Nucleus dorsalis superficialis (lateralis dorsalis) of the thalamus and the limbic system in man

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SYNOPSIS Although the earlier supposition was that the n. dorsalis superficialis (n. lateralis dorsalis) of the thalamus projected to the parietal region, more recent evidence has linked it to the posterior cingulate gyrus and possibly adjacent regions near the splenium of the corpus callosum. An afferent supply from lower levels was in more doubt, although some report had been made of cell and fibre degeneration in the n. dorsalis superficialis after extensive temporal resections and section of the fornix in lower primates. The five human hemispheres of the present study all had lesions of long duration below the level of the splenium of the corpus callosum in the posteromedial temporal region. All showed marked degeneration in the fornix and n. dorsalis superficialis. In favourably stained cases, gliotic fascicles could be followed from the descending column of the fornix to the n. dorsalis superficialis via the region lateral to the stria medullaris thalami. The cell loss in the nucleus thus appeared to be an instance of anterograde transynaptic degeneration. These cases provided an interesting instance in which human infarctions provided natural lesions that would have been hard to duplicate in experimental animals.

In man, the n. dorsalis superficialis (n. lateralis dorsalis) lies on the superior surface of the thalamus above the n. medialis (n. medialis dorsalis) and is contiguous with the pulvinar posteriorly. Anteriorly, it extends a conical process medial to the posterior tapering extension of the anterior nuclei. It is separated from the thalamic surface and the adjacent nuclei by a thin and somewhat variable medullated lamina. In general, the background myelination of the nucleus is very light, making it readily distinguishable by the naked eye on myelin preparations. However, a variable pattern of fascicles may enter the nucleus from the stratum zonale lateral to the nucleus or the ventral myelinated lamina. This may lead to a parcellated or marbled appearance accounting for the designation, n. disseminati dorsalis, used by Riley (1943).

In the early work there was little to suggest that the nucleus belonged to the limbic system. Walker (1938a, p. 185) concluded that, 'It is quite apparent that this nucleus [n. lateralis dorsalis] is largely related to the posterior part of the postcentral convolution and, to a lesser

extent, to the cortex of areas 5 and 7.' Support for this concept was supplied by studies in the macaque (Walker, 1938a), chimpanzee (Walker, 1938b, c), and in man (Papez, 1939; Clark and Russell, 1940; Hartmann and Simma, 1952; Szabo, 1952). On the other hand, some discrepancies appeared. Ranson *et al.* (1941) reported a case of removal of the lateroposterior frontal, parietal, anterior occipital, and posterior temporal cerebral cortex including the opercula and the cortex of the insula in the macaque that had caused no degeneration in the n. lateralis dorsalis.

Closer inspection of the positive material gives some hint as to the basis for the discrepancy in results. Of Walker's three cases with degeneration in LD, two (experiments 12L and 17) had extension of the parietooccipital ablation to include the medial surface down to the corpus callosum. In the remaining case (12R), the cortical removal extended down the midline only to the callosomarginal sulcus resulting in cell loss in the inferior part of LD but leaving the dorsal part intact.

Some of the human material (Clark and Russell, 1940; Sheps, 1945; Szabo, 1952; Simma, 1954) with degeneration in n. dorsalis superficialis quite obviously had extension of the lesion onto the medial aspect of the hemisphere. This was not so, however, in the cases of Papez (1939) and Hartmann and Simma (1952). In these cases, however, the lesion extended down to the wall of the cerebral ventricle and thus would be in a position to interrupt thalamo-cortical fibres looping around the superolateral aspect of the ventricle to reach the medial aspect of the hemisphere.

The likelihood that the n. dorsalis superficialis has important efferent connections to the medial aspect of the parietal region—that is, cortex bordering the interhemispherical sulcus—receives support from studies in the macaque. Krieg (1963) reported that after lesions in the retro- and suprasplenial cortex (areas 23 and 31) there was cell degeneration in LD (n. lateralis dorsalis or n. dorsalis superficialis). Locke *et al.* (1964) confirmed this in cases of posterior cingulate ablations. Niimi and Tsutsui's (1962) observations in a single animal were similar. Both Krieg and Locke *et al.* noted lack of complete degeneration in LD after lesions of the posterior cingulate region, suggesting the possibility of additional areas of projection.

Afferent connections to the n. dorsalis superficialis have also been found from the posterior cingulate region. With the Marchi technique, Larson (1962) noted a sparse but definite projection to the nucleus from area 23 in the macaque. With similar preparations, Krieg (1963, p. 223, 230) reported fibres from both the retro- and suprasplenial cortex (areas 23 and 31) to the n. dorsalis superficialis. Domesick (1969) in the rat traced fibre degeneration from lesions in the dorsal part of the posterior cingulate region (Rose's agranular retrosplenial cortex) to LD.

A final interesting observation has been made by Pasik *et al.* (1960) and Siqueira (1965) in the monkey. After extensive temporal lobectomies, degeneration was apparent in the n. dorsalis superficialis which they felt was proportional in intensity to the degree of damage to the hippocampal formation. One may remember that Krieg (1963) found no Marchi evidence of corticothalamic projection from the posterior

hippocampal gyrus and anterior lingula (cases 149, 150, 151, 152).

The present report presents in detail the serial section reconstructions of five human hemispheres, all of which had degeneration of the n. dorsalis superficialis and fornix in association with lesions in the medial posterior temporal region below the level of the splenium of the corpus callosum. The lesion was thus outside the commonly accepted posterior limbic projection area of the nucleus.

