

CLINICO-PATHOLOGICAL STUDIES

ON 101 CASES OF LEUCOTOMY.

By

Turner McLARDY, M.B.E.,  
B.Sc., M.B., Ch.B.,  
D.P.M.

ProQuest Number: 13855751

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 13855751

Published by ProQuest LLC (2019). Copyright of the Dissertation is held by the Author.

All rights reserved.

This work is protected against unauthorized copying under Title 17, United States Code  
Microform Edition © ProQuest LLC.

ProQuest LLC.  
789 East Eisenhower Parkway  
P.O. Box 1346  
Ann Arbor, MI 48106 – 1346

## FOREWORD.

These studies have been carried out by the writer whilst working, since April 1946, in the Department of Neuropathology at the Maudsley Hospital, London.

All macroscopic and histological investigations of the brain material (except of 7 cases reported on by Meyer and Beck in 1945) were made in the first instance by the writer in person and subsequently checked by other members of the Department. All the clinical data were personally abstracted from the original case notes.

Studies of some aspects of the earlier cases have already been published in association with other members of the Department. Where this is the case the tables and discussions have been brought up to date in the light of increased material, improved methodology and progressive extension of histological investigation. The whole of the data have been re-surveyed and co-ordinated and several new aspects are reviewed and discussed for the first time.

Profound thanks are due to Dr. Alfred Meyer for his instruction, encouragement and criticism throughout the studies and grateful acknowledgement is made to Mrs. E. Beck for her cross-checking and photography of anatomical findings, to Mr. G.W. Cox and Miss H. Warmington for their highly skilled technical assistance and to Mrs. M. Booth for her painstaking abstracting and other most efficient secretarial services.

T. McL., November, 1948.

INDEX.

	Page
Foreword	2
Introduction: Objectives	4
Previous Literature	6
Material: (a) Brains, (b) Clinical Records	8
Section I: <u>Direct Post-operative Deaths</u>	11
(1) Infection	15
(2) Cause and Prevention of Fatal Haemorrhage	15
Section II: <u>Methods of Analysis of the Lesions</u>	22
(1) Topographical use of Brodmann's Map	22
(2) Plane of Cut	22
(3) White Matter Segments	24
(4) Secondary Degeneration in the Thalamus	26
Section III: <u>Posterior Cuts</u>	30
(1) Undesirable Physiological Sequelae of Leucotomy	36
(2) Delayed Post-operative Death	42
Section IV: <u>Post-operative Personality Change</u>	47
(1) Anatomical Correlates of Different Degrees of Personality Change	47
(2) Anatomical Correlates of Different Kinds of Personality Change	53
(3) "Anatomical Basis" of Personality Change	55
Section V: <u>Post-operative Improvement and Relapse</u>	58
(1) Anat. Correlates in Predominantly Affective Conditions	62
(2) Anat. Correlates in Mixed, mainly Paranoid, Psychoses	64
(3) Anat. Correlates in Schizophrenias of early onset	65
General Conclusions	75
References	78
Appendix	81

## INTRODUCTION.

The importance of macroscopic and histological determination of what precise lesions have been created during, or have developed after, leucotomy operations is manifest, - - and may conveniently be looked at from the following four aspects, the first three of which have been taken as the main Objectives of the studies reported here:-

1. To determine the causes of operative catastrophe in particular instances, for the enlightenment of the surgeons and clinicians concerned and in general, towards suggesting methods of their avoidance.

2. To search for any constant relationship between other undesirable sequelae (physiological or psychological) and attributes of the lesions, - towards being able to advise regarding the practical avoidance of such sequelae and the more academic end of elucidating any principles of localisation of function (physiological or psychological) within the frontal lobes.

3. To make valid\* correlation between clinical improvement and the position, extent and other features of the operative lesions and, if any positive anatomical correlates of improvement

Footnote. \*Clinico-surgical correlation studies without at least a fair sample autopsy check of the actual lesions cannot be considered valid especially in this country where practically all leucotomy operations are performed blindly with a minimal utilisation of internal landmarks, - resulting in enormous unintentional variations in the lesions which are not appreciated until post mortem (see Section I).

are found, to try to determine the optimal, minimal, lesions for the best clinical results, bearing in mind that these may be different in different types of mental illness.

4. To utilise these surgical lesions in structurally healthy brains towards extending general knowledge of the anatomy of the human frontal lobe through investigation of secondary degenerative changes. Such studies in pure anatomy will not be described in the present thesis, except the findings from that part of them which concerns the "projection parcellation" of the nerve cells of the dorsomedial nucleus of the thalamus and permits determination of what areas of prefrontal cortex have been isolated by circumscribed lesions situated posteriorly in or close to the anterior limb of the internal capsule.

-----o-----

### PREVIOUS LITERATURE.

Apart from publications from the Maudsley Hospital (Meyer and Beck, 1945; Meyer and McLardy, 1947; Meyer, McLardy and Beck, 1948; Meyer and McLardy, 1948) no clinico-pathological correlation study involving post mortem determination of the actual lesions created has appeared in the literature. Heath and Pool (1948) have described the precise cortical regions resected and the early results in four cases submitted to a bilateral open operation and many similar reports are to be expected soon from other workers in the United States and elsewhere who are increasingly employing an open operation with well defined destruction of grey matter or amputation of grey and white matter.

