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How to run a brain bank
A report from the Austro-German brain bank

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Summary. The sophisticated analysis of and growing information on the human brain requires that acquisition, dissection, storage and distribution of rare material are managed in a professional way. In this publication we present the concept and practice of our brain bank. Both brain tissue and information are handled by standardized procedures and flow in parallel from pathology to neuropathology and neurochemistry. Data concerning brain material are updated with clinical information gained by standardized procedures.

Introduction

The ever-more sophisticated analysis of the pathology of the human brain by chemical, biochemical, pharmacological, molecular and pathological methods requires that the acquisition, dissection, storage and distribution of rare material are managed in a professional way.

The effective implementation of this objective had until relatively recently posed several problems. However, the practice of "brain banking", which developed in the early seventies (Pope, 1982) has solved some of these problems. The relative rarity of material has been overcome by the collection of material and information according to standardized procedures from many centres. Standardized dissection procedures are performed by experienced neuropathologists in order to subdivide regions of interest according to updated neuroanatomical and cytochemical findings. This allows the inclusion of regions into the protocol which may be of future interest or are of interest in diseases other than the ones investigated. Tissue storage in deep-freezers is afflicted with minor problems such as the time

spent searching for tissue at very low temperatures. The problem of distribution of rare material is essentially one of inter-scientist contact and communication. A database with addresses of scientists, their subjects of interests and available methods, which is affixed to the brain bank, will help to facilitate communication.

In the present publication we look at the concept and practice of our brain bank which runs mainly in Austrian-German cooperation.

Material and methods

Organisation media

Hardware. An IBM-compatible computer with 80386 processor running on 25 MHz is used. Working memory is 4 MB, storage capacity on hard disk drive is 200 MB (Highscreen, Vobis, Aachen, F.R.G.).

Software. The database was developed with dBase IV 1.5 program (Ashton Tate/ Borland, F.R.G.).

Storage media for tissue

Eight deep freezers (1 Revco 1386-VOD, 2 Revco ULT 1786-3-VUA, 1 Revco ULT 1786-VOE, 1 Revco 1790-UNM and 3 Revco 1790-VNP, Revco Scientific Inc., Asheville, U.S.A.) run at −80°C.

Dissection equipment

Frozen brain material is dissected on a metal plate (Haake K/F3, Karlsruhe, F.R.G.) cooled to −20°C with brain temperature between −10 and −5°C.

Brain material

Tissue is obtained from control subjects, i.e. subjects without neurological or psychiatric diseases, metabolic diseases, alcoholism, CNS trauma and long-term agonal states, and from patients who suffered from neurological and psychiatric diseases including Parkinson's, Huntington's and Alzheimer's diseases, senile dementia of the Alzheimer type, vascular or multi-infarct dementia, alcoholism, epilepsy, depression and schizophrenia, and a few samples of metabolic encephalopathies, storage diseases, and other rare neuropsychiatric diseases.

Brain bank practice

Brain bank concept

The brain bank cannot function in isolation. It requires demand from chemical, biochemical and molecularbiological laboratories and supply by pathological units of tissue and information (Fig. 1). The brain bank and the dissection or neuropathological centre should work in close communication.

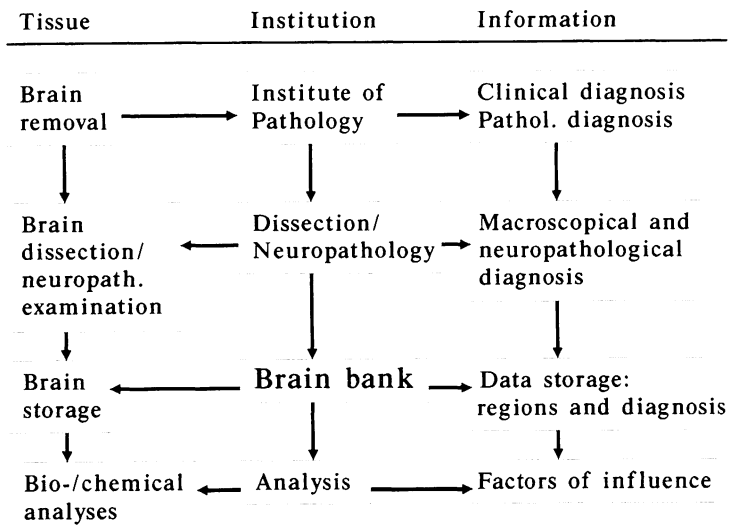

Fig. 1. Conceptional flow chart for tissue and data flow within the brain bank

It is particularly important that data flow must parallel the flow of material. Details to the flow chart presented in Fig. 1 are given below.

Acquisition centres

Acquisition centres are pathological units of general, neurological and psychiatric hospitals. The body should be placed in the mortuary refrigerator at 4°C within 3 hours of death until removal of the brain, noting time and date. Removal of brain and other body tissue should take place as soon as possible, preferably between 4 and 12 hours after death [limits: frozen (for biochemistry) 18 to 24 hours, fixed 72 hours]. The brain is removed, and the brainstem and cerebellum separated, ideally above the IIIrd nerve nuclei, and weighed separately. Care should be taken not to disrupt the subthalamic nucleus and midbrain. Another possibility is to section the brain, brainstem and cerebellum sagittally in half, making the cut from the base to obtain a correct mid-sagittal cut through the brainstem. One half of the brain is fully immersed in 10% neutral or buffered formalin. Spinal cord (including autonomic ganglia when appropriate) with the dorsal root ganglia, peripheral nerves and muscle or other organs may be removed too.

Undissected hemispheres are frozen in a deep freezer at −80°C for chemical, biochemical and molecular biological investigations. For biochemical and pharmacological examinations, i.e. autoradiography, immunocytochemistry, in situ hybridization etc., brains are frozen in dry ice-cooled isopentane. For neuropathological examinations, i.e. immunocytochemistry etc., regions of interest are cut out of the hemisphere and immediately frozen in liquid nitrogen. The material gained with one of the above pro-

cedures is stored at −80°C in a deep freezer and transported to the brain bank on dry ice (−70°C).

Case report: pathology

Information concerning the patient is gained according to a standardized protocol (see Table 1). To ensure legal protection the name of the patient is coded into a registration number which includes the number of the acquisition center (first two numbers), the number of the dissection currently performed at this centre (next three or four numbers) and the year of dissection (last two numbers). In the standard protocol a preliminary diagnosis is enclosed as classification. Date of birth is recorded for age report of the patient and to test the influence of season of birth on the genesis of various diseases, e.g. schizophrenia (Beckmann and Franzek, 1992). Date of death is required for age calculation and for determination of storage time of tissue, while time of death may provide information on circadian rhythms of the investigated parameters.

Age, sex, post mortem time (time between death and the beginning of the freezing procedure) and duration of storage are known to influence some chemical, biochemical and pharmacological parameters and must therefore be noted. Data on body weight, body length, brain fresh weight

Table 1. Case report — pathological data form

Registration number:	00/000/00;
Classification:	;
Data set number of regions:	;
Data set number of clinical data:	;
Data set number of neuropathology:	;
Date of birth:	;
Date of death:	;
Time of death:	;
Age:	years;
Sex:	;
postmortem time:	hours;
Body weight:	kg;
Body length:	cm;
Brain fresh weight:	g;
Nutritional state:	;
Agonal state:	;
Clinical cause of death:	;
Pathological cause of death:	;
Neuropathological assessment (using appropriate and standardized methods, including special stains, quantification).	
Neuropathological diagnosis should be made in the absence of clinical information, if appropriate.	

and CSF and brain tissue pH (Ravid et al., 1992) should be recorded as well as cause of death, nutritional status and information concerning agonal status.

The preliminary information that is gained during the dissection must later be completed by detailed neuropathological examination of the formalin-fixed hemisphere. Histological diagnosis is based on examination of multiple CNS areas using routine staining techniques and, if necessary, additional immunocytochemistry, cytochemistry, and electron microscopy (see chapter Neuropathology).

Table 2. Case report — clinical data

Registration number:	00/000/00;
Classification:	;
Data set number of regions;	;
Data set number of pathological data:	;
Data set number of neuropathology:	;

DSM-III-R, ICD-9/10; Hachinski Score etc.

Family history
dementia, intellectual impairment, personality disorder, psychoses, movement disorders, Down's syndrome among the patient's siblings and relatives

Social history
activities of daily living, type of household, degree of self-sufficiency, mobility, social contacts

Educational/professional history
school: years and degree, employment, retirement

General history
vascular, cardiovascular, metabolic, pulmonary-respiratory, haematological, neoplastic hormonal, infections, venereal diseases, toxins

Neurological history
pre- and perinatal complications, craniocerebral trauma, epilepsy, hypoxia, ischemia, hemorrhage, movement disorders, hydrocephalus, motor neuron disease, stroke

General physical history/Neurostatus
general physical state of health, nutritional state, respiration, cardiovascular function, metabolism, vigilance, orientation, aphasia, hypomimics, cranial nerve function, tonus, reflexes, sensibility, crude force, dexterity, pyramidal, frontal and cerebellar signs, tremor, muscular atrophies

Psychiatric history
inherited diseases of early childhood, manic-depressive disorder, schizophrenia, psychoses of unknown origin, psycho-reactive and neurotic diseases, personality disorders, suicide attempts, hallucinations, mnestic problems, concentration

History by family/health care giver questionaire
personality changes, paranoid symptoms, mood, slowing of thinking, memory and concentration, alterations in speech, delusion

Medication history
antidepressants, sedatives, hypnotics, neuroleptics, anticonvulsants, stimulating agents, digitalis, analgesics (name, dosage, duration)

Laboratory tests
EEG, CCT, MRT, blood chemistry, CSF, etc.

Neuropsychological assessment/Psychostatus
Mini-Mental Score, Blessed Score

Case report: clinical information

The clinical case report (Table 2) should be based mainly on information regarding the last 8 weeks prior to death. It should also include details of the *family history*. Diseases and disabilities of neuropsychiatric interest in the patient's family should be recorded, i.e. dementia, intellectual impairment, personality disorders, psychoses, movement disorders, Down's syndrome, lymphomas, age of mother and father, etc.

The *social history* is also recorded. Type of household (living with partner, family, alone or in a health care unit), degree of self-sufficiency, mobility and social contacts should be documented.

The *educational/professional status* is noted. This is indicated by the number of years and type of schooling, the highest school or university degree achieved and the employment or retirement status.

In the *general history information* is taken on cardiovascular, metabolic, pulmonary-respiratory, haematological, hormonal, infectious and venereal diseases, laboratory tests, e.g. EEG, CCT, MRT, blood chemistry, CSF etc. and the consumption of noxious substances, i.e. nicotine, alcohol or drugs, which may influence postmortem brain analysis.

The *neurological history* is comprised of pre- or perinatal complications, handedness, activities in trauma-prone sports (e.g. boxing), craniocerebral injury, meningoencephalitis, epilepsy, hypoxia, ischaemia, transient ischaemic attack, reversible ischemic neurologic deficit, stroke, cerebral haemorrhage, movement disorders, hydrocephalus or other neurological disorders.

The *general physical and neurostatus* includes data on general physical state of health, nutritional state, respiration, cardiovascular functioning and metabolism. Mnestic status, vigilance, orientation, aphasia, hypomimics and cranial nerve function are documented. This is followed by the report on tonus, reflexes, sensibility, crude force, dexterity, diadochokinesis, arm holding, pyramidal, frontal and cerebellar signs and tremor.

In the *psychiatric history* inherited diseases of early childhood, endogenous disorders such as manic-depressive disorder or schizophrenia, exogenous psychiatric disturbances, psychoses of unknown origin, psychoreactive and neurotic diseases are recorded. Personality disorders, suicide attempts, hallucinations, mnestic problems and problems in concentration are also noted.

Information from family members or health care givers on personality changes, paranoid symptoms, mood changes, slowing of thinking, memory and concentration, alterations in speech, delusion or other pronounced changes is recorded.

Finally the *medication history* is documented. Questions concern treatment with antidepressants, sedatives, hypnotics, neuroleptics, anticonvulsants, stimulating agents, digitalis, analgesics or other therapeutic agents of interest. Compound name, dosage and duration of medication (long-term or short-term treatment) are recorded.

Case report: neuropathology

All brains, both pathological and normal controls, undergo histological examination. From formalin-fixed brains 8 to 15 blocks from different areas are routinely dissected and processed for neuropathology using routine histological techniques. Light microscopical studies are performed by an expert neuropathologist. If necessary, additional histochemical or electron microscopical studies are performed. Material from "controls" is only used for chemical analyses after histopathological studies have revealed absence of any abnormal findings. Material from "pathologic" cases is used for analyses when neuropathology has confirmed the clinical diagnosis and other unrelated major pathological changes of the CNS have been histologically excluded.

The neuropathological diagnosis is recorded as text on a paper hardcopy. Access by the brain bank is via the registration number. In the next step of the brain bank development we plan to encode the text for easy use in the database.

Dissection centres

Dissection centres, which are usually identical to acquisition centres if experienced neuropathologists are present, are best located at the site of the brain bank. The decision of which brain areas are dissected is determined by the requirements from research groups.

Frozen hemispheres (−80°C) are thawed to −10 to −5°C and dissected on a cooled metal plate (−20°C) according to a standard procedure (Table 3), which is presented in the case of a male 75-year old patient who suffered from cerebrovascular insufficiency. The fresh brain weight was 1,280 g and postmortem delay was 3.4 hours. For region identification an anatomical atlas is used (Heimer, 1983; Nieuwenhuys et al., 1988).