As is often the case with human material, lesions tend to be multiple. In the present study, the associated infarcts of the lingula and n. ventralis caudalis thalami were the most troublesome. The importance of these extraneous lesions has been discounted by the authors on the basis of the appearance of degeneration in n. dorsalis superficialis when these regions were intact and experience with other cases (Van Buren and Borke, 1972a) which serve as control material.

METHODS

The five hemispheres had been prepared with immersion fixation, total embedding in celloidin and serial section at 35 μ m. Adjacent sections at 20 section intervals were stained respectively with cresyl violet and for myelin (Loyez method) and mounted on large glass slides.

Reconstruction work was begun by making prints of every 100th section of the myelin series at about 4 $\times$ and every 40th section through the thalamus at 12 $\times$ of the cresyl violet series on Kodak Photo-mechanical T paper. The 10 second processor available for this paper was a great convenience. On these prints the areas of damage and degeneration were marked with a soft pencil after inspection with a stereomicroscope (10–40 diameter magnification). Thus the term 'neuronal degeneration' used here refers quite simply to loss of neuronal population of varying degree. No attempt was made to evaluate intrinsic cell change—for example, chromatolysis. Postmortem autolytic changes made such evaluations of doubtful value. 'Gliosis' refers to areas of definite increase in glial nuclei giving the region a darker background than adjacent areas. 'Myelin loss' was likewise a designation made on low power observation. The cardinal concept applied to the studies was that the changes were of three-dimensional nature and thus must be visible in sequential sections of the series. Adherence to this principle tended to mini-

TABLE 1
PRESENT HUMAN THALAMIC AND
HYPOTHALAMIC NOMENCLATURE*

A pr	N. anteroprincipalis (combined n. anteromedialis and n. anteroventralis)
Ce	N. centralis (n. centrum medianum)
Co	N. commissuralis (n. centralis medialis)
D c	N. dorsocaudalis (n. lateralis posterior)
D o	N. dorsooralis (n. ventralis lateralis, dorsal part)
D sf	N. dorsalis superficialis (n. lateralis dorsalis)
Fa	N. fasciculosus (n. ventralis anterior, medial part)
G l	Corpus geniculatum laterale
G m	Corpus geniculatum mediale
H	Habenula
H m	N. habenularis medialis
Li	N. limitans
L po	N. lateropolaris (n. ventralis anterior, lateral two-thirds)
M	N. medialis (n. medialis dorsalis)
Pf	N. parafascicularis
Pu	N. pulvinaris
Pv	N. paraventricularis hypothalami
R	N. reticularis thalami
So	N. supraopticus hypothalami
V c	N. ventrocaudalis (n. ventralis posterior, posterior part)
V c pc	N. ventrocaudalis parvocellularis (n. ventralis posterior medialis, medial part or n. ventralis posterior medialis parvocellularis of Olszewski, 1952)
V im e	N. ventrointermedius externus (n. ventralis intermedius, lateral part; the term was later neglected by Walker and the region included as the anterior part of n. ventralis posterior)
V im i	N. ventrointermedius internus (n. ventralis intermedius, medial part—see above)
V o e	N. ventrooralis externus (n. ventralis lateralis, ventro-lateral part)
V o i	N. ventrooralis internus (n. ventralis lateralis, ventro-medial part)

* Terms which are not in general Anglo-American usage have been given approximate equivalents from Walker's (1938a) nomenclature for the macaque thalamus.

mize effects of inattention or the preconceptions of the observers.

Once the areas of damage were outlined on the prints, they were traced, and ink diagrams were prepared to form the montages.

NOMENCLATURE Since there have been no all-inclusive studies of the human nervous system, the present terminology is a composite. Tract terminology is taken from Riley (1943) and the names of the gyri of the human brain from Economo and Koskinas (1925). It may be noted that the latter use the term gyrus limbicus superior, for the more currently used cingulate gyrus.

The decision further to burden thalamic anatomy with a modification of terminology was thrust upon us by the cytoarchitectural realities of the human thalamus which do not fit the classical descriptions of the lower primate thalamus used in the Anglo-American literature. The most difficult region is the lateroventral portion of the thalamus. Even in the

macaque, Olszewski (1952) was forced to add a 'nucleus X' in this area.

The present system essentially follows that of Vogt and Vogt (1941) including a few of the many modifications introduced by Hassler (1959). In the authors' experience many of the smaller divisions of serial section reconstructions of the human thalamus. They thus appeared more as features of a particular specimen brain rather than the general human thalamus. The details and justification for this system are given elsewhere (Van Buren and Borke, 1972a). For the present account, the equivalents of the present thalamic system in terms of Walker's (1938a) macaque nomenclature are given in Table 1. The terms taken from Riley (1943) and Economo and Koskinas (1925) have been used according to the definitions given by these authors.

RESULTS

The clinical aspects of these cases were of some interest and have been reported elsewhere (Van Buren and Borke, 1972b).

The areas of Destruction and Secondary Degeneration are outlined in Tables 2 and 3 respectively. The anatomical findings may be summarized as follows:

CASE LS LXXII From a large aneurysm of the basilar artery emboli appeared to have arisen which occluded branches of both posterior cerebral arteries as well as some posterior thalamic branches. Infarcts occurred in both hippocampal gyri as well as in the lingula and cuneus on the left and the cornu Ammonis on the right. The temporal loops of the optic radiations were interrupted on both sides and there was degeneration of the splenium of the corpus callosum (Figs 1, 2, and 3).