The only relevant anatomical studies on leucotomy material so far published have been those of Meyer, Beck and McLardy (1947) based on eight hemispheres and the description by Freeman and Watts (1947) of the gross and histological findings in four lobotomy cases with some general conclusions regarding parcellation of the cells of the dorsomedial nucleus of the thalamus derived from these and another eight cases.

Le Gros Clark (1932), Le Gros Clark and Boggon (1933, 1935), Walker (1938, 1940) and Mettler (1947) have made important contributions to knowledge of the prefrontal connections of the thalamic nuclei of, chiefly, the macaque monkey. By none

of these workers, however, has the resultant "projection parcellation" of the cells of the dorsomedial nucleus subsequently been applied in reverse as a method of deducing what prefrontal regions of cortex have been isolated from the thalamus in cases where macroscopic inspection of the primary lesion cannot determine it.

-----o-----



## MATERIAL.

### A. Brains.

98 of the 101\* brains were received from some 35 mental hospitals throughout England, Scotland and Wales, the remaining 3 from Malta, (where the operations had been performed by a visiting English neurosurgeon).

The cases range in post-operative survival from 5 hours to about 5 years, but cannot be taken as representative of all leucotomy patients who have died within 5 years of the operation. They are probably representative of all cases dying within one month, i.e. the period during which even post-operatively uneventful cases are usually retained in hospital, but they are certainly not a "fair sample" of cases surviving beyond that period. This is because almost none of the brains was received from a case where death occurred at home or in a general hospital. Collection of brains has depended largely on the initiative of mental hospital medical officers who realised the importance of systematic investigation of such material. Practically all the cases had either never left, or never lost touch with, the mental hospital in which the operation had been performed. Two notable consequences of this non-random selection of material which should be borne in mind are that the all-over grade of post-operative improvement in the present series of cases is

Footnote. \* The serial numbers of the cases run to 102 because one lobectomy case (No. 6) was originally included in the series.

lower, and the proportion of cases of "direct post-operative death" vastly higher, than in the "leucotomised population" in general.

The variety of the cuts in this brain material gives an opportunity of studying the clinical sequelae of very different frontal lesions indeed.

#### B. Clinical Records.

The original case records were generously made available for perusal and abstracting by the large majority of the hospitals concerned. In the remaining cases summaries were furnished.

Since a majority of the cases were operated on during war years when medical and nursing staffs were severely taxed the records are inevitably in many cases sketchy. This applies particularly to information regarding premorbid personality, and physiological, psychometric and general psychological observations before and after operation. Hence only rather gross signs and symptoms unlikely to have passed unrecorded even in these circumstances can be dealt with in the present studies. Abstracting and evaluation of all the case notes by the same person, the writer, has helped it is hoped to smooth out the wide differences in diagnostic assessment and terminology.

---

---

I. INTRODUCTION

-----

II. SCOPE OF THE STUDY

(Contents face page 11.)

1. Introduction	"	"	=	1
2. Scope of the Study	"	"	=	5
3. Methodology	"	"	=	10
4. Results and Discussion	"	"	=	15
5. Conclusion	"	"	=	20