Topographic approach to tissue sampling

Lateral aspect of the hemisphere

From the lateral hemisphere in the frontal lobe the polar region (Brodmann area (BA) 10; Brodmann, 1925; Fig. 2) and the orbital gyri (BA 11; Fig. 3; Penfield and Rasmussen, 1950) are removed. Both areas are heteromodal, high-order association areas (Mesulam, 1985), involved in complex integrative functions (Fuster, 1980). From the convex part of the frontal lobe the superior frontal gyrus (BA 8 and 9; Fig. 4) is used. This is part of the premotor area and is involved in combination of movements of the body (Brinkman and Porter, 1983). If required the medial frontal gyrus, coordinating eye movements is removed. In addition, the precentral gyrus

Table 3. Standard dissection procedure

Registration number:	00/000/00;
Classification:	;
Data set number of pathological data:	;
Data set number of clinical data:	;
Data set number of neuropathology:	;
Storage:	
Deep-freezer number:	;
Container number:	;
Dissectionist:	;
Assisted by:	;
Hemisphere side:	;
Lateral hemisphere:	
Frontal cortex, complete:	;
or:	
Frontal cortex, polar region: (BA 10)	;
Frontoorbital gyri: (BA 11)	;
Frontal cortex, convex part: (BA 8, 9)	;
Precentral gyrus: (BA 4)	;
Temporal Cortex, complete:	;
or:	
Superior temporal gyrus: (BA 41, 42, 38, 22)	;
Medial temporal gyrus: (BA 21)	;
Inferior temporal gyrus: (BA 20)	;
Parietal cortex, complete:	;
or:	
Superior parietal lobule: (BA 7)	;
Postcentral gyrus: (BA 1–3)	;
Angular gyrus: (BA 39)	;
Supramarginal gyrus: (BA 40)	;
Occipital cortex, complete:	;
or:	
Occipital cortex, polar region: (BA 17, 18)	;
Medial hemisphere:	
Superior gyrus of calcarine sulcus:	;
Inferior gyrus of calcarine sulcus:	;
Cingulate gyrus: (BA 23, 24)	;
Corpus callosum:	;
Hypothalamus:	;
Habenular complex:	;
Mamillary body:	;
Brain stem and cerebellum:	
Raphe nuclei:	;
Locus coeruleus:	;
Cerebellar cortex:	;
Dentate nucleus:	;
Coronal slices:	
Caudate nucleus, complete:	;
or:	
Head of the caudate nucleus:	;
Body of the caudate nucleus:	;

Table 3. *Continued*

Tail of the caudate nucleus:	;
Putamen, complete:	;
or:	
Anterior putamen:	;
Medial putamen:	;
Posterior putamen:	;
Accumbens:	;
Globus pallidus, complete:	;
or:	
Anterior globus pallidus:	;
Lateral globus pallidus:	;
Medial globus pallidus:	;
Substantia innominata:	;
Septum nuclei:	;
Amygdaloid body:	;
Entorhinal cortex:	;
Hippocampus:	;
Plexus chorioideus:	;
Substantia nigra, complete:	;
or:	
Substantia nigra, compact part:	;
Substantia nigra, reticulate part:	;
Red nucleus:	;
Subthalamic nucleus:	;
Thalamus, complete:	;
or:	
Anterior thalamic nucleus:	;
Ventral anterior thalamic nucleus:	;
Ventral lateral thalamic nucleus:	;
Medial thalamic nucleus:	;
Centromedial thalamic nucleus:	;

BA Brodmann area

(BA 4; Fig. 5; Lorente de Nó, 1949), the region that is important in voluntary movements (Penfield and Jasper, 1954), is prepared.

From the temporal lobe the superior gyrus (BA 41, 42, 38 and 22; Fig. 6), which contributes to the acoustic system (acoustic centre of speech and primary and secondary auditory centres) (Merzenich and Brugge, 1973; Pandya and Sanides, 1973; Hefner and Masterton, 1975; Benson et al., 1981), the medial gyrus (BA 21; Fig. 7), which appears to be responsible for the alertness to acoustic stimuli, (Kleist, 1934) and the inferior temporal gyrus (BA 20; Fig. 8), which plays a role in face recognition (Damasio, 1985) are removed. The latter two are heteromodal association areas (Mesulam, 1985).

The parietal cortex is subdivided into the postcentral gyrus (BA 1–3; Fig. 9), which represents the somatosensory cortex (Dykes and Ruest, 1986). The supramarginal gyrus (BA 40; Fig. 10) and the angular gyrus (BA 39; Fig. 11), deficits within which cause alexia and agraphia (Benson and Geschwind, 1985), are prepared. The last parietal area is the superior

parietal lobulus (BA 7; Fig. 12), which is a secondory sensory center (Burton, 1986).

From the occipital cortex the polar region (BA 17 and 18; Fig. 13) is dissected followed by the medial site of the hemisphere.

Medial aspect of the hemisphere

From the medial site of the hemisphere within the occipital lobe the superior (cuneus; Fig. 14) and inferior gyri (medial occipitotemporal gyrus; Fig. 15) of the calcarine sulcus (BA 17 and 18) are removed. These three regions belong to the visual cortex (Hubel, 1967; Damasio, 1985). The cingulate gyrus (BA 23 and 24; Fig. 16) is prepared next. This area belongs to the limbic system (Stephan, 1964) and bilateral lesions of the region cause transitory memory disorders which have been compared to the confabulations observed in the course of Korsakoff's syndrome (Whitty and Lewin, 1960) and deficits of recall of recent experiences in correct temporal order (Signoret, 1985). Then the corpus callosum (Fig. 17), the massive fibre bundle that transmits information from one hemisphere to the other (Innocenti, 1986) and whose destruction causes severe amnesic syndromes (Zaidel and Sperry, 1974), is prepared.

Regions of the diencephalon and mesencephalon that are accessible from the medial aspect of the hemisphere, are then removed. The hypothalamus (Fig. 18), the link between neuronal and endocrine systems (Akert, 1959), is prepared in toto (De Wulf, 1971; Morgane and Panksepp, 1979) without the hypophysis, as this part remains mainly within the sella turcica during removal of the brain from the skull. Tumors within the hypothalamus cause an amnesic syndrome with disorders of attention and vigilance (Williams and Pennybaker, 1954). Various disturbances in feeding, drinking, thermoregulation and sexual behaviours have also been discussed in context with hypothalamic pathology (Plum and Van Uitert, 1978; Saper, 1985). The habenular complex (Fig. 19), which may be an important link between the limbic forebrain and the midbrain-extrapyramidal motor system (Sandyk, 1991), is also cut off from the medial site. The mamillary body (Fig. 20), which belongs to the limbic system through its connection within the hippocampo- mamillo- thalamo- cingulo- hippocampal system (Papez, 1937), is the last area removed from the upper surface of the medial aspect.

Parasagittal lamination of the hemi-brainstem exposes the locus coeruleus, which is characterized by its dark structure (Fig. 21). This noradrenaline producing region is removed completely (Nobin and Björklund, 1973; Olson et al., 1973; Bogerts, 1981; Pearson et al., 1983; Konradi et al., 1989). When the brain, in particular the brain stem, is exactly medio-sagittally severed, the serotonergic raphe nuclei (Olszewski and Baxter, 1954; Braak, 1970; Nieuwenhuys, 1974) are removed. Deficits of the neurotransmitters noradrenaline and serotonin are discussed in neurochemical hypotheses on depression. Theories concerning the role of nor-

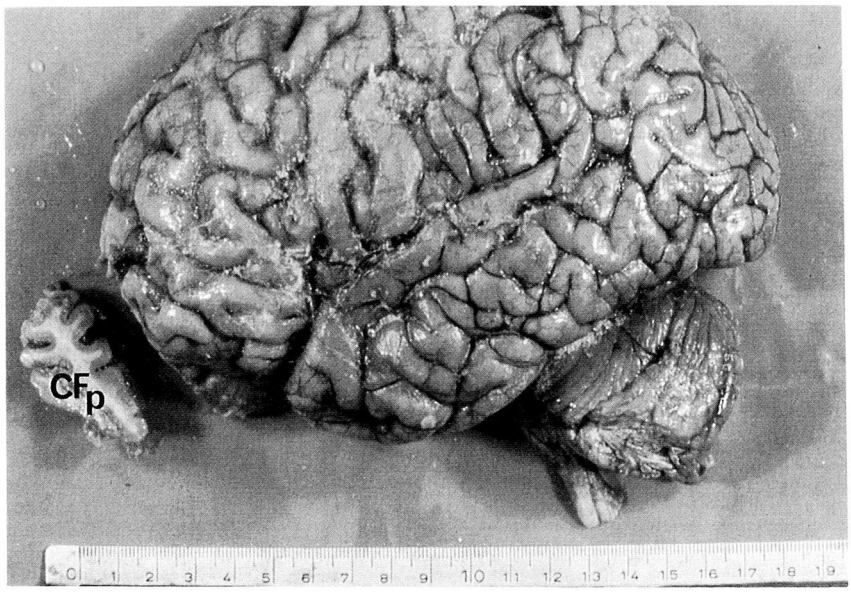

Fig. 2. Dissection of the polar region (CF_p) of the frontal lobe

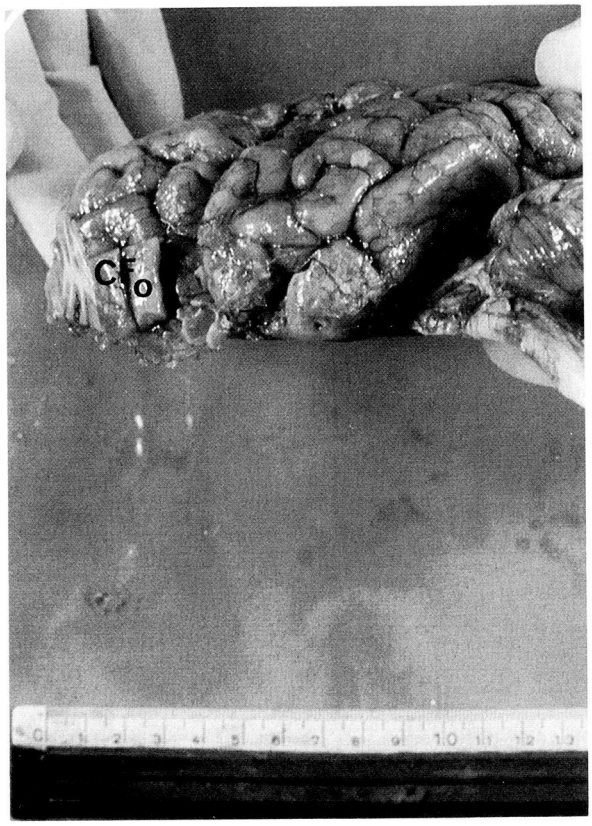

Fig. 3. Dissection of the fronto-orbital region (CF_o). The gyrus rectus is included

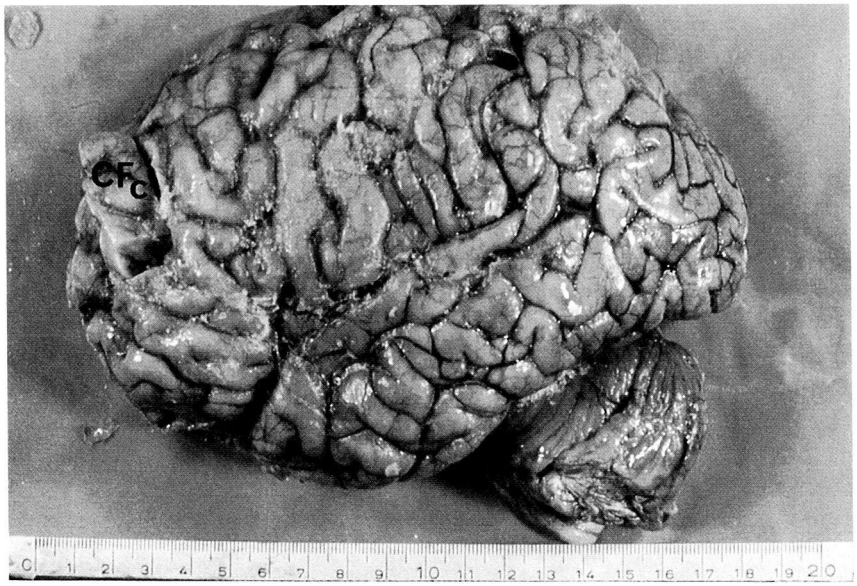

Fig. 4. Dissection of the convex region of the frontal lobe (CF_c)

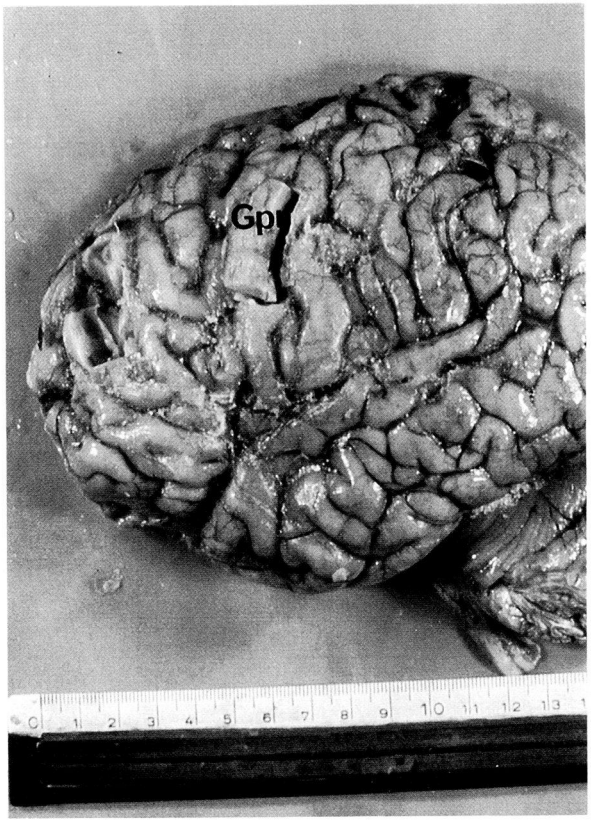

Fig. 5. Dissection of the precentral gyrus (Gpr)