The demyelination of the left alveus and fimbria could be followed into the fornix and approximately one quarter of the fornix remained myelinated. The relative positions of this myelinated remnant in the body of the fornix can be followed in Fig. 4.

The left n. dorsalis superficialis showed mild reduction in size with cell loss in the posterior portion. Gliosis extended the full length of the nucleus largely in the lateral areas. No certain loss was seen in the adjacent portions of the stratum zonale thalami (Figs 5 and 6).

The complete destruction of the posterior

TABLE 2
LIST OF STRUCTURES SHOWING PRIMARY DAMAGE IN THE FIVE HEMISPHERES

		Destructive lesions				
		LS LXXII		MU-64-64		MU-66-64:
		left hemisphere	right hemisphere	left hemisphere	right hemisphere	left hemisphere
<i>Cerebrum and brain-stem</i>						
B cj	Brachium conjunctivum					
C cl s	Corporis callosi splenium	x	x			
C cl t	Corporis callosi truncus	x	x			
Cl	Clastrum			x		
C m	Corpus mamillare					
Cn A	Cornu Ammonis		x	x	x	x
Cor r	Corona radiata			x		
Cp e	Capsula externa			x		
Cp i a	Capsulae internae crus anterior					
Cp i p	Capsulae internae crus posterior		x			
Cu	Cuneus	x				
F ₂₀	Pars orbitalis of F ₂				x	
F	Fornix		x			
Fus	Gyrus fusiformis				x	
g sg i	Gyrus sagittalis cunei inferior					x
g sg m	Gyrus sagittalis cunei medius					x
Hi	Gyrus hippocampi	x	x	x	x	x
Lg	Lingula	x		x	x	x
L (sa)	Gyri limbici superioris pars anterior			x		
O ₁	Gyrus occipitalis primus					x
O ₂	Gyrus occipitalis secundus					x
Pd r th	Pedunculus rostralis thalami					
Put	Putamen			x		
Ru	N. ruber					
S b mc F	Subst. medullaris cerebri frontalis			x	x	
S b mc O	Subst. medullaris cerebri occipitalis			x	x	x
S b mc P	Subst. medullaris cerebri parietalis			x		x
S b mc T	Subst. medullaris cerebri temporalis		x	x	x	
S m th	Stria medullaris thalami					
S n	Substantia nigra					
S rcr	Stratum reticulolum coronae radiatae		x			
S sc	Stratum subcallosum		x			
S s o e	Stratum sagittale occipitale externum		x	x	x	x
S s o i	Stratum sagittale occipitale internum		x			x
Str z	Stratum zonale thalami					x
Tp	Tapetum			x		
<i>Thalamus</i>						
A pr	N. anteroprincipalis					
Ce	N. centralis		x			
Co	N. commissuralis					
D c	N. dorsocaudalis					
D o	N. dorsooralis					
D sf	N. dorsalis superficialis					
G l	Corpus geniculatum laterale					
G m	Corpus geniculatum mediale					
H m	N. habenularis medialis					
iLa	N. intralamellaris	x				
L po	N. lateropolaris					
M	N. medialis					
Pu	N. pulvinaris				x	x
V c	N. ventrocaudalis	x	x		x	x
V im e	N. ventrointermedius externus	x				

hippocampus on the *right* side resulted in complete demyelination of the body of the fornix. From the descending portion of the fornix, demyelinated and gliotic fascicles ascended toward the pedunculus rostralis thalami and the ventrolateral margin of the anterior nucleus of the thalamus but could not be followed further

posteriorly. The internal medullary lamina, ventrolateral to the anterior nucleus showed gliosis back to section 2141. No degeneration was seen in the stria medullaris thalami.

The *right* n. dorsalis superficialis showed complete cell loss apart from the posterior quarter. The stratum zonale lateral and posterior to the

TABLE 3

LIST OF STRUCTURES SHOWING SECONDARY DEGENERATION IN THE FIVE HEMISPHERES

		Secondary degeneration				
		LS LXXII		MU-64-64		MU-66-64:
		left hemisphere	right hemisphere	left hemisphere	right hemisphere	left hemisphere
<i>Cerebrum and brain-stem</i>						
B cj	Brachium conjunctivum				x	
C cl s	Corporis callosi splenium	x	x	x	x	x
C cl t	Corporis callosi truncus	x				
Cl	Clastrum					
C m	Corpus mamillare		x			
Cn A	Cornu Ammonis	x		x	x	x
Cor r	Corona radiata					
Cp e	Capsula externa					
Cp i a	Capsulae internae crus anterior		x		x	
Cp i p	Capsulae internae crus posterior	x	x		x	
Cu	Cuneus					
F ₂₀	Pars orbitalis of F ₂					
F	Fornix	x	x	x	x	x
Fus	Gyrus fusiformis					
g sg i	Gyrus sagittalis cunei inferior			x		
g sg m	Gyrus sagittalis cunei medius					
Hi	Gyrus hippocampi					
Lg	Lingula			x		
L (sa)	Gyri limbici superioris pars anterior					
O ₁	Gyrus occipitalis primus					
O ₂	Gyrus occipitalis secundus					
Pd r th	Pedunculus rostralis thalami		x	x	x	
Put	Putamen					
Ru	N. ruber		x			
S b mc F	Subst. medullaris cerebri frontalis			x	x	
S b mc O	Subst. medullaris cerebri occipitalis			x	x	x
S b mc P	Subst. medullaris cerebri parietalis			x	x	x
S b mc T	Subst. medullaris cerebri temporalis			x	x	
S m th	Stria medullaris thalami					x
S n	Substantia nigra		x			
S rcr	Stratum reticulosum coronae radiatae	x	x			
S sc	Stratum subcallosum	x	x	x	x	
S s o e	Stratum sagittale occipitale externum		x	x	x	x
S s o i	Stratum sagittale occipitale internum	x	x	x	x	x
Str z	Stratum zonale thalami	x		x	x	x
Tp	Tapetum			x	x	x
<i>Thalamus</i>						
A pr	N. anteroprincipalis			x		
Ce	N. centralis					x
Co	N. commissuralis			x		
D c	N. dorsocaudalis	x				
D o	N. dorsooralis	x				
D sf	N. dorsalis superficialis	x	x	x	x	x
G l	Corpus geniculatum laterale	x	x	x	x	x
G m	Corpus geniculatum mediale				x	x
H m	N. habenularis mediale					x
iLa	N. intralamellaris			x		
L po	N. lateropolaris	x				
M	N. medialis			x	x	
Pu	N. pulvinaris	x	x	x	x	x
V c	N. ventrocaudalis				x	
V im e	N. ventrointermedius externus					
R	N. reticularis			x		x