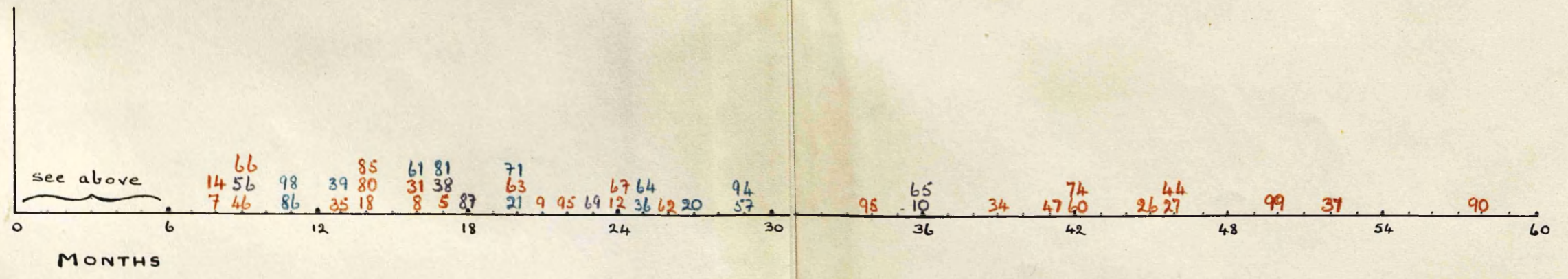
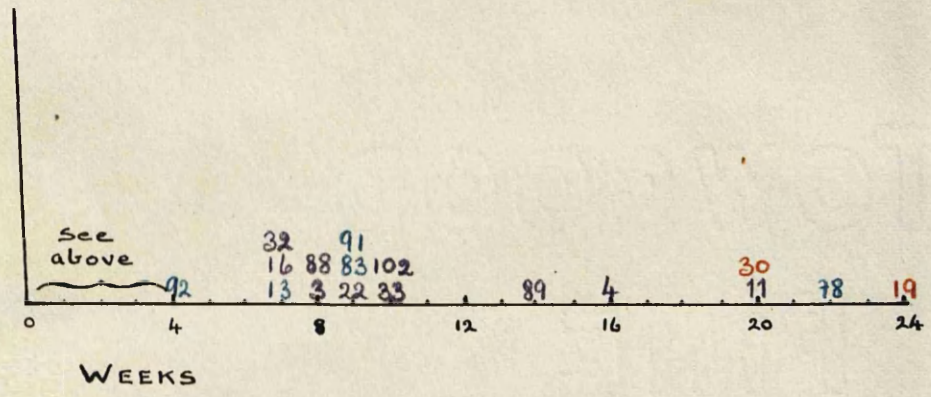
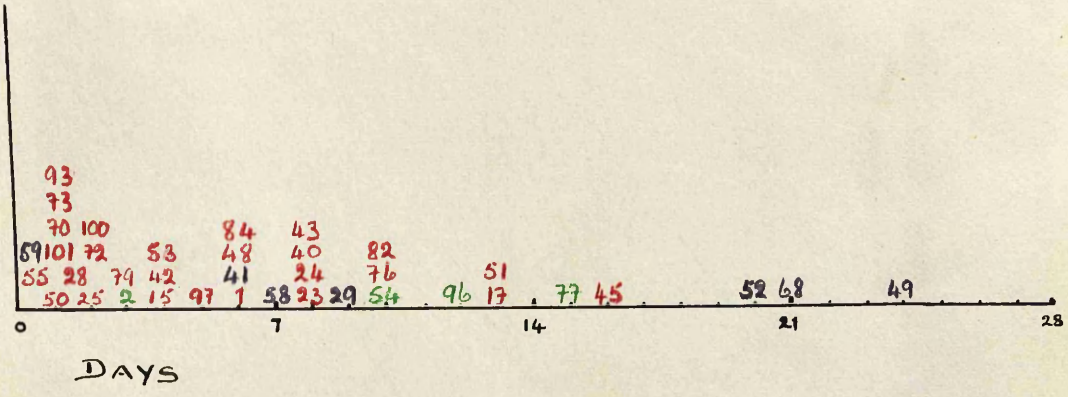


TABLE I.

POST-OPERATIVE SURVIVAL PERIOD

and TYPE of DEATH.

- Green = Death from Infection.
- Red = " " Haemorrhage.
- Purple = " " Bilateral Posterior Cuts.
- Blue = " " Unilateral Posterior Cut.
- Brown = " " Intercurrent Disease.

## SECTION I.

### DIRECT POST-OPERATIVE DEATHS.

Table I (facing) shows the distribution of the 101 cases in respect of their length of survival after operation. There are three periods at which the deaths tend to cluster: firstly in the 1st and 2nd week; secondly about the 8th week; and thirdly, and more diffusely, around a period whose mean is 17 months after operation. The latter two clusters will be discussed in Section III: the first only will be considered here.

This first cluster is made up of the majority of the recognised "operative" deaths, i.e. all those due to infection or haemorrhage. Actually all such deaths in the series occurred within the first three post-operative weeks. They are represented by their serial numbers in red or green in Table I. Table II (page 12) gives detailed analysis of their aetiology as ascertained by dissection and histological check for infection and vascular pathology.

TABLE II - Direct Post-operative Deaths.

A. INFECTION:	Meningitis .....	2
	Abscess .....	$\frac{2}{4}$
B. HAEMORRHAGE:	Anterior Cerebral Artery*, Right ...	6
	" " " , Left ....	3
	" " " Right & Left .	2
	Middle Cerebral Artery*, Right .....	7
	" " " , Left .....	2
	" " " Right & Left ...	3
	Right Ant. Cer. & Left Mid. Cer. Arts.	2
	Undetermined source, probably venous	$\frac{2}{27}$

Notes.

In 2 cases the cerebral vessels displayed severe arterio-sclerosis: in 2 moderate sclerosis.

A conspicuous "cerebellar cone" constricting the blood supply of the medulla was found in most of the cases with haemorrhage.

In 3 of the cases with haemorrhage a "dorsal approach" had been employed: in 4 a rotating-blade leucotome had been used.

\* or major branches of these.



Figures 1 to 4 illustrate the main different types of lesion:-

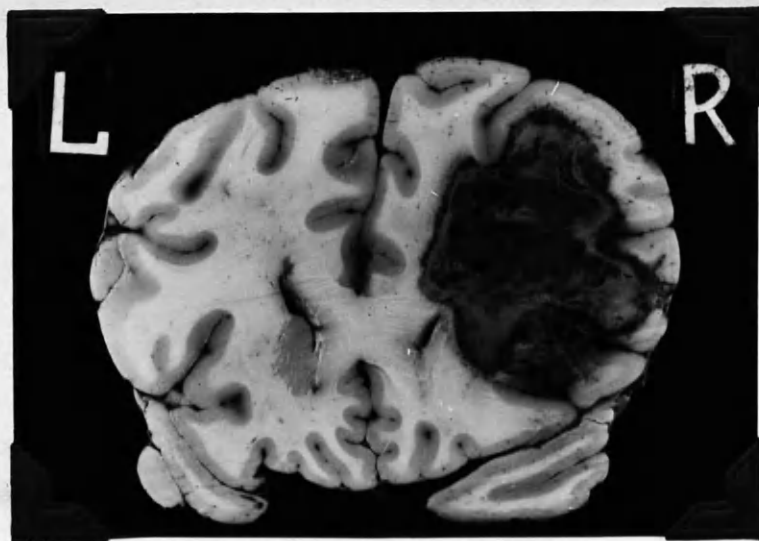


Fig. 1. Cerebral Abscess developing in the right leucotomy lesion of Case No. 54.

