 11:492–510

Matricali B (1961) A new stereotactic coordinate system for the rabbits brainstem. The medial lemniscus of the rabbit, its course through the brainstem and origin, fibre content and termination of its components. Thesis, J. Noorduijn en Zn. NV, Gorinchem

Massopust LC, Hauge DH, Ferneding JC, Doubek WG, Taylor JJ (1985) Projection systems and terminal localization of dorsal column afferents: an autoradiographic and horse radish peroxidase study in the rat. J.Comp.Neurol 237, 533–544

Matsushita M, Ikeda, M (1975) Central cervical nucleus as cell origin of a spinocerebellar tract arising from cervical cord-study in cat using horse-radish-peroxidase. Brain Res. 100:412–417

Matsushita M, Ikeda M (1987) Spinocerebellar projections from the cervical enlargement in the cat, as studied by anterograde transport of wheat germ agglutinin-horseradish peroxidase. J. Comp. Neurol. 263:223–240

Matsushita M, Tanami T (1987) Spinocerebellar projections from the central cervical nucleus in the cat, as studied by anterograde transport of wheat germ agglutinin-horseradish peroxidase. J. Comp. Neurol. 266:376–397

Matsushita M, Hosoya Y, Ikeda M (1979) Anatomical organization of the spinocerebellar system in the cat, as studied by retrograde transport of horseradish peroxidase. J. Comp. Neurol. 184:81–106

Matsushita M, Ikeda M, Tanami T (1985) The vermal projection of spinocerebellar tracts arising from lower cervical segments in the cat: An anterograde WGA-HRP study. Brain Res. 360:389–393

Matzke HA (1951) The course of the fibers arising from the nucleus gracilis and cuneatus of the cat. J Comp Neurol 94:439–452

Meessen H, Olszewski J (1949) Cytoarchitektonischer Atlas des Rautenhirns des Kaninchen. Pp: 52, Charger, Basel, NY

Mehler WR, Fefferman ME, Nauta WJH (1960) Ascending axon degeneration following anterolateral cordotomy: An experimental study in the monkey. Brain, 83:718–750

Mehler WR (1962) The anatomy of the so-called 'Pain tract' in man: An analysis of the course and distribution of the ascending fibers of the fasciculus anterolateralis. Basic Research in Paraplegia. pp 2655 (JD French and RW Posters eds) Thomas, Springfield, Illinois

Mehler WR (1966) The posterior region in man. Confin. Neurol 27:18–29

Mehler WR (1974) Central pain and the spinothalamic tract. Adv. Neurol. 4: 127–146

Mesulam NM (1981) Appendix D: The application of silver degeneration techniques to the human brain in: de Olmos, J.S., Ebbesson, S.O.E., Heimer, L. Silver methods for the impregnation of degenerating axoplasm. In Heimer.L, Robards, M.J. Neuroanatomical tract tracing methods. Plenum Press New York. (pp. 158–166)

Miklossy J, Clarke S, Van der Loos H (1991) The long distance effects of brain lesions: visualization of axonal pathways and their terminations in the human brain by the NAFTA method. J.Neuropathol.Exp.Neurol. 50:595–614

Molenaar I (1977) An anatomical study of the propriospinal connections in the cat. Thesis Rotterdam

Mott FW (1895) Experimental inquiry upon the afferent tracts of the central nervous system of the monkey Brain 18:1–20

Mott FW (1897) Die zufuhrenden Kleinhirnbahnen des Ruckenmarks bei dem Affen. Neurol Centralbl. 16:1097–1098

Nauta HJW (2000) Punctate midline myelotomy for the relief of visceral cancer pain J.Neurosurg 92, Suppl 2:125–130

Nauta WJH, Gygax PA (1951) Silver impregnation of degenerating axon terminals in the central nervous system: (1) Technics. (2) Chemical 'Notes. Stain Technology 26:5-11

Nauta WJH, Ebbesson SOE (1970) The selective silver-impregnation of degenerating axons and their synaptic endings in nonmammalian species. Contemp. Research Methods. Springer Verlag. New York, Berlin: 132–161