nucleus showed thinning and gliosis which were continuous with the destruction of this layer over the infarction in the pulvinar (Figs 5 and 7).

CASE MU 64-64 There was damage on the *left* in the lateral hippocampus and demyelination

which could be followed into the lateral portion of the fornix. Anterior to the thalamus gliotic bundles separated from the descending portion of the fornix and ascended to enter the internal medullary lamina inferolateral to the n. antero-principalis. The stria medullaris thalami was

FIG. 1. Case LS LXXII L. The extent of the lesion in the left hemisphere. Black = necrosis of tissue; horizontal hatching = cell loss; vertical hatching = myelin loss; diagonal hatching = gliosis. See Tables 1-3 for summary and nomenclature.

FIG. 2. Case LS LXXII R. The extent of the lesion in the right hemisphere. Black=necrosis of tissue; horizontal hatching=cell loss; vertical hatching=myelin loss; diagonal hatching=gliosis. See Tables 1-3 for summary and nomenclature.

FIG. 3. Case LS LXXII L and R. Details of the topography of the medial temporal lesions. Black = necrosis of tissue; horizontal hatching = cell loss; vertical hatching = myelin loss; diagonal hatching = gliosis.

FIG. 4. Case LS LXXII. Relative position of the remaining myelinated remnant in the body of the left fornix. Compare section numbers with Figs 1 and 5. R=right; L=left.

FIG. 5. Case LXXII. Relative size of the n. dorsalis superficialis on the two sides. Loyez stain for myelin. Section 2340.

FIG. 6. Case LS LXXII L. Left thalamus. Black = necrosis of tissue; horizontal hatching = cell loss; vertical hatching = myelin loss; diagonal hatching = gliosis.

FIG. 7. Case LS LXXII R. Right thalamus. Black = necrosis of tissue; horizontal hatching = cell loss; vertical hatching = myelin loss; diagonal hatching = gliosis.

FIG. 8. Case MU 64-64 L. The extent of the lesion in the left hemisphere. Black = necrosis of tissue; horizontal hatching = cell loss; vertical hatching = myelin loss; diagonal hatching = gliosis. See Tables 1-3 for summary and nomenclature.

FIG. 9. Case MU 64-64 L and R. Details of the topography of the medial temporal lesions. Black = necrosis of tissue; horizontal hatching = cell loss; vertical hatching = myelin loss; diagonal hatching = gliosis.

normal. There was no direct damage to the stratum zonale thalami, but this structure showed some thinning and pallor (Figs 8, 9, and 10).

The *left* n. dorsalis superficialis showed rather general gliosis with cell loss which was most marked in the posteromedial portion (Fig. 11).

On the medial side of the *right* temporal lobe an infarct completely destroyed the hippocampus, hippocampal gyrus, and fusiform gyrus. There was secondary degeneration (Figs 12 and 13) and shrinkage of the alveus, fimbria, and fornix.

In the *right* thalamus demyelinated and gliosed fascicles could be traced from the descending fornix upward and laterally into the lamina medullaris interna inferolateral to the anterior nucleus. From this region they passed posteriorly

toward the n. dorsalis superficialis. Practically no nerve cells remained within the n. dorsalis superficialis, although the nucleus was clearly outlined on the myelin series. Thinning and pallor of the stratum zonale thalami was seen which was similar to that on the left side (Fig. 14).

CASE MU 66-64 In the *left* hemisphere an infarct transected the hippocampus at the level of the splenium of the corpus callosum (Figs 15 and 16). The damage extended forward with diminishing size to end at the junction between the hippocampal gyrus and hippocampus just behind the anterior extremity of the temporal horn. Despite the extensive hippocampal damage some fibres remained in the superomedial portion of the fornix. From the descending fornix gliotic

FIG. 10. Case MU 64-64 L. Gliotic bundles of degenerating fibres passing from the descending column of the left fornix toward the anterior pole of the thalamus. Gliosis appeared in the region of the pedunculus thalami and the internal medullary lamina. Cresyl violet stain.

fascicles could be followed into the stria medullaris thalami (Fig. 17). Posteriorly, this degenerated area was contiguous with the cell loss in the n. dorsalis superficialis. Myelin loss was seen in the stria medullaris thalami and stratum zonale thalami near the nucleus.

The *left* n. dorsalis superficialis showed complete cell loss with heavy gliosis and shrinkage in the outline of the nucleus (Figs 18 and 19).