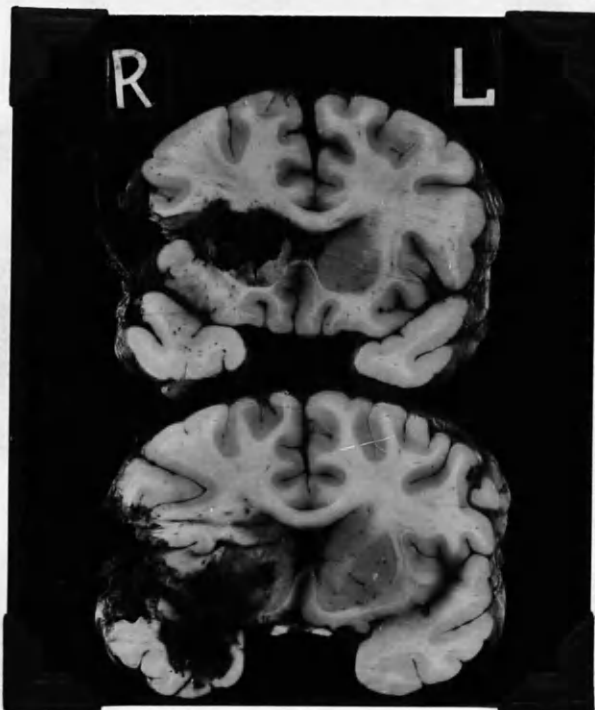


Fig. 2. Haemorrhage from the Right Middle Cerebral Artery in Case No. 73: leucotome entry mark in the posterior part of Area 44.

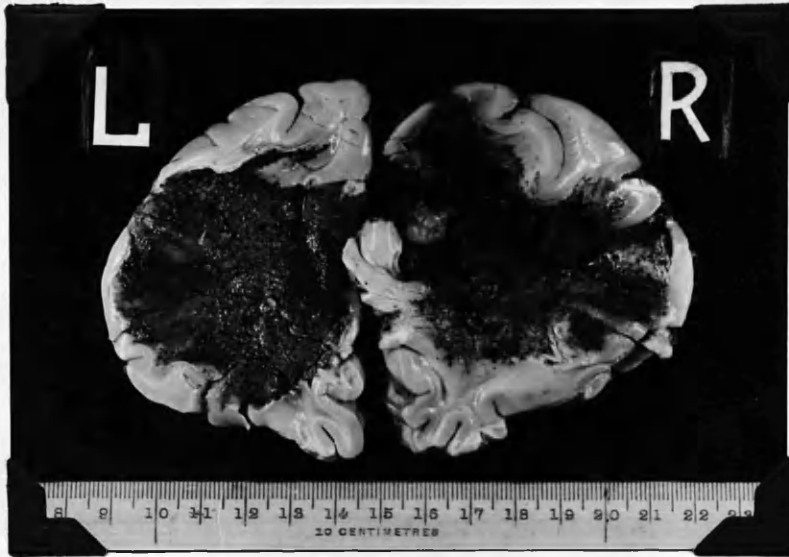


Fig. 3. Haemorrhage from both Anterior Cerebral Arteries in Case No. 1: usual lateral approach through "pars triangularis".