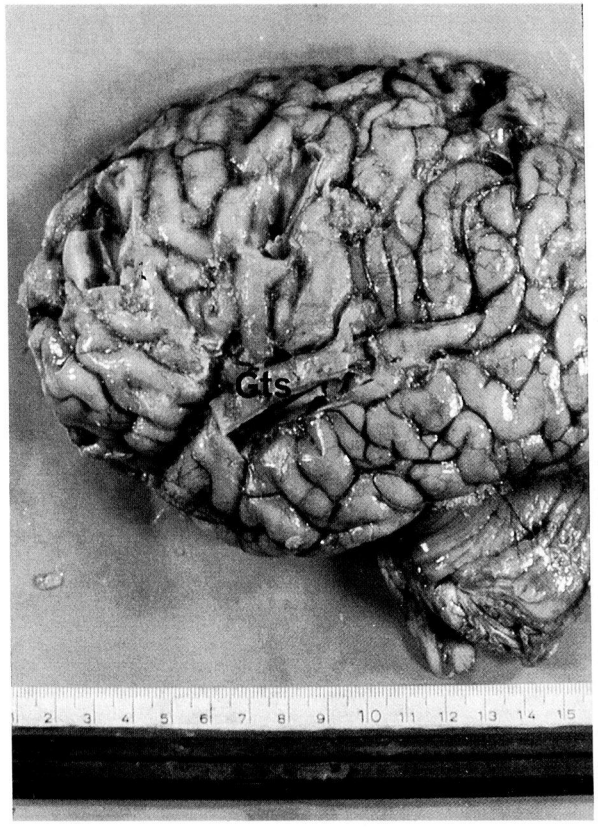

Fig. 6. Dissection of the superior temporal gyrus (Gts)

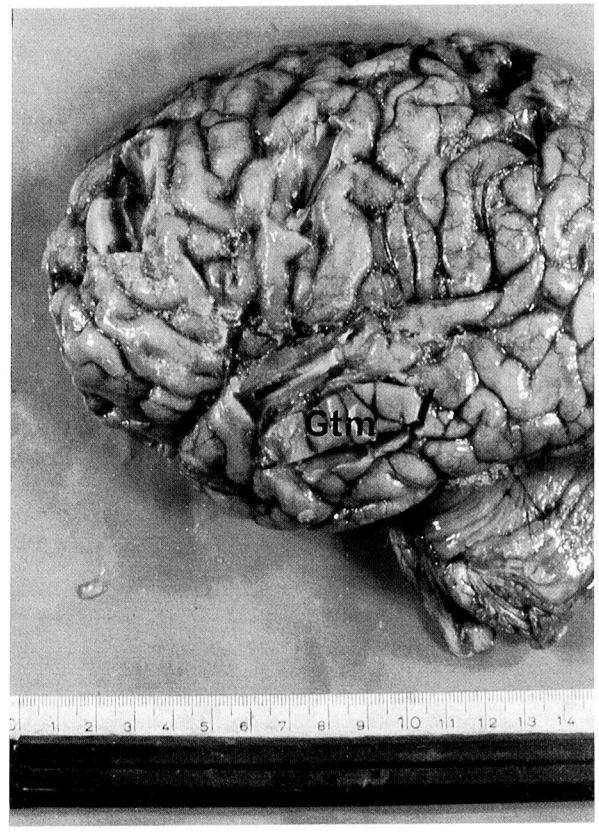

Fig. 7. Dissection of the medial temporal gyrus (Gtm)

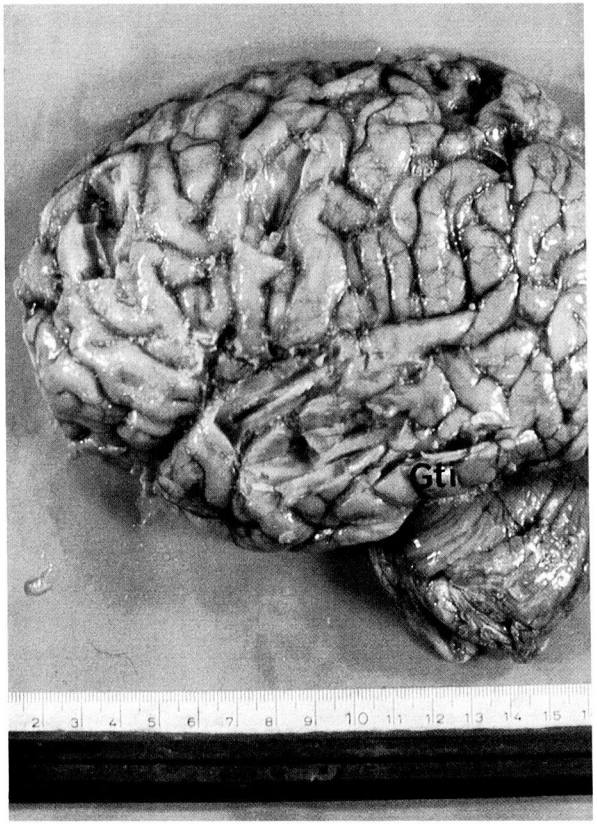

Fig. 8. Dissection of the inferior temporal gyrus (Gti)

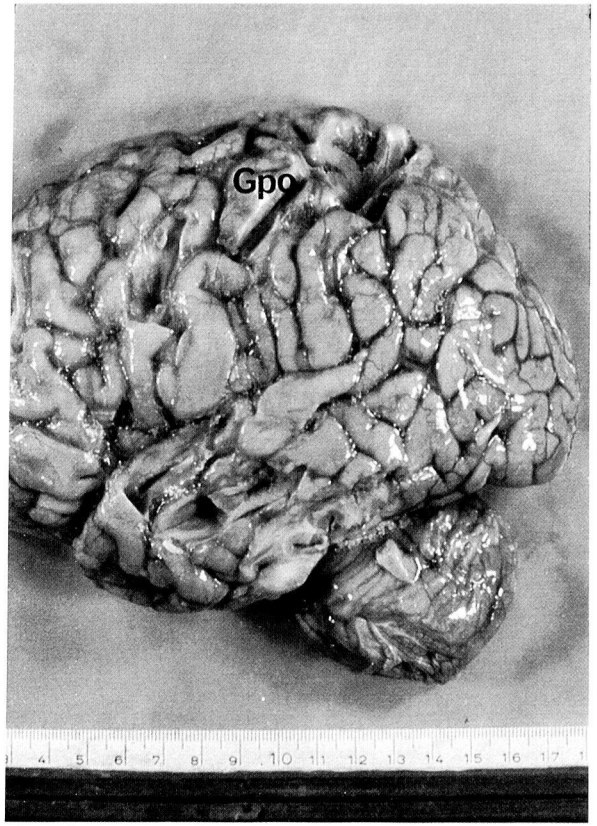

Fig. 9. Dissection of the postcentral gyrus (Gpo)

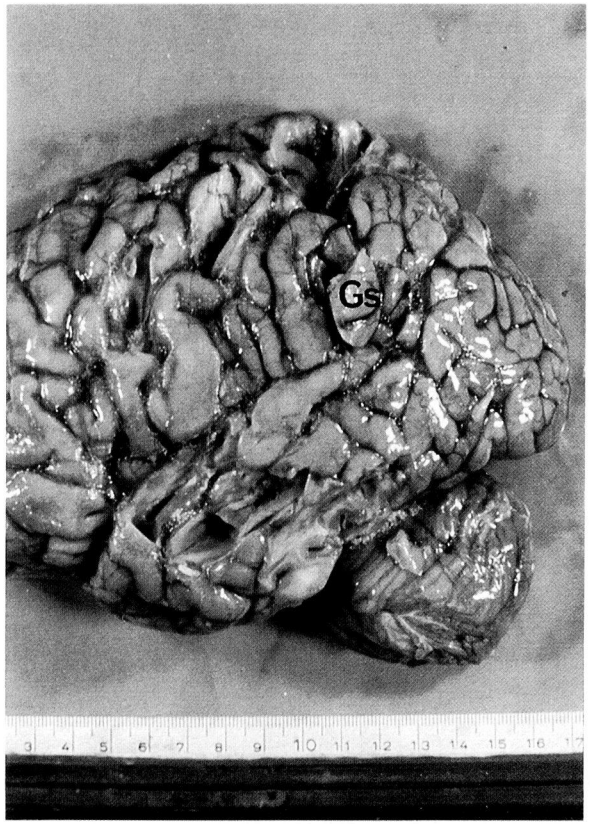

Fig. 10. Dissection of the supramarginal gyrus (Gs)

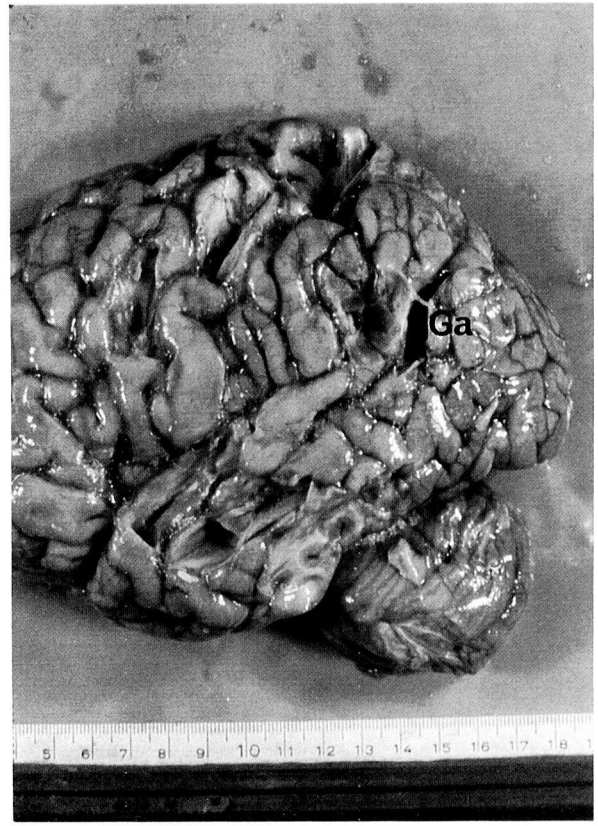

Fig. 11. Dissection of the angular gyrus (Ga)

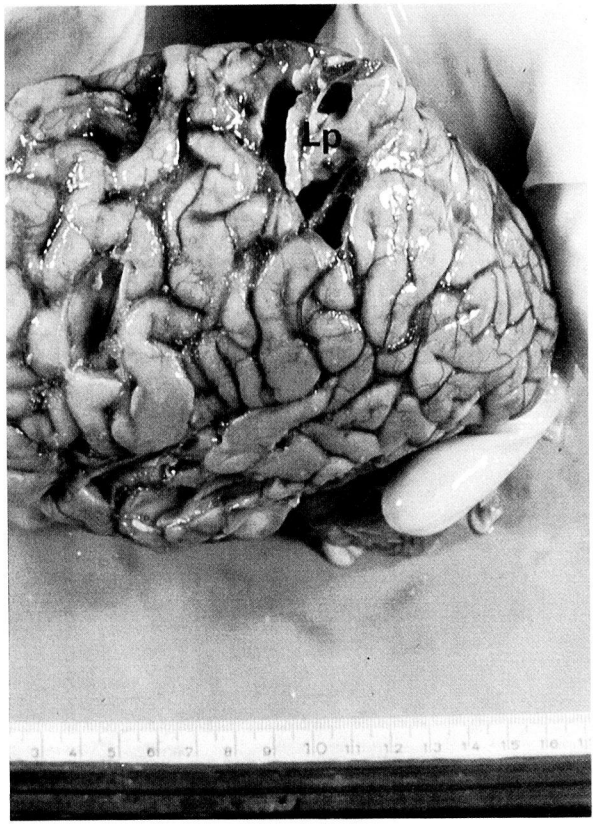

Fig. 12. Dissection of the superior parietal lobule (Lp)

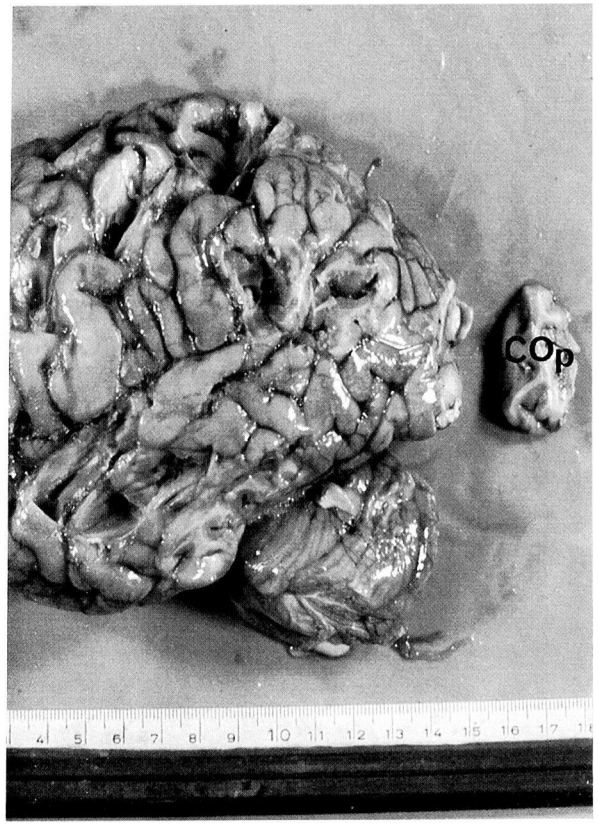

Fig. 13. Dissection of the polar region of the occipital lobe (CO_p)