Detailed descriptions of the hemispheres were as follows:

DESCRIPTION OF LEFT HEMISPHERE OF LS LXXII
CEREBRUM In the cortex there was a small area of

loss in the hippocampal gyrus which extended through the full thickness of the cortex and became confluent with the ventricle. This lay at the level of the splenium (nos 2800–3000) and continued posteriorly into the anterior portion of the lingula. From here it passed upward and posteriorly to affect the inferior calcarine cortex. Behind this the damage extended upward to destroy the posterior cuneus as well as the lingula. Within the temporal lobe there was cell loss in Sommer's sector of the hippocampus (nos 2400–2600) with degeneration of the polymorph cells in the hippocampus (H_5) and pallor of the cells in the dentate gyrus. Demyelination of the alveus and fimbria (omitted in drawings nos 2400–2800) could be followed into the fornix, but the degree of

FIG. 11. Case MU 64-64 L. Left thalamus. Black=necrosis of tissue; horizontal hatching=cell loss; vertical hatching=myelin loss; diagonal hatching=gliosis.

demyelination was less than on the left side and approximately a quarter of the fornix remained.

In the corpus callosum the splenium was essentially destroyed. Demyelination was present in the stratum reticulatum coronae radiati, stratum subcallosum, and internal capsule similar to that in the right hemisphere. In addition there was degeneration in the stratum sagittale internum, whereas the tapetum and stratum sagittale externum were intact.

BASAL GANGLIA In the anteromedial portion of the substantia nigra there was a small area which showed some free pigment but without outstanding cell loss. The nucleus ruber also showed a somewhat uncertain patchy cell loss.

THALAMUS The changes were somewhat difficult to interpret because the thalamus was involved by several microinfarcts as well as areas of frank secondary cell degeneration. The decision was particularly difficult in the nucleus dorsooralis and nucleus dorsocaudalis. As a rule, the areas of cell loss without gross disruption of the background pattern

of myelinated fibres were considered as secondary cell degeneration.

The midline nuclei were intact.

In the ventrolateral thalamic region loss was seen in the nucleus lateropolaris and its posteromedial quadrant adjacent and passing into the n. dorsooralis (no. 2061). Within the latter nucleus loss lay largely in the inferomedial portion (no. 2101). Gliosis with little cell loss lay in the inferomedial quadrant of the nucleus dorsocaudalis and passed posteriorly into the adjacent portions of the pulvinar (nos 2381, 2421). Within the pulvinar the cell loss lay along the posterior margins of the n. centralis and n. ventrocaudalis, then passed along the ventrolateral portions of this nucleus adjacent to n. limitans to the posterior pulvinar pole.

Microinfarcts were noted in the n. intralamellaris (no. 2261), the anterosuperior aspect of the n. ventralis intermedius externus (no. 2261), and the central portion of the n. ventrocaudalis (no. 2421-2541).

The n. dorsalis superficialis showed reduction in size with major cell loss in the posterior portion. Gliosis extended the full length of the nucleus largely

FIG. 12. Case MU 64-64 R. The extent of the lesion in the right hemisphere. Black = necrosis of tissue; horizontal hatching = cell loss; vertical hatching = myelin loss; diagonal hatching = gliosis. See Tables 1-3 for summary and nomenclature.

FIG. 13. Case MU 64-64 R. Degenerating fibres from the descending column of the right fornix (F) are shown ascending to enter the region of the pedunculus rostralis thalami. Cresyl violet stain.

in the lateral areas. No certain loss was seen in the adjacent portions of the stratum zonale thalami.

In the corpus geniculatum laterale degeneration affected the lateral half and reached its maximum severity posteriorly. This destroyed all but a few of the larger cells lying in both the parvocellular and magnocellular layers.

DESCRIPTION OF RIGHT HEMISPHERE OF LS LXXII

CEREBRUM The cortical loss involved the hippocampal gyrus posterior to the uncus and extended into the inferior horn of the lateral ventricle. This destroyed the lateral half of the hippocampus (nos 2500-2900). In the anterior portion of the hippocampus there was cell loss in Sommer's sector, but this loss was less extensive than on the left side.

The fornix and alveus were completely demyelinated as was the splenium of the corpus callosum. There was extensive myelin loss in the stratum subcallosum lateral to the body of the lateral ventricle which could be followed into the frontal lobe and extended into the stratum reticulatum coronae radiati. Demyelination could also be followed into the occipital lobe in the internal and external sagittal strata.

From the region of the pons an area of demyelination and gliosis could be followed up the medial portion of the pes pedunculi toward the anterior crux of the internal capsule. Likewise the posterior limb of the internal capsule had a rather spongy appearance with small spaces between the myelinated bundles (without cellular reaction) which had rather the appearance of a postmortem artefact.

FIG. 14. Case MU 64-64 R. Right thalamus. Black = necrosis of tissue; horizontal hatching = cell loss; vertical hatching = myelin loss; diagonal hatching = gliosis.

THALAMUS From the descending, completely demyelinated fornix, demyelinated and gliotic bundles could be seen ascending toward the pedunculus rostralis thalami and the ventrolateral margin of the anterior nucleus but beyond this could not be followed with certainty. There was, however, gliosis in the internal medullary lamina ventrolateral to the anterior nucleus as far back as no. 2141. The stria medullaris thalami was normal.

Although the anterior nuclei were intact, the n. dorsalis superficialis showed complete loss of cells apart from the most posterior portions. Immediately lateral and posterior to this nucleus the stratum zonale showed thinning and gliosis which was continuous with the destruction of this layer over the pulvinar.