Nauta WJH, Mehler WR (1966) Projections of the lentiform nucleus in the monkey. Brain Res. 1, 3–42

Nauta WJH, Ryan LF (1952) Selective silver impregnation of degenerating axons in the central nervous system. Stain Technology, 27:175–179

Olzsewski J, Baxter D (1954) Cytoarchitecture of the human brain stem. S. Karger, Basel, N.Y

Oscarsson O, Uddenberg N (1964) Identification of spinocerebellar tract activated from forelimb afferents in cat. Acta Physiol. Scand. 62:125–136

Oscarsson O (1973) Functional organization of spinocerebellar paths. In: Handbook of Sensory Physiology Vol II. Somatosensory system (Ed. A. Iggo) pp. 339–380. Springer Verlag, Berlin

Oscarsson O, Uddenberg N (1965) Properties of afferent connections to the rostral spinocerebellar tract in cat. Acta Physiol. Scand. 64:143–153

Palecek J, Paleckova V, Willis WD (2002) The role of pathways in the spinal cord lateral and dorsal funiculi signaling nociceptive somatic and visceral stimuli in rats. Pain 96:297–307

Palecek J, Paleckova V, Willis WD (2003) Fos expression in spinothalamic and postsynaptic dorsal column neurons following noxious visceral and cutaneous stimuli. Pain 104:249–257

Patterson JT, Head PA, McNeill DL, Chung K, Coggeshall RE (1989) Ascending unmyelinated primary afferents in the dorsal funiculus. J.Comp Neurol 290:384–390

Paxinos G, Huang XF (1995) Atlas of the human brainstem. Academic Press, San Diego

Paxinos G, Tòrk J, Halliday G, Mehler WR (1990) Human homologs to brainstem nuclei identified in other animals as revealed by acetylcholinesterase. In: The human nervous system, cd. G. Paxinos, Acad., Press San Diego. pp. 149–202

Peerbolte ML (1932) De loop van de achterwortelvezels, die in de achterstrengen van het ruggemerg opstijgen. Thesis Leiden

Petit D (1972) Postsynaptic fibers in the dorsal columns and their relay in the nucleus gracilis Brain Res 48:380–384

Petras JM, Cummings JF (1977) Origin of spinocerebellar pathways. 2: Nucleus centrobasalis of cervical enlargement and nucleus dorsalis of thoracolumbar spinal cord. J. Comp. Neurol. 173:693–715

Peyron R, Laurent B, Garcia-Larrea (2000) Functional imaging of brain responses to pain. A review and meta-analysis. Pain 30:263–288

Probst M (1900) Experimentelle Untersuchungen ueber die Schleifendigung die Haubenbahn, das dorsale Längsbündel und die hintere Kommissur. Arch f.Psychiat 33:1-57

Pubol BH, Welker WI, Johnson JI (1965) Somatic sensory representation of forelimb in dorsal root fibers of raccoon, coatimundi and cat. J.Neurophys 28:312–341

Quensel F (1898) Einfall von Sarcon der Dura spinalis Beitrag zur Kenntniss der secundären degenerationen nach Rueckenmarkcompression. Neurol. Centralbl. 17:482–493

Ramon y Cajal (1911) Histologie du systéme nerveux de l'homme et des vertèbrès, part I. Edition française, Instituto Ramon y Cajal, Madrid, (facsimile from 1952)

Rasmussen AT, Peyton WT (1941) The location of the lateral spinothalamic tract in the brainstem of man. Surgery. 10:699–710