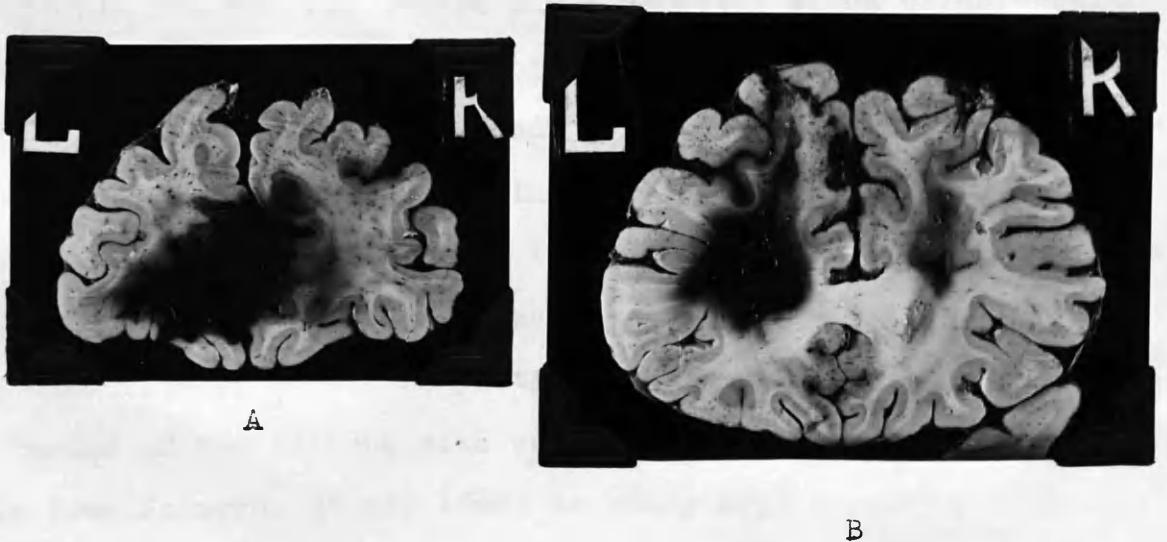


Fig. 4. Haemorrhage from the Left Anterior Cerebral Artery (Photo A) after dorsal approach through Area 8 (Photo B) in Case No. 45.



## Discussion.

### 1. Infection.

Since the proportion of direct post-operative deaths (31%) in this series is some 10 times higher than in all leucotomy operations performed in this country (e.g. Board of Control, 1947) and the brains received from cases of death within the first month of the operation are probably a fair sample of all such deaths, it can reasonably be deduced that death from infection occurs in under 0.5% of all leucotomy operations in this country.

A point of note is that only the two fatal cases (out of the whole 101) displayed evidence of abscess formation in the leucotomy scars. This is strikingly different from the state of affairs in America and Sweden where clinical signs of cerebral abscess are a frequent sequel of the operation (personal communications) apparently because radio-opaque substances are routinely injected into the track of the leucotome by some surgeons. There is no record of any such injection in the present two cases. The responsible factor in at least one of them was apparently contamination by an actinomycotic organism. The possibility that perfusion of the lesions with concentrated penicillin may play a role (see Johnson, et al, 1946) is being kept in mind.

### 2. Haemorrhage.

A curious little point is the predominance of damage to arteries of the right hemisphere. Whether this is due to pure chance or to some technical factor (vide infra), or can be

accounted for by the surgeon being less cautious in the, usually, non-dominant hemisphere, is obscure. Certainly there is no recognised anatomical asymmetry which might explain it.

The most striking and important feature is that at least 23 out of the 31 deaths can be attributed without doubt to the surgeon's instrument. This calls for scrutiny of the operative procedure. The usual leucotomy cut in this country is made through a burr hole orientated by means of skull measurements alone and is intended to commence at an entry point situated about the middle of pars triangularis of the inferior frontal gyrus (Brodmann's Area 45) and to extend throughout most of the white matter within the coronal plane passing through that point. Figure 5 illustrates the actual (unintentional) variability of the lesions (in the left hemisphere) in both position and extent as established post mortem in a group of cases operated on by various surgeons (a) in 1943 and (b) in 1947. It at the same time demonstrates the absence of improvement in accuracy over the years which characterises the whole series.