The pulvinar showed flattening of its normally convex dorsal outline with maximum degeneration both medially and laterally in the superior posterior portions. This seemed related to the destruction of white matter lateral and posterior to the corpus geniculatum laterale (nos 2540, 2580) which appeared in a position to destroy the fibres connecting this region of the pulvinar. The pars oralis and intergeniculatus of the pulvinar appeared largely normal.

In the lateral half of the corpus geniculatum

laterale, cell loss was seen which was of increased intensity in the lateral portions of the nucleus. Occasional larger cells remained in this region.

A small infarction involved the inferomedial portion of the nucleus ventrocaudalis and the adjacent region of the n. centralis (nos 2301–2501).

In the more inferior portions the corpus mamillare was much reduced in size on the right. The cells were sparser and arranged in irregular clumps, contributing a rather spongy appearance to the nucleus.

In the anteromediosuperior portion of the substantia nigra there was a small area of pigment deposition and cell loss. This area appeared to receive the ascending demyelinated fibres from the pons. The comb fibres appeared symmetrical on the two sides without evidence of loss. Mild patchy cell loss was noted in the n. ruber.

DESCRIPTION OF BRAIN-STEM AND CEREBELLUM OF LS LXXII

BRAIN-STEM The position of the basilar artery aneurysm is indicated below the brain-stem on sections nos 2600–3300.

FIG. 15. Case MU 66-64 L. The extent of the lesion in the left hemisphere. Black = necrosis of tissue; horizontal hatching = cell loss; vertical hatching = myelin loss; diagonal hatching = gliosis. See Tables 1-3 for summary and nomenclature.

In the midbrain an infarct destroyed the locus caeruleus and the lateral lemniscus near its junction with the medial lemniscus on the right at the tegmental-tectal junction. Superiorly the lesion extended into the inferior colliculus (nos 3000-3200).

The left ventrolateral aspect of the pons was deformed by the aneurysm and cell loss and demyelination were seen in the adjacent portions of the tegmentum. A cystic area of degeneration lay at the lateral pole of the inferior olive superomedial to

the pyramid on the left. This was associated with rather generalized loss in the left inferior olivary nucleus with complete cell loss in a small sector on the superolateral aspect of no. 3701. The right inferior olivary nucleus showed partial cell loss in the inferior half, particularly in the posterior portions.

The corticospinal fibres were extensively damaged on the left side in the pons. This could be followed down into the left pyramid and upward into but not beyond the level of the left cerebral peduncle.

FIG. 16. Case MU 66-64 L. Details of the topography of the medial temporal lesion. Black=necrosis of tissue; horizontal hatching=cell loss; vertical hatching=myelin loss; diagonal hatching=gliosis.

CEREBELLUM On the left the superior cerebellar peduncle showed myelin loss in the anterolateral aspect. The left brachium pontis was also destroyed by infarct (nos 3300, 3400).

The left cerebellum had major cortical damage on the inferolateral aspect. This extended into a cystic cavity adjacent to the dentate nucleus and there was neuronal loss in the contiguous portions of this nucleus (no. 3800). The adjacent portions of the left restiform body were also destroyed here.

On the right side the anterosuperior cerebellar cortex was extensively infarcted and the dentate nucleus showed severe cell loss in the lateral part. An area of myelin loss also involved the lateral two-thirds of the right superior cerebellar peduncle (no. 3300).

DESCRIPTION OF LEFT HEMISPHERE OF MU 64-64

CEREBRUM In the anterior portion of the left hippocampus Sommer's sector was degenerated and the population of polymorph cells in the curve of the dentate gyrus was reduced in comparison with the right side. These defects became more striking posteriorly and by no. 2000 the lateral portion of the hippocampus and the white medullary core of the fusiform and hippocampal gyri were destroyed by infarct. The infarct spread laterally to the stratum sagittale externum in its most inferior portion (nos 2000-2300) and passed posteriorly to undercut the anterior lingula (nos 2500-2700) and the gyrus sagittalis cunei inferior (nos 2800-3100). From here it continued posteriorly and became confluent with the cortical lesion occupying the posterior two-thirds of the lingula (nos 2900-3400).

From the damage in the lateral hippocampus, demyelination could be followed into the lateral portion of the alveus and fimbria and thence into the lateral portion of the body of the fornix. Gliotic fascicles separated from the descending portion of the fornix and ascended to enter the internal medullary lamina inferolateral to the nucleus antero-principalis. There was also gliosis in the pedunculus rostralis thalami. The stria medullaris thalami was normal.

There was complete demyelination in the splenium of the corpus callosum from no. 1961 posteriorly. Fibre loss also appeared in the tapetum and adjacent white matter in the area of the temporoparieto-occipital junction and further posteriorly in the occipital lobe.

Coming forward, a slit-like infarct was seen in the substantia medullaris of the paracentral lobule (nos 1500-2000).

A third infarct in the form of a vertical lamina lay in the lateral aspect of the anterior putamen and the

FIG. 17. Case MU 66-64. In section 1900 the extensive demyelination of the stria medullaris thalami is indicated between arrows. The relative atrophy of D sf is indicated under the arrow in section 2060. Note the thinning of the stratum zonale thalami and the stria medullaris thalami on this side. R=right; L=left. Loyez stain for myelin.