Rasmussen AT, Peyton WT (1946) Origin of the ventral external arcuate fibers and their continuity with the striae medullaris of the fourth ventricle of man. J.Comp.Neur., 84:325–337
Rasmussen AT, Peyton WT (1948) The courses and termination of the medial lemniscus in man. J. Comp Neurol 88:411–424
Reil JC (1809) Die vödern Schenkel, das vördere Marksegel und die Schleife. Reil's. Arch. f.d. Physiol. 9:505–514
Russell JSR (1898) Contributions to the study of some afferent and efferent tracts in the spinal cord. Brain 145
Rustioni A (1973) Non-primary afferents to the nucleus gracilis from the lumbar cord of the cat. Brain Res. 51:81–95
Rustioni A (1974) Non-primary afferents to the cuneate nucleus in the brachial dorsal funiculus of the cat. Brain Res. 75:247–259
Rustioni A (1977) Spinal neurons project to the dorsal column nuclei of Rhesus monkey. Science 196:656–658
Rustioni A, Kaufman AB (1977) Identification of cells of origin on non-primary afferents to the dorsal column nuclei of the cat. Exp. Brain Res. 27:1-14
Rustioni A, Hayes NL, O'Neill S (1979) Dorsal column nuclei and ascending spinal afferents in macaques. Brain 102:95–125
Sadjapour K, Brodal A (1968) The vestibular nuclei in man. A morphological study in the light of experimental findings in the cat. J. Hirnfors. 10:299–323
Schachter SC (2001) Evaluation of the first seizure. http://www.medscape.com/Up to Date/2001. 09–12–2004
Schaffer K (1938) Beitrag zur feineren Anatomie des Kleinhirnanteils der Pyramidenbahn. Z. Anat. 109:278–281
Schoen, JHR (1964)Comparative aspects of the descending fibre systems in the spinal cord. In: Eccles JC, Schadé JP (eds) Progress in Brain Research II:Organization of the spinal cord. Elsevier, Amsterdam pp 203–222
Schoen JHR (1969) The corticofugal projection of the brainstem and spinal cord in man. Psychiat. Neurol. Neurochir. 72:121–128
Schoen JHR (1970) The aspect of the rubrospinal tract in man. Acta Morphol. Neerl. Scand. 7:330–331
Schoenen G, Grant G (1990) Spinal Cord: Connections In: G. Paxinos (ed) The human nervous system. pp. 77–92. Acad. Press San Diego
Schwank RL (1934) The relationship between the circumolivary pyramidal fascicles and the pontobulbar body in man. J. Comp. Neurol. 60:309–317
Schwartz HG, O'Leary JL (1941) Section of the spinothalamic tract in the medulla with observations on the pathway of pain. Surgery 9:183–193
Schwartz, H.G. and O'Leary, J.L. (1942) Section of the spinothalamic tract at the level of the inferior olive. Arch. Neurol. Psychiat. 47:293–304
Shintani C, Tsuruoka S, Shiigai T (2000) Pure sensory stroke caused by a cerebral hemorrhage: Clinical-radiologic correlations in seven patients. Am.J. Neuroradiol 21:515–520
Sie Pek Giok (1956) Localization of fiber systems within the white matter of the medulla oblongata and the cervical cord in man. Thesis Leiden
Smith MC (1957) Observations on the topography of the lateral column of the human cervical spinal cord. Brain 80:263–272
Smith MC, Deacon P (1984) Topographical anatomy of the posterior columns of the spinal cord in man. Brain 107:671–698

Snyder RL, Faull RLM, Mehler WR (1978) A comparative study of the neurons of origin of the spinocerebellar afferents in the rat, cat and squirrel monkey based on the retrograde transport of horseradish peroxidase. J. Comp. Neurol. 181:833–852

Snow PJ, Wilson P (1991) Plasticity in the somatosensory system of developing and mature mammals. Springer Verlag, Berlin. Progress in Sensory Physiol. 11 pp. 482

Takamutsu K, Takizawa T (1991) Bilateral cheiro-oral sensory syndrome: report of two cases. Prog Comput Tomogr 13:104–106

Takezawa N, Makino M, Segawa T (1990) Pure sensory stroke due to a pontine lacune. Neurol Med Chir (Tokyo) 33:278–280

Thiele FH, Horsley V (1901) A study of the degeneration observed in the CNS in a case of fracture dislocation of the spine. Brain 24:519–531

Theodor WH, Fisher RS (2004) Brain stimulation for epilepsy. Review. The Lancet (Neurology) 3:111–118