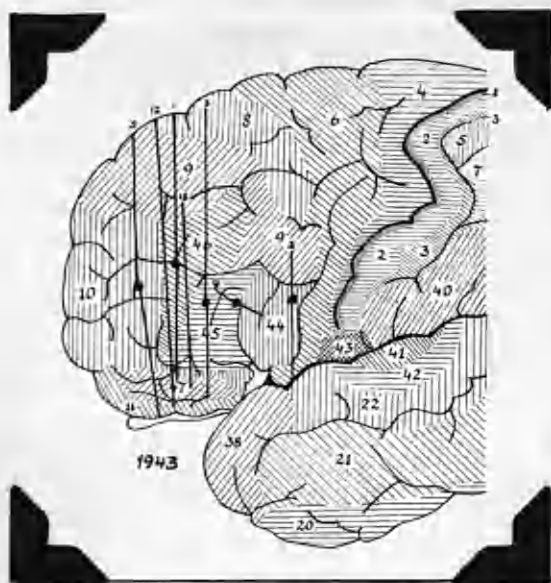


Fig. 5a

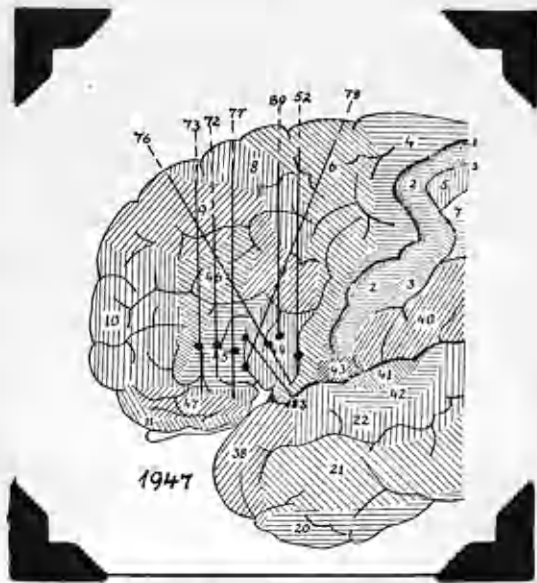


Fig. 5b

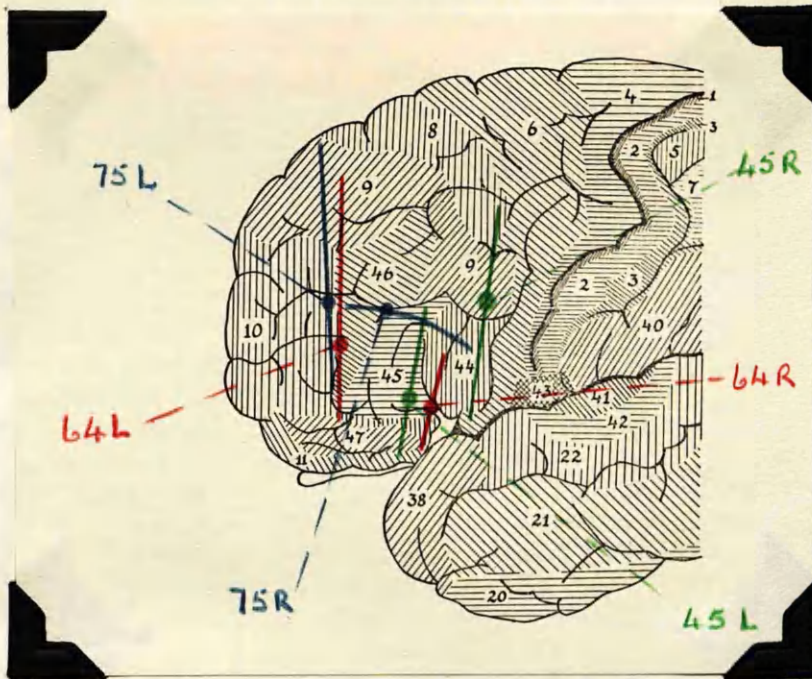


Fig. 6.

Figure 6 illustrates the unintentional variability between the cuts in the Left and Right hemisphere frequently found in the same brain. A series of cases all operated upon by the same surgeon in the belief that he was performing an identical operation revealed almost as wide ranges of variation as in Figures 5 and 6. By contrast, in the U.S.A. Lyerly (1944), by utilising a ~~much~~ more open exposure and additional internal land-marks, appears to obtain appreciably more accurate placement of his cuts and a ~~much~~ lower incidence of fatal haemorrhage, whilst Poppen (1948) with his suction-tipped instrument under direct vision suffered only two deaths from haemorrhage in a series of 470 leucotomies. There would seem, therefore, strong presumptive evidence for concluding that the blindness of the operation is a major factor in determining the occurrence of vascular catastrophies.

Before, however, attributing these catastrophies to the

poverty of operative land-marks alone there would seem to the writer to be at least three other factors which should be scrutinised as being possibly contributory to, and perhaps sometimes wholly responsible for, the fatal consequences of at least one of the two cuts:-

(1) Cortical atrophy, a common feature in chronic deteriorated psychotics, can in the writer's experience cause, for instance, Area 45 to lie unusually posteriorly over part of the insula and its related branches of the middle cerebral artery. Dax and Radley-Smith (1943) reported three cases of unsuspected, shrunken frontal lobes at leucotomy operation; Alexander (1943) was surprised to find conspicuous cortical atrophy in the first group of schizophrenics he operated upon; Fleming (1944) recorded two personal cases; Heath and Pool (1948) found atrophy in three out of four cases of functional psychosis (one aged 22); and it was recorded in five of the cases in the present series. In all but one of these last cases organic atrophy was definitely excluded post mortem. It would appear therefore that pseudo-cortical atrophy, presumably due to temporary dehydration, can occur during anaesthesia or operation and as seriously invalidate cortical landmarks as may organic atrophy.

(2) Oedema or other form of swelling within the first frontal lobe operated upon might result in distortion of the large arteries of the opposite frontal lobe from their normal position, and



certainly the fact that most of the brains under discussion had bilateral cuts would indicate that the bleeding was mainly from the second side operated on.

(3) Movement of the brain within the skull during the operation has apparently never been systematically investigated, (e.g. by radiography at different stages of the operation with the anterior horns of the ventricles filled with air and lead pellets fixed to the scalp), although more than one neurosurgeon has remarked that the firmness to palpation (Heath and Pool, 1948) or the resistance to cutting (personal communications) differs enormously from patient to patient for no known reason. Whatever may be the circumstance of anaesthesia, or the individual reaction to operative interference, responsible for such differences, (presumably not unrelated to pseudo-cortical atrophy), the remarkable discrepancy sometimes found between the surgeon's stated intention and the lesions found in the laboratory (see Fig.7)



Fig. 7: Position of the lesions in Case No. 59, illustrating the discrepancy between the surgeon's intention (coloured lines) and the actual post mortem finding.

strongly suggests that semi-blunt leucotomes can, and do on occasions, lever the white matter about very considerably. Such traction might well cause rupture of at least the anterior cerebral artery or its branches.

Systematic investigation of these three factors would seem highly desirable. Whichever, if any, of them plays a material part in causing misplaced or otherwise fatal cuts there can be no doubt that open\* operation would minimise the danger of any of them not being observed and allowed for.

In view of the recent developments in the field of circumscribed rostral leucotomy it should perhaps be added that in such operations misplacement of the cuts, from whatever of the causes discussed above, cannot be at all so dangerous because firstly the cerebral arteries diminish in size as the frontal pole is approached and secondly, in at least the transorbital operation (Freeman, 1948a, b) or its obverse from the dorsal aspect (being performed by McKissock: personal communication), using a straight semi-blunt leucotome swung through a single short arc, large vessels are extremely unlikely to be severed even if encountered.