FIG. 18. Case MU 66-64. On the left *D sf* is outlined with dots and appears normal. On the right the nucleus is shrunken and heavily gliosed.

adjacent portion of the external capsule and claustrum. As it progressed posteriorly this was shifted upward into the coronae radiati between the caudate corpus and the superior edge of the putamen. In this position it may well have severed fibres from the limbic cortex to the nucleus antero-principalis.

The fourth major lesion was a surgical cavity in the frontal lobe arising from the orbital surface of the first and second frontal gyri and ascending to occupy the inferior two-thirds of the frontal lobe. Medially the cortex of the limbic gyrus at the rostrum of the corpus callosum (nos 600–1000) was punctured.

Secondary demyelination ran anteriorly from this lesion nearly to the frontal pole and backward into the stratum subcallosum and substantia medullaris of the frontal lobe. From here it continued into the genu of the corpus callosum and a more ventral degenerated arm was seen to pass into the crus anterior of the internal capsule and then to the most medial portion of the pes pedunculi.

THALAMUS The midline nuclei were intact apart from loss of cells to the left of the midline in the n. commissuralis (no. 1641). This lay in the anterior portion of the nucleus and continued into the adjacent regions of the n. intralamellaris (pars paracentralis).

Within the n. anteropincipalis cell loss and gliosis were seen in the inferolateral quadrant of the anterior portion. The laminar portion (n. antero-dorsalis) could be identified.

The n. medialis showed cell loss in the anterior two-thirds of the nucleus. This was in the form of a

wide lamina running from an inferomedial position posteriorly to a superolateral position anteriorly.

Within the anterior portion of the n. dorsalis superficialis there was rather general gliosis, but in the posterior half this was accompanied by cell loss in the medial part.

The pulvinar showed extensive degeneration including a small infarct near but not continuous with the ventricular surface of the posterior third (no. 1961). The posterior half of the nucleus showed nearly complete degeneration except for a small area of sparing on the medial aspect. Anteriorly this medial sparing enlarged and spread anteriorly so that the anterosuperior portion was essentially spared. The corpus geniculatum laterale showed extensive degeneration of all parts except for a small superomedial segment near the apex of the nucleus.

When the specimen was compared with a normal of similar age, considerable thinning and pallor of the stratum zonale were apparent over the posterior half of the thalamus. In no region, however, was it completely missing, and review of the serial sections, particularly between no. 1900 and no. 2000 showed no spread of the pulvinar infarct to the surface.

DESCRIPTION OF RIGHT HEMISPHERE OF MU 64-64

CEREBRUM On the medial aspect of the temporal lobe an infarction completely destroyed the hippocampus, hippocampal gyrus, and fusiform gyrus. There was secondary degeneration in the alveus and fimbria. Throughout its course the fornix showed marked degeneration and shrinkage.

The splenium was completely demyelinated and

traced into the medial fifth of the pes pedunculi. An additional infarction was noted on the postero-inferolateral aspect of the cerebellar cortex which directly involved the inferomedial quadrant of the dentate nucleus at no. 2800. In the superior cerebellar brachium (no. 2400) gliosis and demyelination were apparent in the superomedial corner, but this could not be followed beyond the decussation of the brachium conjunctivum.

THALAMUS Gliotic and demyelinated bundles could be traced from the descending fornix in the region of the pedunculus rostralis thalami and superolaterally into the lamina medullaris interna inferolateral to the anterior nucleus. From this region they passed posteriorly in the direction of the n. dorsalis superficialis. Within the n. dorsalis superficialis practically no nerve cells remained, although the myelin series served clearly to outline the nucleus.

Anteriorly in the n. medialis gliosis and cell loss were seen on the lateral margin, which tended to migrate to a central position in the nucleus more posteriorly but could not be followed behind the anterior third of the nucleus.

Small infarcts were present in the n. ventrocaudalis (nos 1801–1921) as well as some patchy areas of cell loss. In view of the infarcts, the significance of the cell loss was doubtful.

A small infarct was also seen in the pulvinar (no. 1881). This, however, was entirely separate from cell loss and gliosis which affected the posteroinferolateral quadrant of the nucleus. This area was contiguous with gliotic fibre bundles entering from the white substance.

The anterosuperolateral angle of the corpus geniculatum mediale showed a small region of cell loss in one section (no. 1961) but this could not be followed in adjacent sections.

Loss within the corpus geniculatum laterale was more marked posteriorly particularly in the lateral half.

See remarks in the discussion of the left thalamus regarding the apparent symmetrical thinning of the stratum zonale of each thalamus.

DESCRIPTION OF LEFT HEMISPHERE OF MU 66-64

CEREBRUM Just behind the anterior extremity of the temporal horn a small area of infarction lay along the junction between the hippocampal gyrus and hippocampus (no. 2100). This extended posteriorly and completely transected the hippocampus at the level of the splenium of the corpus callosum. From this level the infarct extended posteriorly destroying the cortex within the calcarine fissure with a small extension into the lingula and the gyrus sagittalis

cuneus inferior. At the occipital pole the infarct curved around its posterior aspect and destroyed cortex bordering the second occipital sulcus. It extended as deep as the lateral aspect of the occipital horn of the ventricle (nos 3200–2800).

Despite the complete transection of the hippocampus (no. 2201), some fibres remained in the medial and superior portion of the fornix. More could be seen crossing from the right side posteriorly and further anteriorly in the fornix descending from the fornix dorsalis. From the descending column of the fornix gliotic fascicles could be followed into the stria medullaris thalami and posteriorly this degenerated area was contiguous with the cell loss in the n. dorsalis superficialis. Degeneration was noted in the septal nuclei, more pronounced in the large celled lateral subdivision.