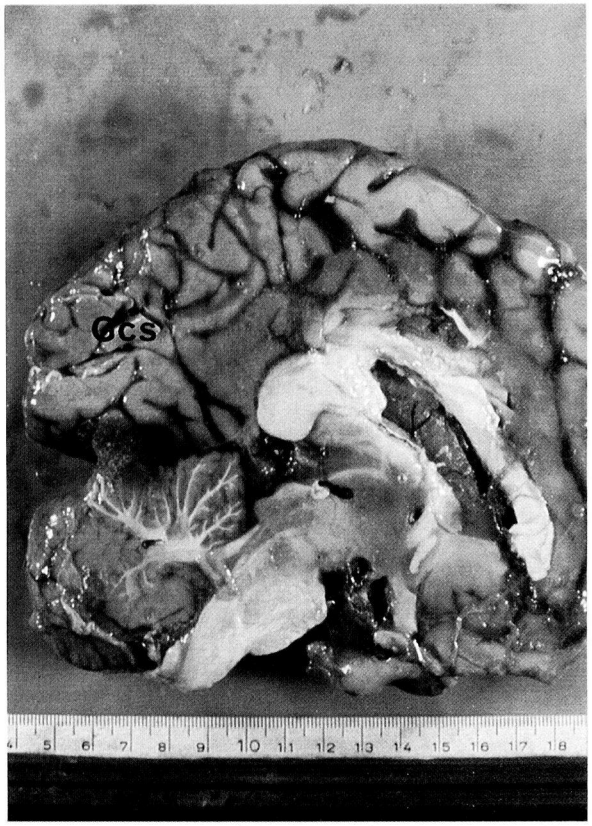

Fig. 14. Dissection of the gyrus superior to the calcarine sulcus (Gcs): gyrus sagittalis inferior

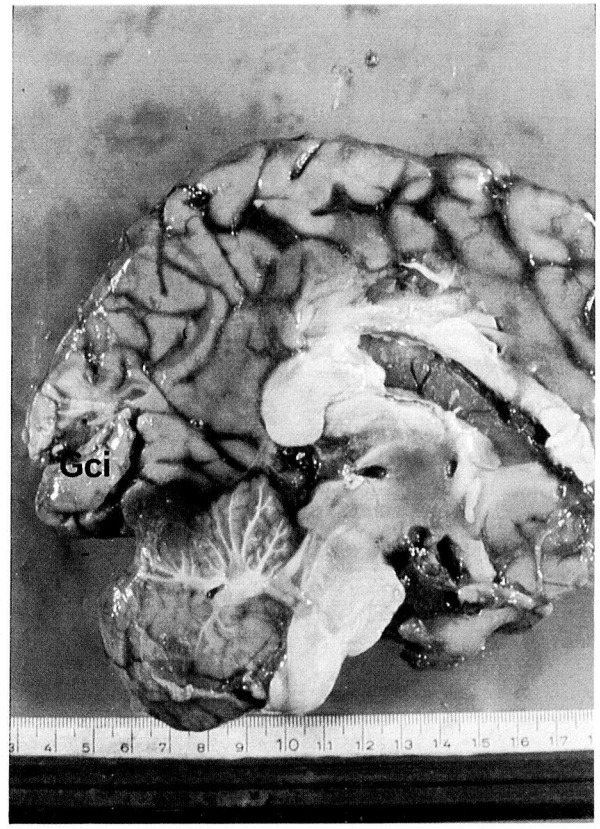

Fig. 15. Dissection of the gyrus inferior to the calcarine sulcus (Gci): gyrus lingualis superior

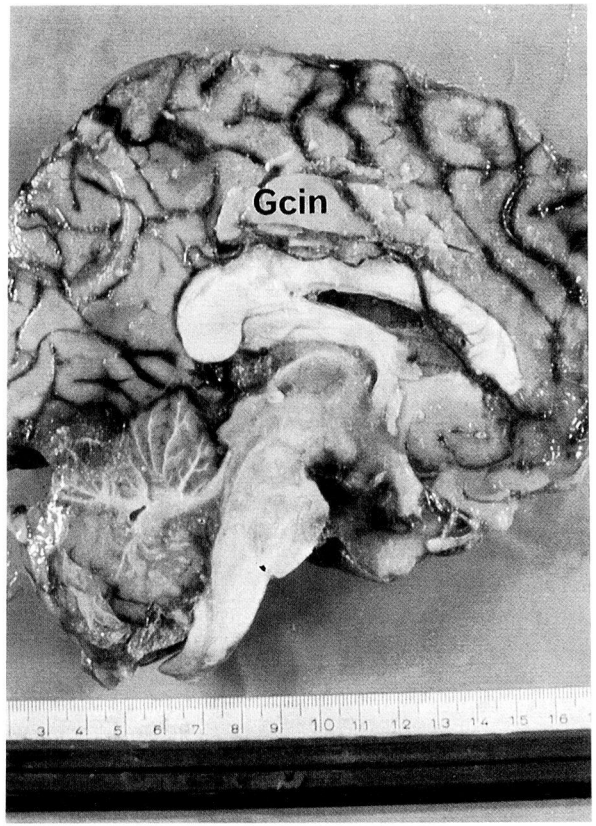

Fig. 16. Dissection of the posterior part of the cingulate gyrus (Gcin, BA 23)

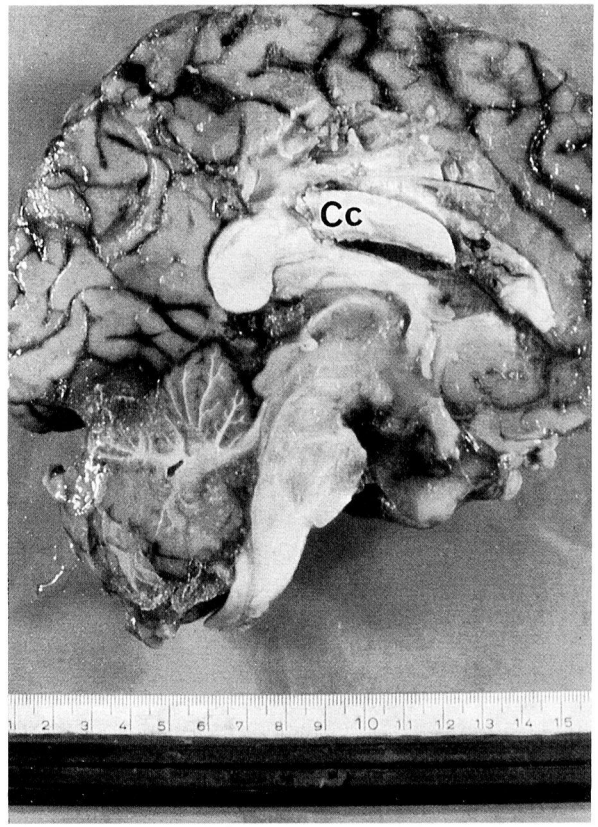

Fig. 17. Dissection of the medial part of the corpus callosum (Cc)

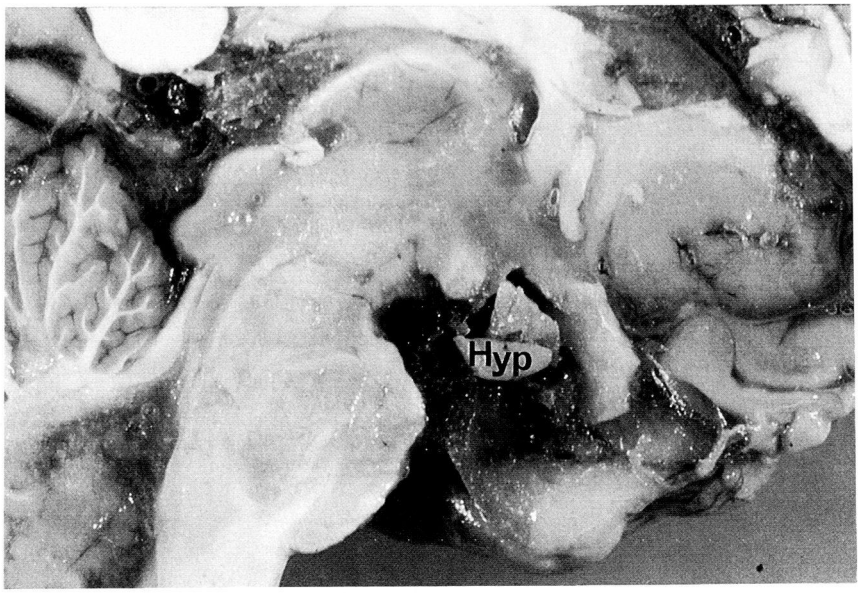

Fig. 18. Dissection of the hypothalamus (Hyp) from the medial aspect of the hemisphere

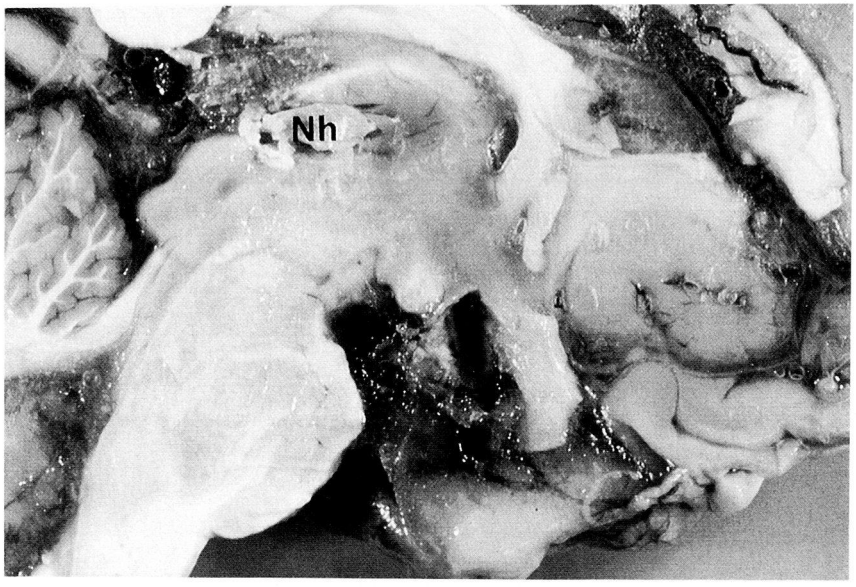

Fig. 19. Dissection of the habenular complex (Nh) from the medial aspect of the hemisphere

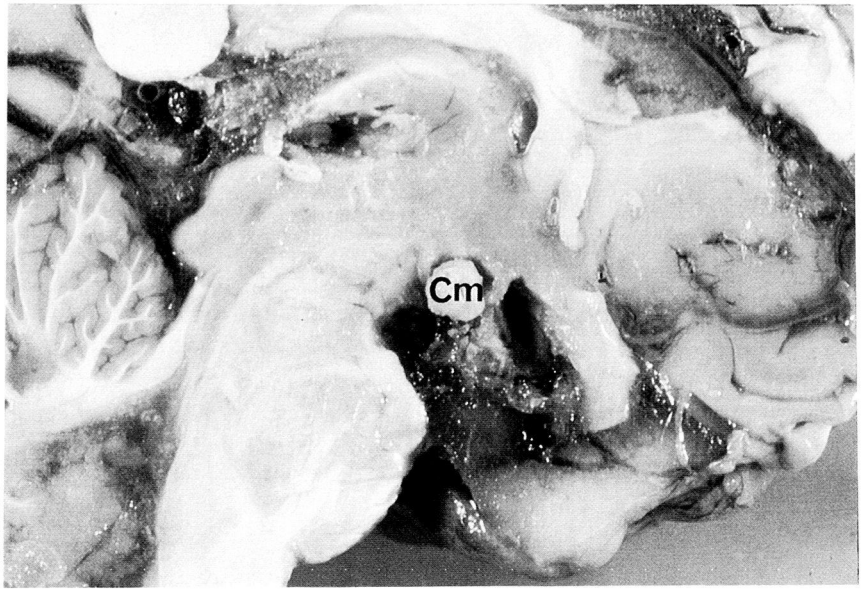

Fig. 20. Dissection of the lateral part of the left mamillary body (Cm)

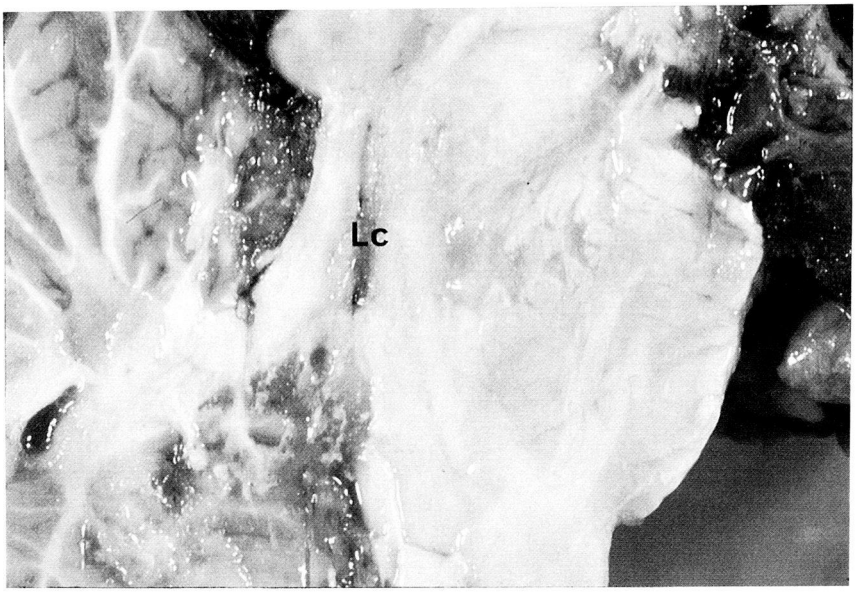

Fig. 21. Hemi-brainstem parasagittal lamination exposes the locus coeruleus (Lc)

adrenaline in depression are based on the early works of Schildkraut (1965), Bunney and Davis (1965) and Matussek (1966), while the serotonergic hypothesis was formulated by Lapin and Oxenkrug (1969).