Thomeer RT, Malessy MJ, Marani E (2002) Nerve root repair. J.Neurosurg Spine 96:138–139

Tschermak A (1898) Ueber den centralen Verlauf der aufsteigenden Hinterstrangbahnen und deren Beziehung zu den Bahnen im Vorderseitenstrang. Arch f Anat u Physiol, Anat Abt, 291–402

Truex RC, Taylor MJ, Smythe MQ, Gildenberg PL (1965) The lateral cervical nucleus of cat, dog and man. J. Comp. Neurol. 139:93–104

Uesaka Y, Nose H, Ida M (1999) Response to bilateral gustatory disturbance caused by a unilateral pontine lesion. Neurology 53:1158–1159

Usunoff KG, Marani E, Schoen JHR (1997) The trigeminal system in Man. Adv. Anat Embryol Cell Biol 136 pp 1–126

Verhaart WJC (1964) A stereotactic atlas of the brainstem of the cat. Van Gorcum & Co, Assen

Verhaart WJC, Sie Pek Giok (1958) The fasciculus centralis tegmenti and the reticular fibre system. Acta Anat. 33, 257–272

Voogd J, Bigaré F. (1980) Topographical distribution of olivary and cortico-nuclear fibers in the cerebellum. A review. In: J. Courville et al. (eds). The inferior olivary nucleus. Anatomy and Physiology. Raven Press N.Y., p. 207–234

Voogd J, Feirabend HKP, Schoen JHR (1990) Cerebellum and precerebellar nuclei. In: The human nervous system, ed. G. Paxinos, pp 321–386, Academic Press, San Diego

Voogd J, Feirabend HKP (1981) Classic methods in neuroanatomy. In: Methods in Neurobiology, R. Lahue (ed) Plenum Press N.Y., London p. 301–364

Wang CC, Westlund KN (2001) Responses of rat dorsal column neurons to pancreatic nociceptive stimulation. Neuroreport 12:2527–2530

Walker AE (1938a) The thalamus of the Chimpanzee: I. Terminations of the somatic afferent systems. Confinia neurol. 1:99–127

Walker AE (1938b) The primate thalamus. Univ. Chicago Press, Chicago, USA

Walker AE (1940) Spinothalamic tract in man. Acta Neurol. & Psychiatr. 43, 248–298

Walker AE, Weaver TA (1942) The topical organization and termination of the fibers of the posterior columns in Macaca mulatta. J.Comp Neurol 76:145–158

Willis and Coggeshall(1991, 2003) Sensory mechanism of the spinal cord. Plenum Press NY, London

Wiksten B (1975) The central cervical nucleus. A source of spinocerebellar fibers, demonstrated by retrograde transport of HRP. Neurosci. Lett. 1:81–84

Winkler C (1920) De bouw van het zenuwstelsel, deel II, De Erven Bohn, Haarlem

Xu Q, Grant O (1994) Course of spinocerebellar axons in the ventral and lateral funiculi of the spinal cord with projections to the anterior lobe: an experimental anatomical study in the cat with retrograde tracing techniques. J. Comp. Neurol. 345:288–302

Xu J, Wall JT (1999) Functional organization of tactile inputs from the hand in the cuneate nucleus and its relationship to organization in the somatosensory cortex. J.Comp. Neurol 411:369–389

Yamashita M, Yamamoto T (2001) Aberrant pyramidal tract in the medial lemniscus of the human brainstem normal distribution and pathological changes. Eur Neurol 45:75–82

Yezierski RP (1988) Spinomesencephalic tract: projections from the lumbosacral spinal cord of the rat, cat, and monkey. J.Comp. Neurol 267:131–146

Zhang D, Carlton SM, Sorking LS, Willis WD (1990) Collaterals of primate spinothalamic tract neurons to the periaqueductal gray. J. Comp. Neurol. 296:277–290

Ziehen (1934) Centralnervensystem. In: Handb. Anat. Menschen, part 4 (2): 1–1546 (v. Eggerling, ed). Fischer Verlag, Jena, Germany

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