Footnote. \* "Open" in this sense would include Poppen's technique where although the trephine hole is small the illumination of the coagulation and suction tip of the instrument remains full throughout the operation.

Summary.

The incidence of post-operative death from infection in this country appears to be relatively insignificant. Of 27 deaths from Haemorrhage (all within the first three weeks of the operation) 85% can be attributed to misdirection of the leucotome in relation to the vessels of the brain. The probable chief cause of this misplacement of the cuts is the blindness of the operation, but it remains possible that changes in brain shape, position and consistency during operation may be contributory factors. Open operation would virtually eliminate all these causes.

---

---

## SECTION II.

### METHODS OF ANALYSIS OF THE LESIONS.

Systematic description and measurement of the lesions resulting from the operation is a first requirement of any investigation involving correlation of anatomical with clinical features, such as undertaken in Sections III to V. The following methods of "quantifying" the lesions have therefore been evolved:-

#### (1) Cortical Topography.

In describing regions of prefrontal cortex Brodmann's internationally known cytoarchitectural maps are employed. This is simply because it is easier to define the position of a region of cortex in terms of Brodmann's numerous "Areas" than in terms of the few named gyri and sulci. That is to say, the Brodmann Areas are employed for their topographical convenience, and not (in the present studies) as implying that any cytoarchitectural investigation has been made.

#### (2) Plane of Cuts.

The plane of cut most usually aimed at in the blind operation, namely perpendicular to the orbital plate and passing through the centre of pars triangularis (Brodmann's Area 45) of the inferior frontal gyrus, is called the Middle plane (see Figure 8, "M"), planes about  $1\frac{1}{2}$  cm. anterior and posterior to it "Anterior" and "Posterior" respectively, and



(Contents face page 24)

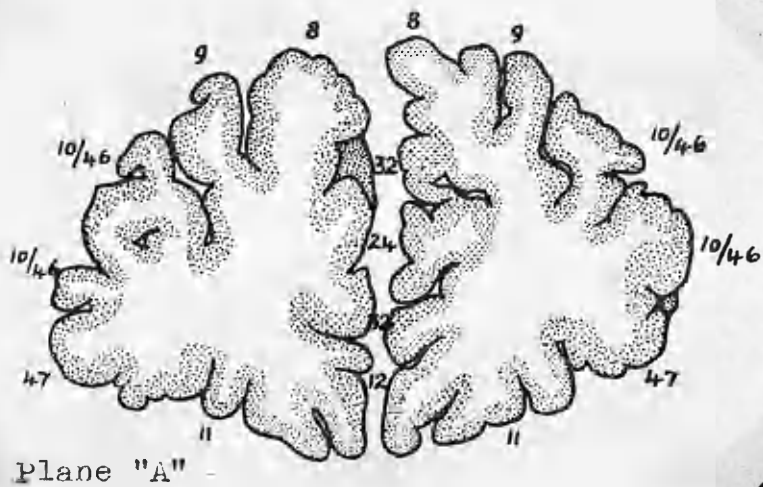


Fig.9:

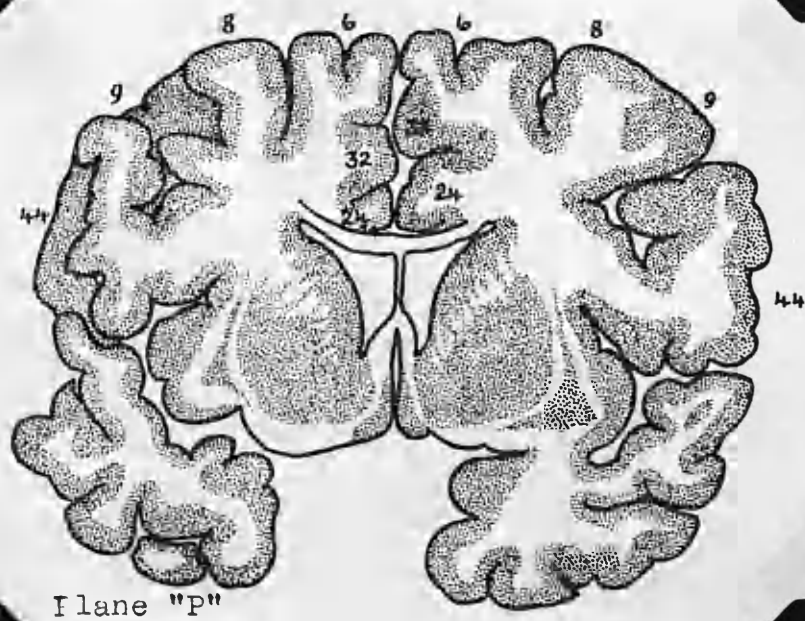
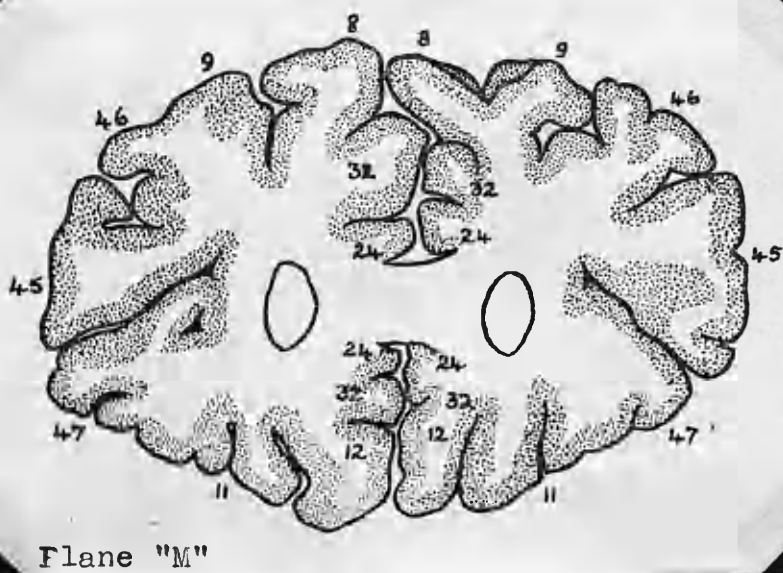