Before coronal sections of the hemisphere are taken, the brain stem and cerebellum are cut off at the pons. From the cerebellum some cortical regions and the dentate nucleus (Fig. 22), which projects to motor nuclei

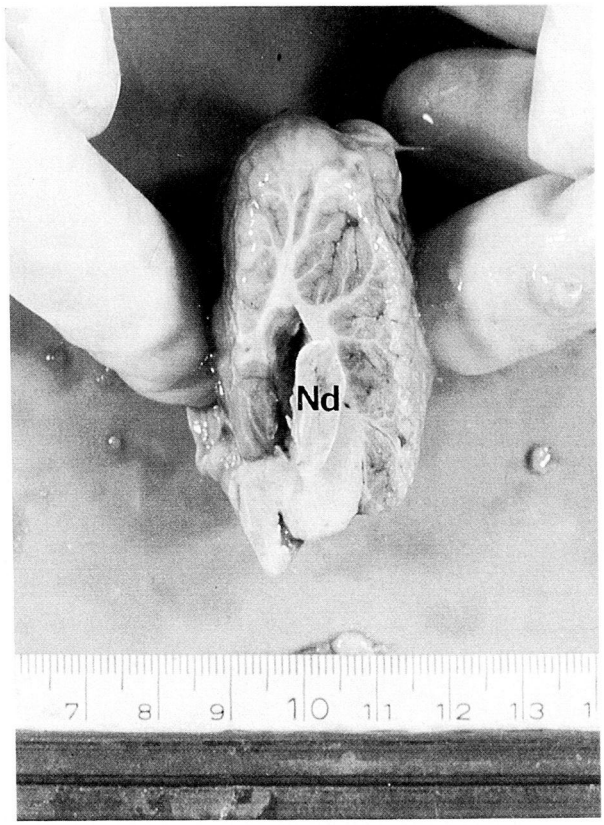

Fig. 22. Dissection of the dentate nucleus (Nd) out of the cerebellum

(ventral anterior and ventral lateral) of the thalamus and the red nucleus (Flumerfelt et al., 1973; Chan-Palay, 1977) are dissected.

Coronal slices

Coronal slicing starts at the pole of the temporal lobe (Fig. 23) and ends at the pulvinar nucleus of the thalamus. Slices are cut either with a rotating knife with a defined thickness of 4 or 6 mm (Fig. 24; first 5 slices), or by manually with a knife at a thickness of about 5 mm.

From these slices the caudate nucleus with its head (Figs. 25–27), body (Figs. 28–31) and tail (Figs. 32–37, 40–41) is dissected. The putamen is also divided into three parts, with the anterior putamen reaching from its rostral part to the beginning of the globus pallidus (Figs. 25–27). The medial putamen extends from the rostral pole of the globus pallidus to the beginning of the pallidal subdivision into lateral and medial parts (Fig. 28). Finally the caudal parts of the putamen (posterior putamen) (Figs. 29–41) are dissected. Caudate nucleus and putamen form the dorsal striatum, which is the major input area of the motor loop. Here somatosensory and premotor stimuli are integrated (Webster, 1965; Alexander et al., 1986).

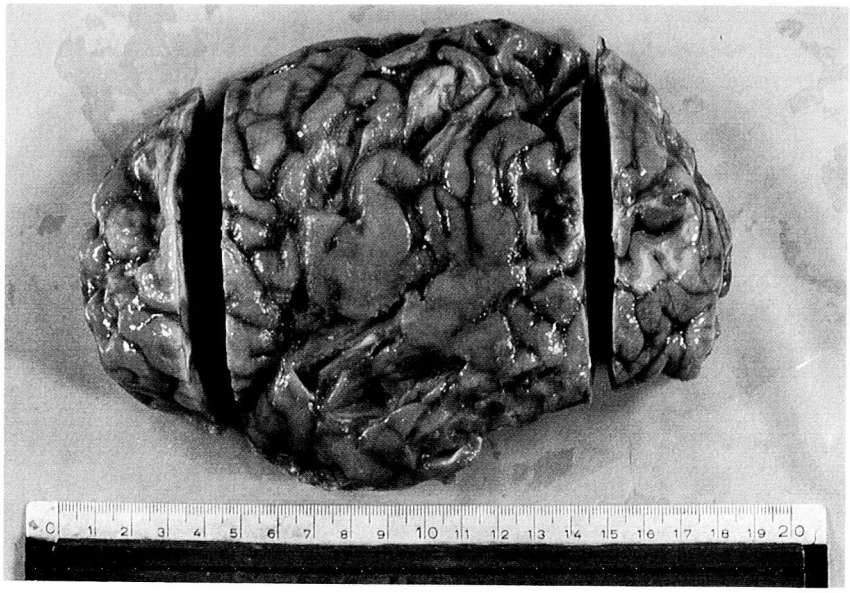

Fig. 23. Preparation of the hemisphere for cutting of coronal slices. The frontal part anterior to the pole of the temporal lobe and the rostral part with the occipital lobe were disposed

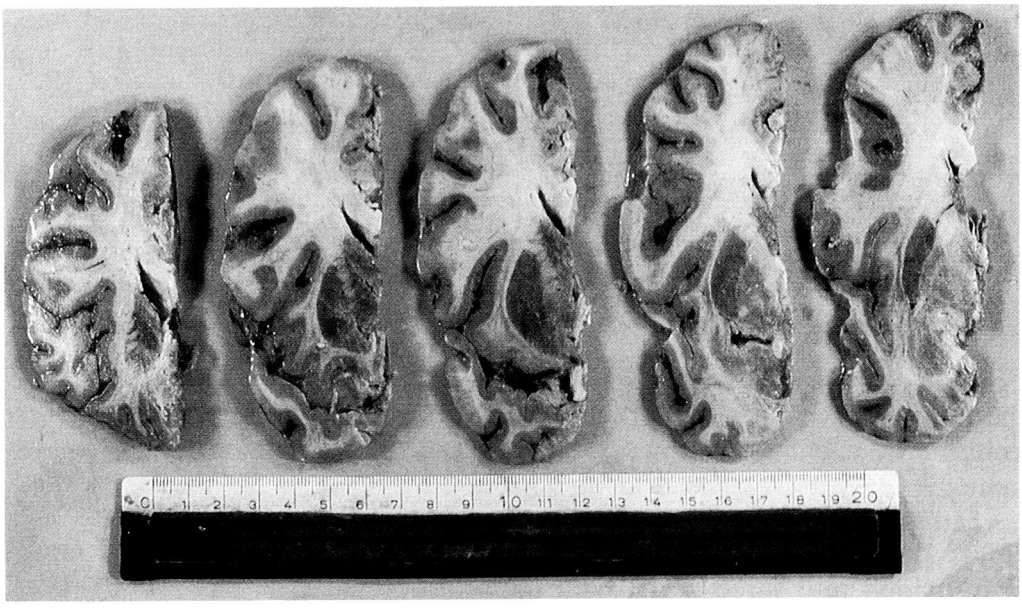

Fig. 24. The first 5 slices cut off the brain, showing the anterior part of the basal ganglia and the rostral parts of the amygdaloid complex

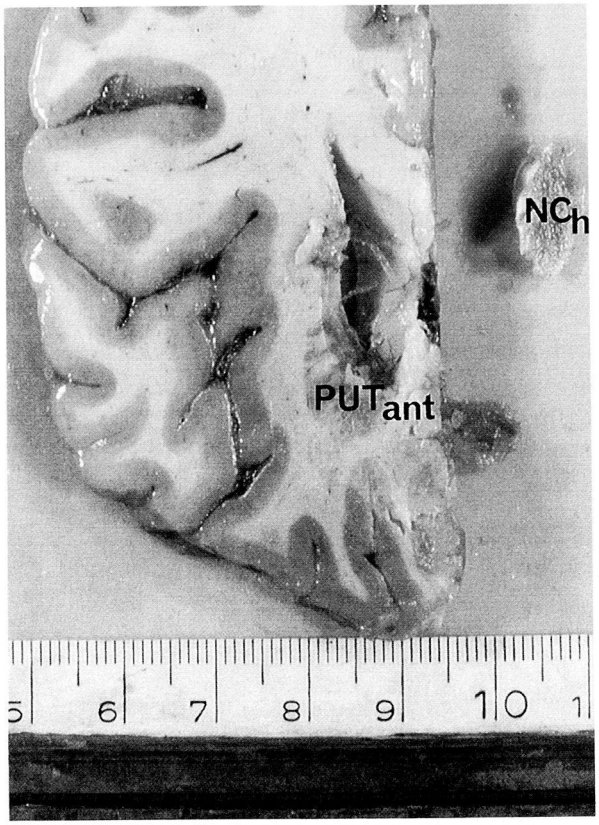

Fig. 25. Dissection of the anterior part of the head of caudate nucleus (NC_h) and the oral parts of the anterior putamen (PUT_{ant}) from the first coronal slice

In Huntington's disease striatal atrophy with selective loss of cholinergic interneurons (Roos, 1986) and progressive degeneration of striatal efferent neurons (Walker et al., 1984; Von Sattel et al., 1985; Reiner et al., 1988; Albin et al., 1990) are observed.

From the ventral striatum, which belongs mainly to the limbic system, the nucleus accumbens (Figs. 26–27), which is rich in dopaminergic D_4 receptors (Sokoloff et al., 1990; Sunahara et al., 1991) is prepared. Caudal to the anterior commissure the substantia innominata (Fig. 29) with the embedded basal nucleus of Meynert, one of the basal forebrain cholinergic nuclei, is dissected. The cholinergic neurones in the basal nucleus undergo a profound and selective degeneration in Alzheimer's disease and senile dementia of the Alzheimer type (Whitehouse et al., 1981; McGeer et al., 1984; Etienne et al., 1986; Gsell et al., 1992). When the two hemispheres have been divided exactly in the median sagittal line the cholinergic nuclei of the septum (Kemper, 1976), which are located fronto-medially of the basal nucleus of Meynert (Fig. 30) can also be prepared.

The globus pallidus is divided into an anterior (Fig. 28), the lateral (Figs. 29–31, 33, 37, 40–41) and the medial part (Figs. 29–41; Fox et al., 1974).

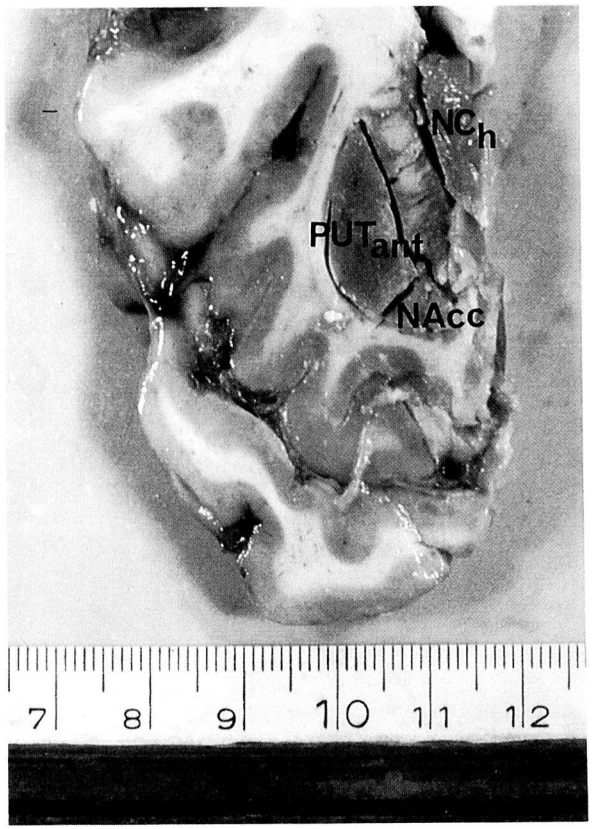

Fig. 26. Dissection of the anterior putamen (PUT_{ant}), of the head of the caudate nucleus (NC_h) and the oral nucleus accumbens (NAcc) from the second coronal slice