There was demyelination in the splenium of the corpus callosum, the forceps major, and both sagittal strata of the occipital lobe. In the external sagittal stratum the myelin loss was virtually complete in the portion inferolateral to the ventricle.

THALAMUS Posterolateral to the thalamus an infarct passed from the white substance into the adjacent pulvinar becoming progressively smaller but still occupying the majority of the lateral portion of the n. ventrocaudalis. From this area of infarction posteriorly the stratum zonale was essentially missing. Anteriorly, although heavily gliotic and demyelinated as far laterally as the stria terminalis, the layer could be recognized. The gliosis and demyelination here could be followed as far anteriorly as the centre of the n. medialis.

Aside from the major infarct in the pulvinar, there was a small area of cell loss in the pulvinar immediately behind the medial nucleus (no. 2181 and no. 2221).

In the parvocellular portion of n. centralis degeneration extended to the infarcted area and in the n. ventrocaudalis there was cell loss and gliosis which affected the lateral portion of the nucleus. It appeared likely that the infarct had severed connections of the n. centralis with the putamen.

The corpus geniculatum laterale showed complete loss of both cells and fibres with similar complete degeneration in the triangular zone of Wernicke.

Only a thin rim of cells in the anteroinferior quadrant (no. 2261) remained in the corpus geniculatum mediale. It was not possible to recognize a magnocellular portion.

The n. dorsalis superficialis showed complete cell loss with heavy gliosis and shrinkage in the nuclear outline. As mentioned above, this area of degeneration was contiguous with the gliosis and demyelina-

tion seen in the stratum zonale and stria medullaris thalami.

The medial nucleus of the habenula showed mild cell loss and there was questionable loss in the lateral division (no. 2161). There was no evident demyelination in the fasciculus retroflexus.

The left mammillary body showed total loss of the lateral nucleus and severe gliosis with cell loss in the medial nucleus. The descending fornix was completely demyelinated and gliosed and could be followed to the lateral aspect of the mammillary body.

DISCUSSION

Perhaps the most difficult portion of the present evidence to evaluate was the importance of degeneration in the stratum zonale thalami. Since this is considered to be the pathway connecting the n. dorsalis superficialis (D sf) with the posterior limbic gyrus, its integrity is essential for the maintenance of cells in this nucleus. Major damage to this layer occurred in LS LXXII R and MU 66-64 L, but in both cases this was posterolateral to the pulvinar and thus probably posterior to the D sf-limbic pathway. However, this point remains uncertain.

Another instance of threat of damage to the cortical projections of D sf was MU 64-64 L, in which there was a slit-like infarct in the paracentral lobule. It appears that this slit was too superficial to interfere with the cortical projections which would be expected to maintain a periventricular position (cf. Krieg, 1963, Fig. 157). The remaining cases seemed without suggestion of direct damage to the stratum zonale thalami.

Apparently as a concomitant of the vascular occlusion responsible for the major lesion in these hemispheres, there were small thalamic infarctions in all cases. LS LXXII R contained the largest lesion in the n. ventrocaudalis which measured $3 \times 5 \times 7$ mm. The remainder were smaller and affected the intralaminar area and adjacent n. ventro-oralis internus (LS LXXII L), the pulvinar (MU 64-64 R and L; MU 66-64 L), and n. ventrocaudalis (LS XXII L; MU 64-64 R; MU 66-64 L). The small size and variable position of these lesions suggests that they did not contribute significantly to consistent degeneration in n. dorsalis superficialis.

Valenstein and Nauta's (1959) experience with lesions of the fornix showed an increasing pro-

jection to n. lateralis dorsalis (D sf) as the phylogenetic series was ascended from guinea-pig to macaque. Two pathways appeared involved in the macaque—that is, the stria medullaris thalami and a more diffuse group entering the thalamic pole which spread both medial and lateral to the anterior nucleus. The present material was obviously not optimal for tracing pathways, but gliosis appeared to involve predominantly the second, more diffuse pathway which we have included under the term pedunculus rostralis thalami.

Perhaps the most significant feature of these cases was that all had lesions below the level of the splenium of the corpus callosum in the posteromedial temporal region accompanied by degeneration in the fornix. The relationship of this lesion to cell loss in the n. dorsalis superficialis may be judged by the fact that degeneration in this nucleus was total in three of the five cases.

The question as to whether the posterior hippocampal gyrus also has connection with the n. dorsalis superficialis cannot be answered with certainty with the present material. The likelihood that degeneration in this nucleus was not dependent upon lesions of the hippocampal gyrus was suggested by MU 64-64 L in which the cortex of the hippocampal gyrus was spared. The evidence, however, remains clouded by an extension of the infarct into the medullary core of the hippocampal gyrus. Three cases have been reported elsewhere in which lesions of the lingula and posterior hippocampal gyri were documented by reconstruction studies without degeneration in the dorsalis superficialis (cases LS LXXIII L, LS LXXIV R, and LS LXXXV R; Van Buren and Borke, 1972a).

It was quite clear, however, that lesions in the temporal gyri including the surface and fissural aspects of the fusiform gyrus were not associated with degeneration in the dorsalis superficialis (Van Buren and Borke, 1972a). LS LXXII R demonstrated that extension of the lesion into the lingula was not necessary to cause total degeneration of the nucleus.

The duration of the lesions (MU 66-64, 15 months; MU 64-64, five years; LS LXXII, six years) was sufficient to suggest that this degeneration was of anterograde transynaptic nature.

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