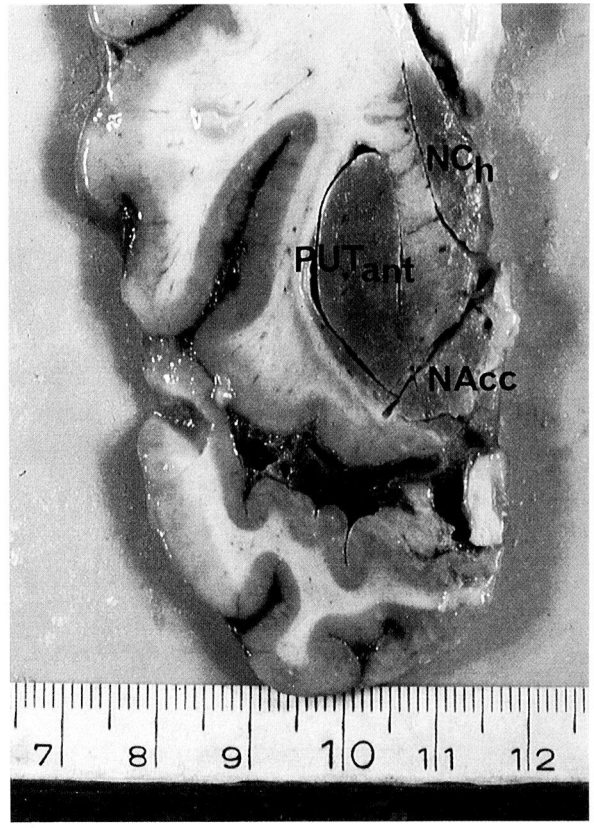

Fig. 27. Dissection of the anterior putamen (PUT_{ant}), head of the caudate nucleus (NC_h) and the nucleus accumbens (NAcc) from the third coronal slice

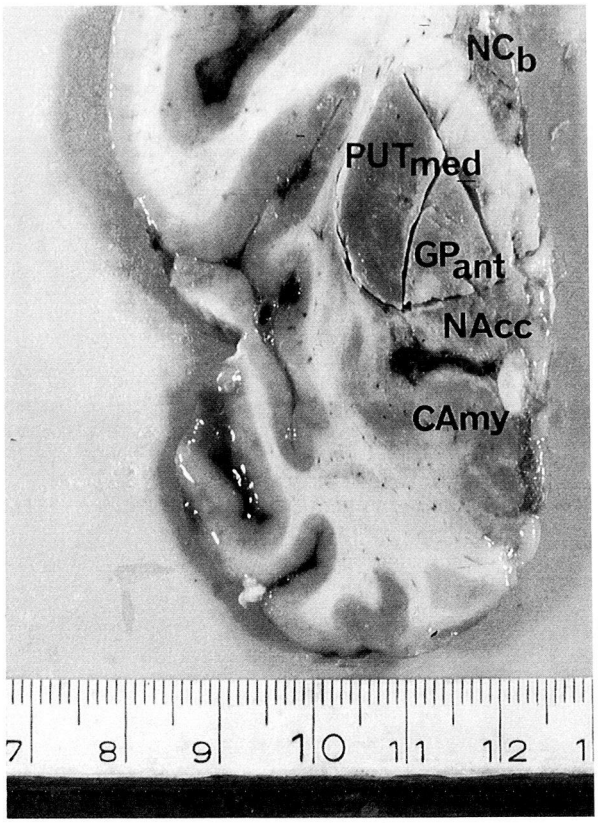

Fig. 28. Dissection of the medial putamen (PUT_{med}), anterior globus pallidus (GP_{ant}), body of the caudate nucleus (NC_b), nucleus accumbens (NAcc) and the anterior portion of the amygdaloid body (CAmy) from the fourth coronal slice

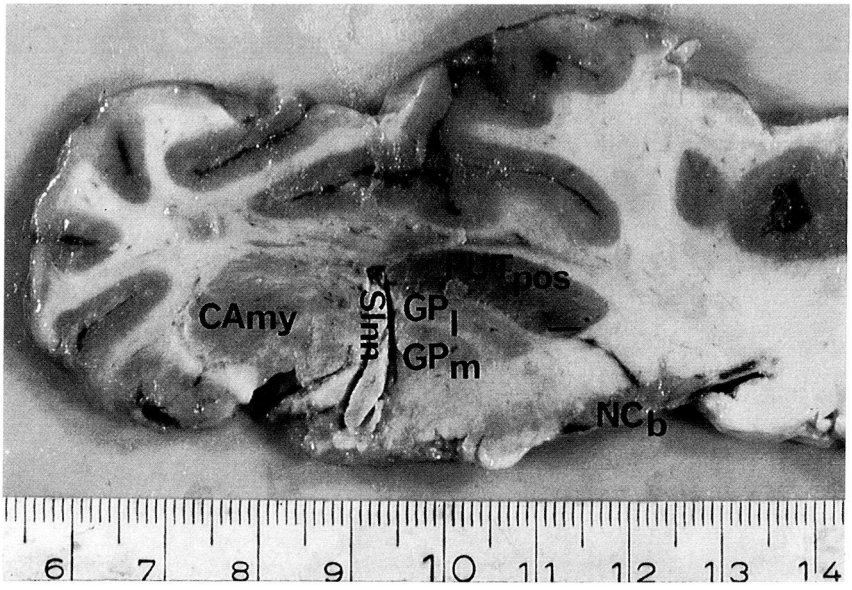

Fig. 29. Dissection of the substantia innominata (SInn) which contains the cholinergic nuclei of the basal nucleus of Meynert. The caudal (posterior) part of the putamen (PUT_{pos}), lateral (GP_l) and medial (GP_m) part of the globus pallidus, body of the caudate nucleus (NC_b) and the amygdaloid body (CAmy) are indicated

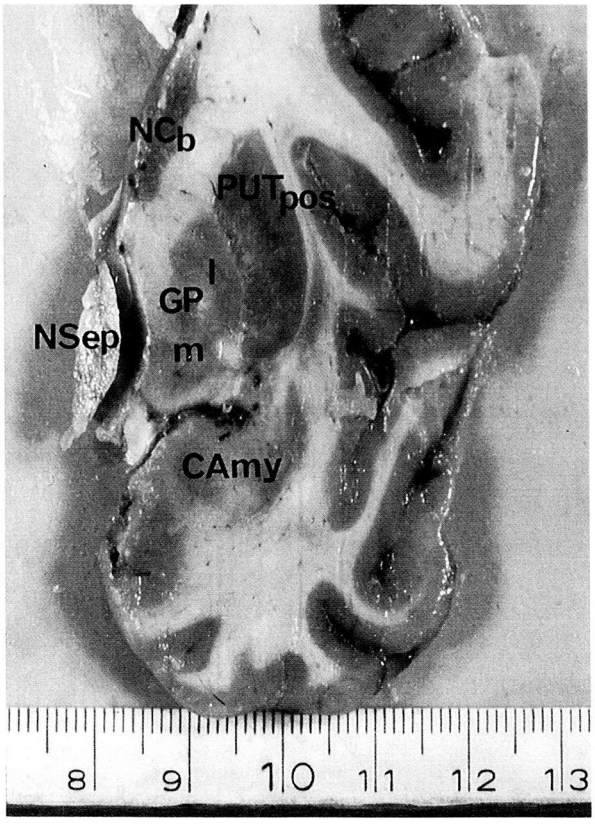

Fig. 30. Dissection of the nuclei of the septum (NSep). The caudal (posterior) part of the putamen (PUT_{pos}), lateral (GP_l) and medial (GP_m) part of the globus pallidus, body of the caudate nucleus (NC_b) and the anterior part of the amygdaloid body (CAmy) are indicated

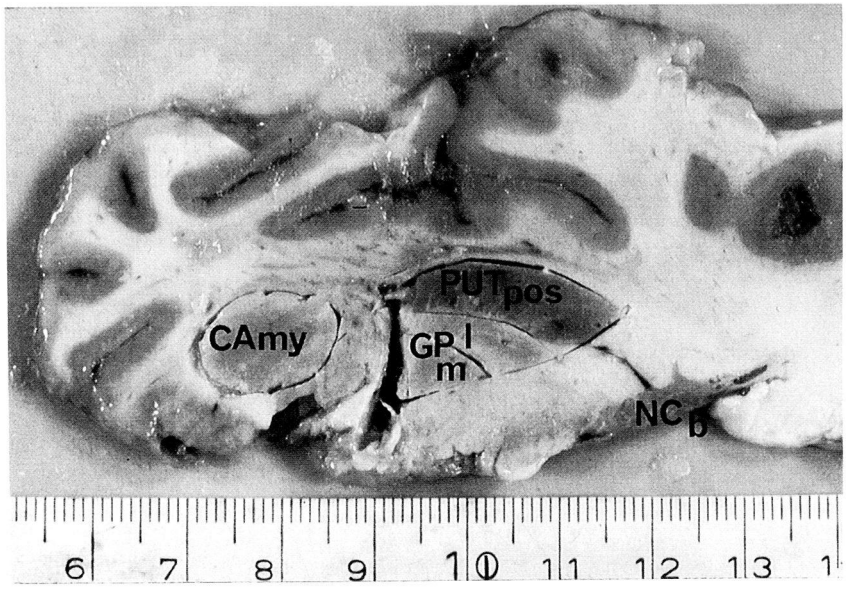

Fig. 31. Dissection of the medial part of the amygdaloid body (CAmy), the body of the caudate nucleus (NC_b), the posterior putamen (PUT_{pos}), and the db lateral (GP_l) and medial (GP_m) globus pallidus

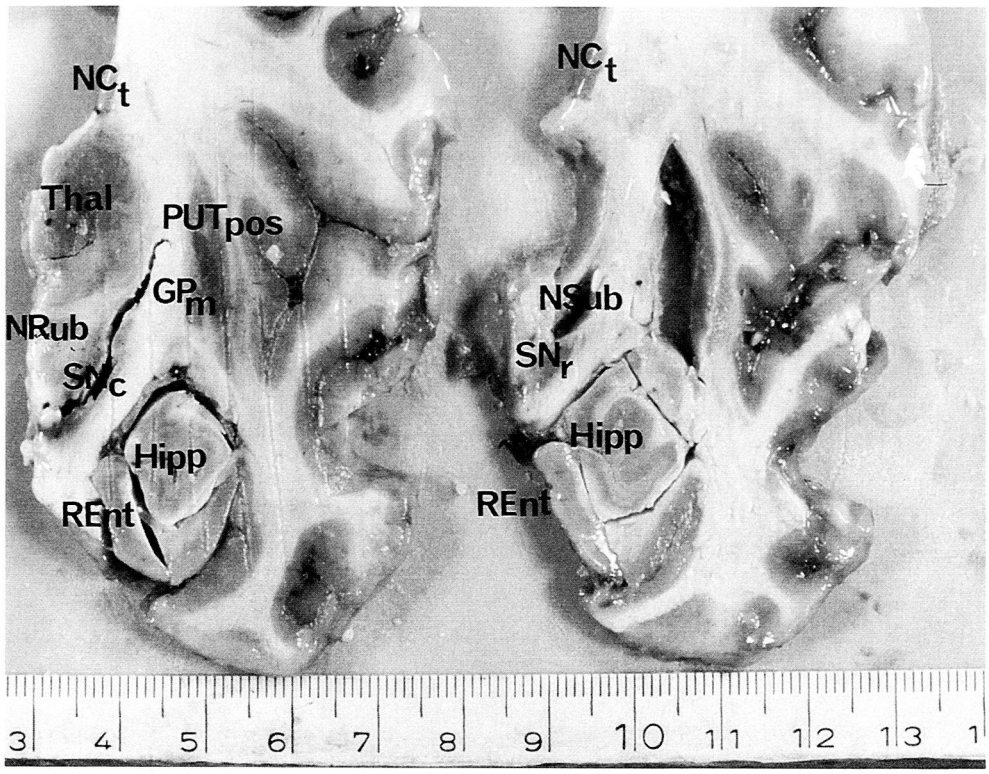

Fig. 32. Dissection of the posterior putamen (PUT_{pos}), medial part of the globus pallidus (GP_m), entorhinal cortex (REnt) and hippocampus (Hipp). On the right slice, the area where the subthalamic nucleus (NSub) has been dissected and the reticulate part of the substantia nigra (SN_r) are shown. On the left slice the red nucleus (NRub), compact part of the substantia nigra (SN_c) and thalamus (Thal) is to be seen. The tail of the caudate nucleus (NC_t) is marked on both slices

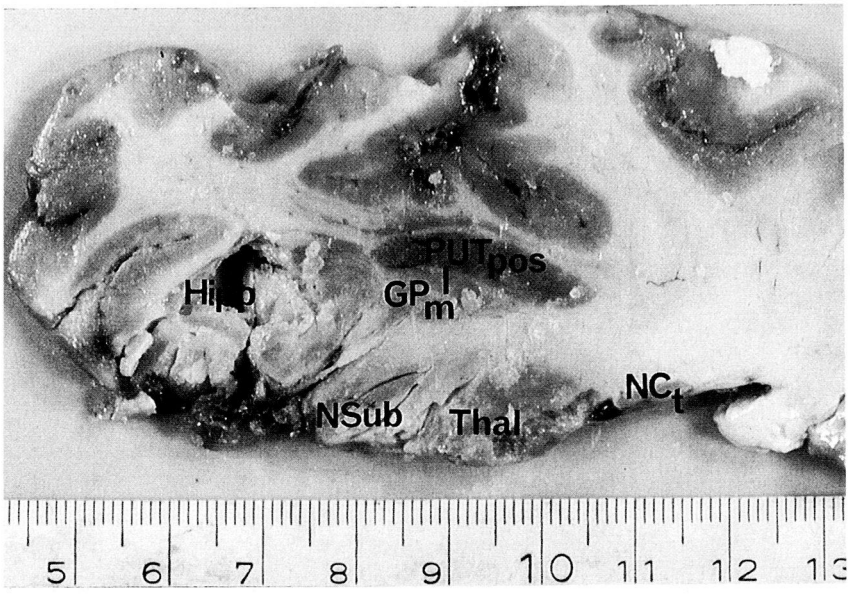

Fig. 33. Dissection of the subthalamic nucleus (NSub). The tail of the caudate nucleus (NC_t), posterior putamen (PUT_{pos}), lateral (GP_l) and medial (GP_m) part of the globus pallidus, hippocampal formation (Hipp), and thalamus (Thal) are indicated

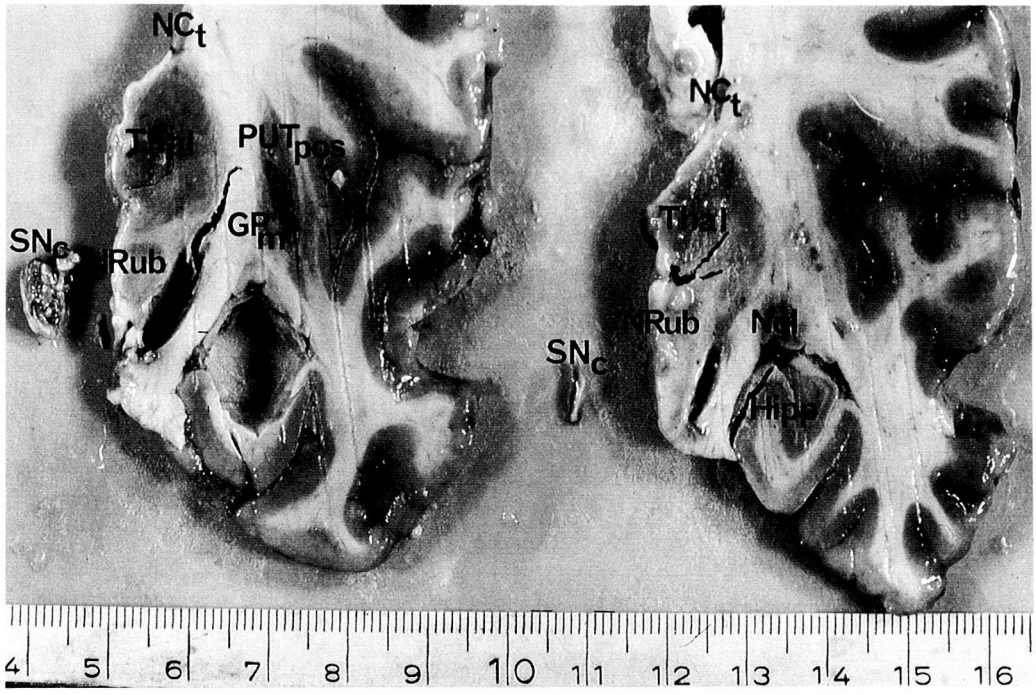

Fig. 34. Dissection of the compact part of the substantia nigra (SN_c). The tail of the caudate nucleus (NC_t), posterior putamen (PUT_{pos}), medial (GP_m) part of the globus pallidus, hippocampal formation (Hipp), lateral geniculate nucleus (Ngl), red nucleus (NRub) and thalamus (Thal) are indicated

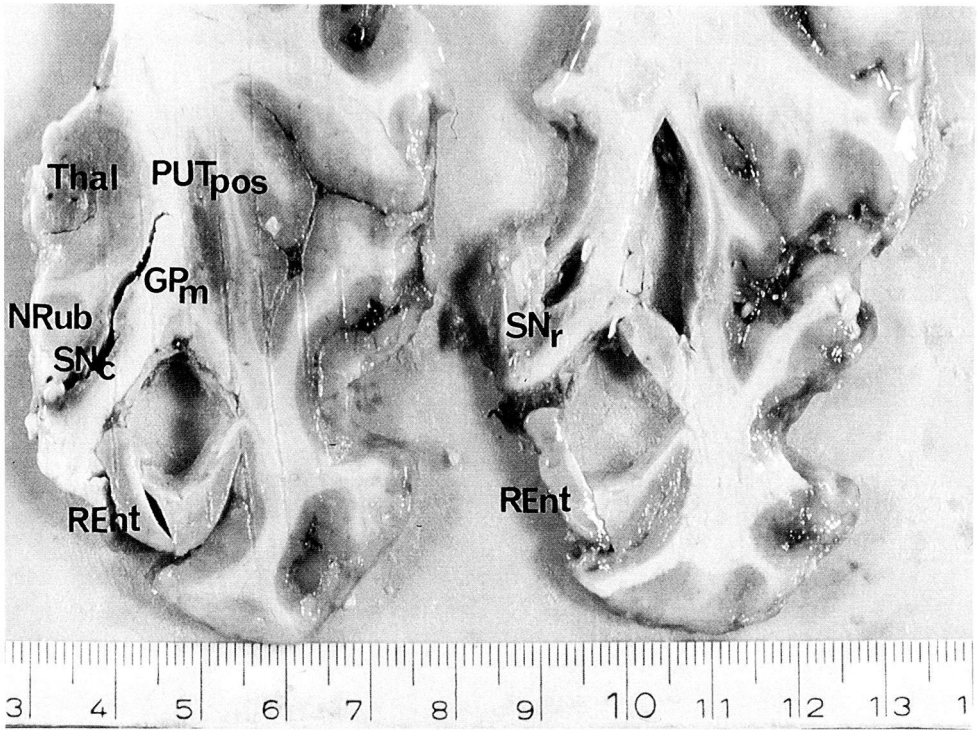

Fig. 35. Dissection of the reticulate part of the substantia nigra (SN_r). The posterior putamen (PUT_{pos}), medial part of globus pallidus (GP_m), thalamus (Thal), red nucleus (NRub), compact part of the substantia nigra (SN_c) and entorhinal cortex are indicated

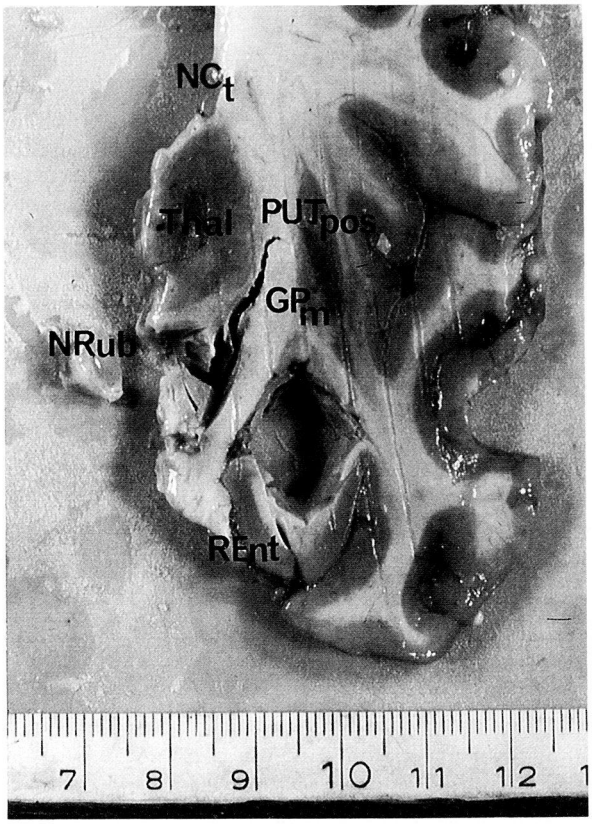

Fig. 36. Dissection of the red nucleus (NRub). The tail of the caudate nucleus (NC_t), thalamus (Thal), medial part of the globus pallidus (GP_m), posterior putamen (PUT_{pos}) and entorhinal region (REnt) are indicated

The latter two belong to the motor loop and integrate GABAergic afferents from the striatum (Alexander et al., 1986).

Limbic structures (Isaacson, 1974) are then dissected. From the anterior part of the temporal lobe the amygdaloid body (Figs. 28–31; Koikegami, 1963; Cowan et al., 1965) is dissected. This area receives convergent input from many brain areas, especially the olfactory part (Rosene and Heimer, 1977), basomedial telencephalon (Cowan et al., 1965) and hypothalamus (Norita and Kawamura, 1980), the thalamus, brain stem and cortical areas (Aggleton et al., 1980). The amygdala itself sends efferent projections to the hypothalamus and medial preoptic area (Berk and Finkelstein, 1981), to the medio-frontal cortex, basal septal region and brainstem (Nauta, 1961; Krettek and Price, 1978), to the magnocellular portion of the medial nucleus of the thalamus (Aggleton and Mishkin, 1984), to the ventral (Heimer, 1978) and dorsal striatum (Kelley et al., 1982), to the cerebral cortex, e.g. the entorhinal cortex and subiculum (Krettek and Price, 1977), to BA 32 (prelimibic), BA 25 (infralimbic), BA 24 (anterior cingulate gyrus) and BA 35 and 36 (perirhinal) (Macchi et al., 1978; Amaral and Price, 1984), the frontal cortex with motor (BA 4; Llamas et al., 1977)

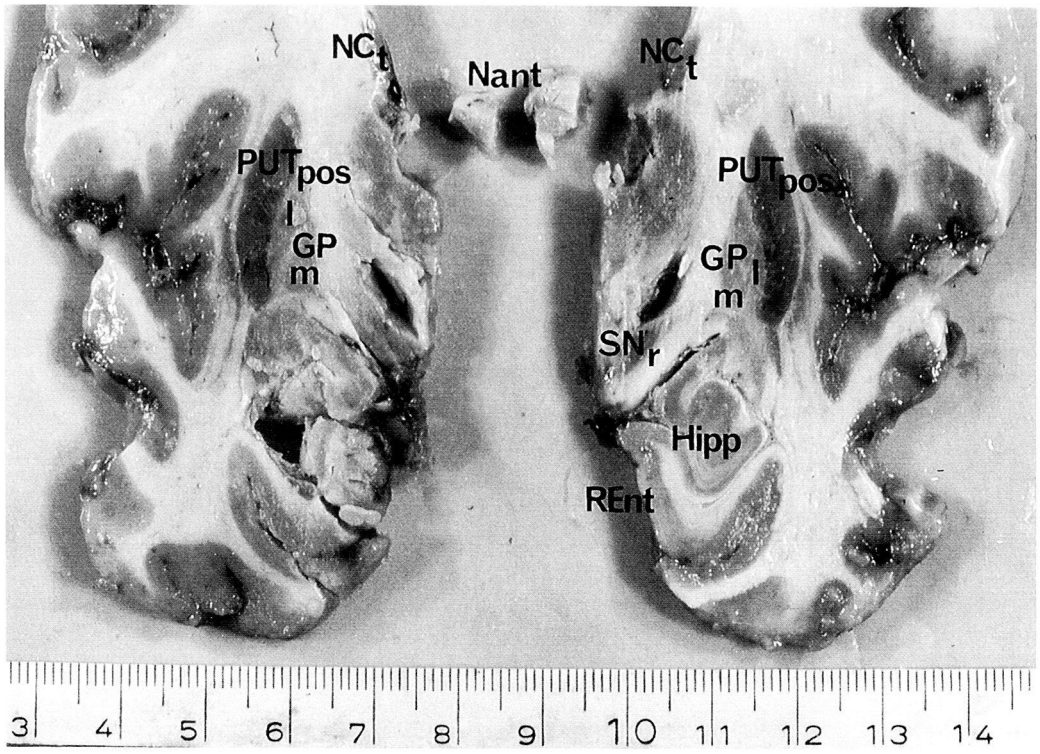

Fig. 37. Dissection of the anterior nucleus of the thalamus (Nant). The tail of the caudate nucleus (NC_t), posterior putamen (PUT_{pos}), medial (GP_m) and lateral (GP_l) part of the globus pallidus, hippocampus (Hipp), entorhinal region (REnt), reticulate part of the substantia nigra (SN_r) and amygdala (CAmy) are indicated

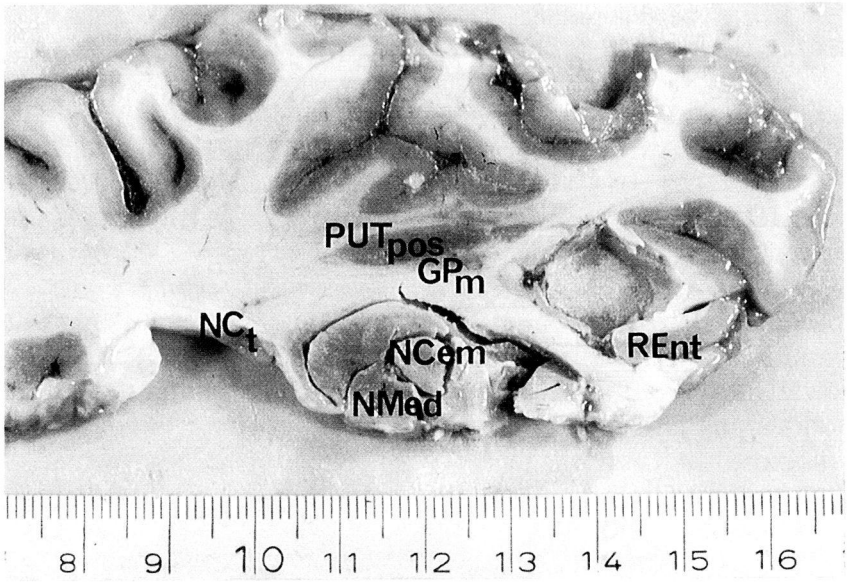

Fig. 38. Dissection of the centromedian nucleus of the thalamus (NCem). The medial nucleus of the thalamus (Nmed), the tail of the caudate nucleus (NC_t), the entorhinal region (REnt), the proterior putamen (PUT_{pos}) and the medial part of the globus pallidus (GP_m) are indicated

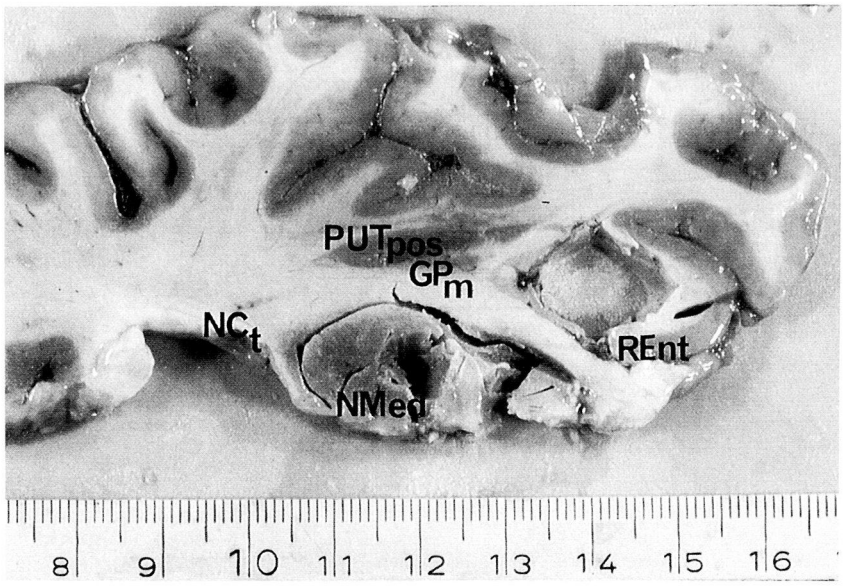

Fig. 39. Dissection of the medial nucleus of the thalamus (NMed). The tail of the caudate nucleus (NC_t), the entorhinal region (REnt), the proterior putamen (PUT_{pos}) and the medial part of the globus pallidus (GP_m) are indicated

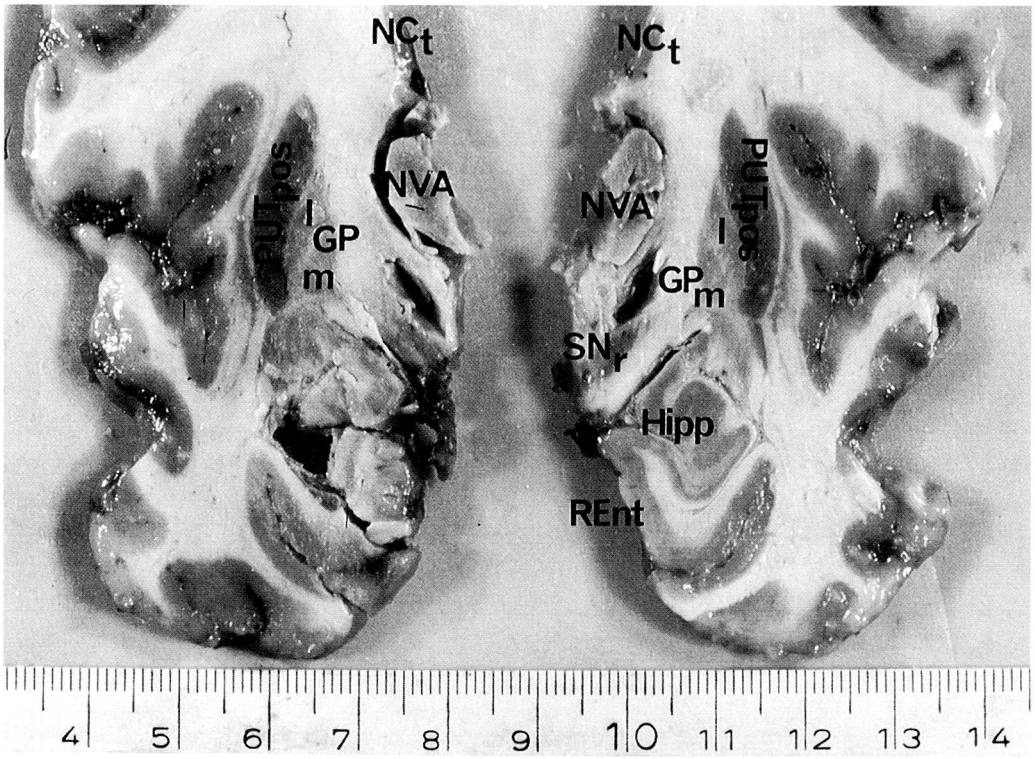

Fig. 40. Dissection of the ventral anterior nucleus of the thalamus (NVA). The tail of the caudate nucleus (NC_t), the entorhinal region (REnt), the hippocampus (Hipp), the reticulate part of substantia nigra (SN_r), the proterior putamen (PUT_{pos}) and the lateral (GP_l) and medial part of the globus pallidus (GP_m) are indicated

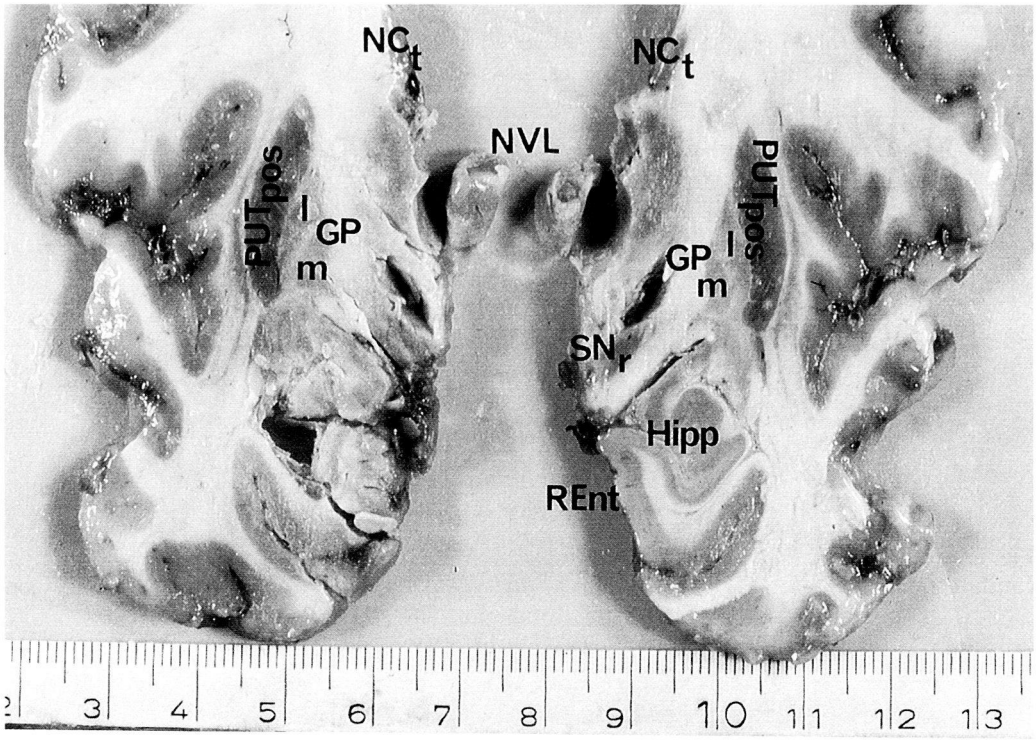

Fig. 41. Dissection of the ventro-lateral nucleus of the thalamus (NVL). The tail of the caudate nucleus (NC_t), the entorhinal region (REnt), the hippocampus (Hipp), the reticulate part of substantia nigra (SN_r), the proterior putamen (PUT_{pos}) and the lateral (GP_l) and medial part of the globus pallidus (GP_m) are indicated

and premotor (BA6; Avendano et al., 1983) regions and most parts of the temporal lobe (Amaral and Price, 1984). The amygdaloid body has numerous connections with other brain areas and its functions are manyfold. It becomes active during times of emergency or extreme stress, provides motivational drive for the execution of movements and is active in pain-control mechanisms (Kuypers, 1982).

From the antero-medial part of the temporal lobe the entorhinal region (Fig. 32) and the hippocampal formation (Fig. 32ff.) are dissected. The entorhinal cortex represents the principal source of cortical input to the hippocampal formation (Van Hoesen and Pandya, 1975a,b; Van Hoesen et al., 1975). In addition, there are indications that cortical areas that project to the hippocampus via the entorhinal cortex are reciprocally connected with the latter (Amaral and Insausti, 1990). Via these connections the hippocampal formation can influence widespread regions within the different cortical lobes. Lesions within the hippocampal formation and entorhinal region are known to cause memory deficits (Penfield and Milner, 1958; Symonds, 1966; Milner, 1970; Squire, 1987) which result from an enduring, polysensory amnesic syndrome. The entorhinal region and parahippocampal area are the first affected areas in Alzheimer's disease and demented parkinsonian patients (Braak and Braak, 1990; Jellinger et al., 1991).

Next the subthalamic nucleus (Fig. 33), the substantia nigra, which is divided into the pars compacta (Fig. 34) and pars reticulata (Fig. 35), and the red nucleus (Fig. 36) are prepared. All of these areas are involved in motor function. The red nucleus with its rubrospinal projections (Edwards, 1972) has an excitatory influence on contralateral flexor motorneurons and inhibits contralateral extensors (Sasaki et al., 1960; Hongo, 1969, 1972). Lesions of the red nucleus and the rubrospinal tract result in motor deficits in the execution of independent movements of the limbs, especially of their distal parts (Lawrence and Kuppers, 1968). The subthalamic nucleus, lying within the motor loop of the extrapyramidal motor-system, receives GABAergic afferents from the lateral part of the globus pallidus and projects into the medial part of globus pallidus and reticular part of substantia nigra. Its degeneration causes hemiballism (Carpenter and Carpenter, 1951; Crossman et al., 1984; Crossman, 1987). A 60–80% destruction of the dopaminergic neurones of the substantia nigra pars compacta (Riederer and Wuketich, 1976) which innervates the striatum, results in clinical symptoms of Parkinson's disease (Ehringer and Hornykiewicz, 1960), i.e. hypokinetic motor dysfunctions such as rigidity and akinesia.

The catecholaminergic neurotransmitter dopamine and the excitatory amino acid neurotransmitter glutamate are discussed in hypotheses on schizophrenia (Kornhuber et al., 1984; Kim et al., 1986).

Dissection of the thalamus of frozen material may be difficult since laminae disappear during postmortem processes. Under these circumstances dissection is performed according to the stereotactic localization of the areas. For the subareas of the thalamus the English/American terminology is used (Van Buren and Borke, 1972; Walker, 1982). The anterior nucleus (Fig. 37), which receives input via mamillary bodies (tractus mamillothalamicus, bundle of Vicq d'Azyr) and connects the limbic system by projections to the cingulate gyrus, is removed first. Thereafter, the centromedian nucleus (Fig. 38), which is an intralaminar nucleus, is dissected. It receives projections mainly from the globus pallidus (Faull and Mehler, 1978; Parent and DeBellefeuille, 1983). The medial nucleus (Fig. 39) is then removed. Its medial magnocellular part is connected to olfactory-related areas (Akert, 1964; Yarita et al., 1980), the amygdaloid body and the entorhinal region (Aggleton and Mishkin, 1984; Russchen et al., 1987). Its lateral parvocellular part receives afferent connections from the substantia nigra among other subcortical areas (Ilinsky et al., 1985) and is connected with the frontal eye field (BA 8) and the prefrontal cortex (Künzle and Akert, 1977; Tanaka, 1976; Schell and Strick, 1984).

The last two areas prepared from the thalamus are the two motor nuclei. The ventral anterior nucleus (Fig. 40) is connected with the frontal eye field and the premotor cortex (Kievit and Kuypers, 1977; Asanuma et al., 1985), while the ventral lateral nucleus (Fig. 41) (posterior part) receives inputs from the cerebellar nuclei (Asanuma et al., 1983). The input from the globus pallidus terminates rostrally to the cerebellar afferents (Kuo and Carpenter, 1973; Nauta, 1979; DeVito and Anderson, 1982; Parent and DeBellefeuille, 1982; Ilinsky and Kultas-Ilinsky, 1984), while between both

terminal areas fibres from the reticulate part of the substantia nigra end (Carpenter et al., 1976; Ilinsky et al., 1985). The ventral lateral nucleus itself projects to BA 4 (precentral gyrus) and BA 6 including the supplementary motor area (Strick, 1973; Schell and Strick, 1984).

Storage

Each brain region is sealed in its own plastic bag located on a freezing-table and stored in a numbered container in a numbered deep-freezer. The database is then updated with information on the prepared regions and the numbers of the storage containers. Thus the information is readily accessible for the planning of research projects and the distribution of material.

Data management

The pathological and clinical case reports are encoded for database use. The database is then updated with clinical, pathological and storage information.

When requested the database is consulted with respect to disease classification, brain region, age, sex, postmortem delay, agonal state, etc. If the number of cases is sufficient for the planned study in accord with statistical assumptions the tissue is removed from its container and sent to the analysis centre. The database must then be updated with the removal of the material.

Data handling with the dBase program also allows easy extraction of data of interest for subsequent statistical data analysis (see also chapter Distribution).

Distribution

The required brain regions of the investigated disease are sent to the laboratories that undertake the analyses. These laboratories also receive the information on pathology, neuropathology and clinical data that they need from the brain bank.

In the next step of the development of the brain bank an informational back flow from the analysis centres to the brain bank is planned. The chemical, biochemical, molecular biological, pharmacological and neuropathological data gained in the analysis centres and obtained by the brain bank will help to maximize information concerning valuable brain material. For example, the combination of the results of different research centres allows statistical correlations between different parameters for the brain regions examined. Possible similarities and differences between neuropsychiatric diseases in regard to chemical, biochemical, pharmacological, molecular biological and neuropathological parameters could be investigated (Riederer et al., 1990).

Acknowledgements

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