Fig. 8a

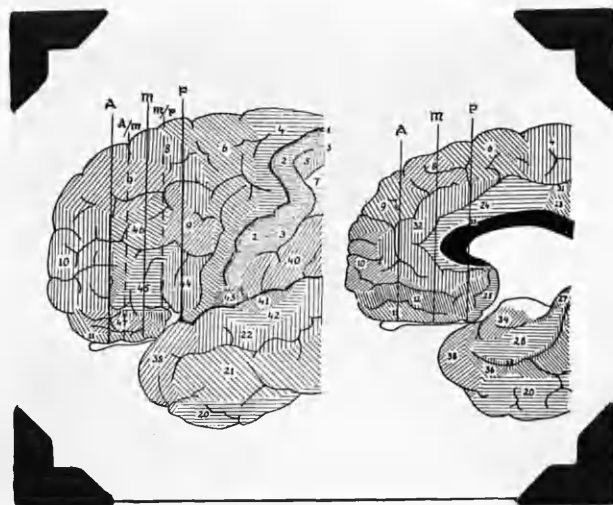


Fig. 8b

the intermediate ones A/M and P/M. Figure 9 (facing) shows the normal structures seen at Planes A, M and P. In many cases the plane allotted to a lesion must represent a mean, for often the final lesion was cystic and frequently it was oblique to the coronal plane.

### (3) White Matter Segments.

Five segments of white matter are differentiated in the ~~(any)~~ coronal plane, namely dorsal, middle, ventral or orbital, cingulate and central (see Figure 10). The cortical surface of the middle segment corresponds roughly to the middle frontal gyrus and that part of the inferior frontal gyrus which lies on the convexity. The cingulate segment incorporates the anterior part of the cingulate gyrus and area 32 of the cingular belt.

Figure 10

D = Dorsal Segment  
 M = Middle "  
 V = Ventral "  
 C = Cingulate "  
 Ruled Area = Central Seg.

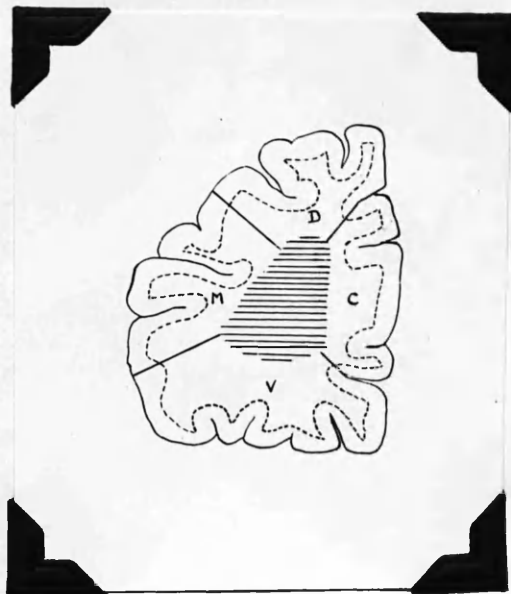


Figure 11 illustrates lesions involving predominantly dorsal plus cingulate (a), middle (b) and ventral (c) segments respectively.

(a)



(b)



(c)



Fig. 11

#### (4) Secondary Degeneration in the Thalamus.

When the cuts take the form of small circumscribed lesions at a posterior level in or close to the anterior thalamic radiation it is impossible to determine by macroscopic examination what prefrontal regions have been severed from their thalamic connections. An indirect method of determination must be sought, - and has been evolved in the writer's laboratory.

By selecting some 30 leucotomy cases with fairly circumscribed lesions near the cortex and making serial sections of the thalamus it has been possible to correlate cortical areas with parts of the dorsomedial nucleus showing secondary degeneration (disappearance of nerve cells and proliferation of neuroglia) and so to arrive at a complete scheme (not yet published in full and still liable to progressive refinement) of the location of the different cells of the dorsomedial nucleus which project to different regions of prefrontal cortex. These are indicated by the appropriate Brodmann numbers in Figures 12a and b.

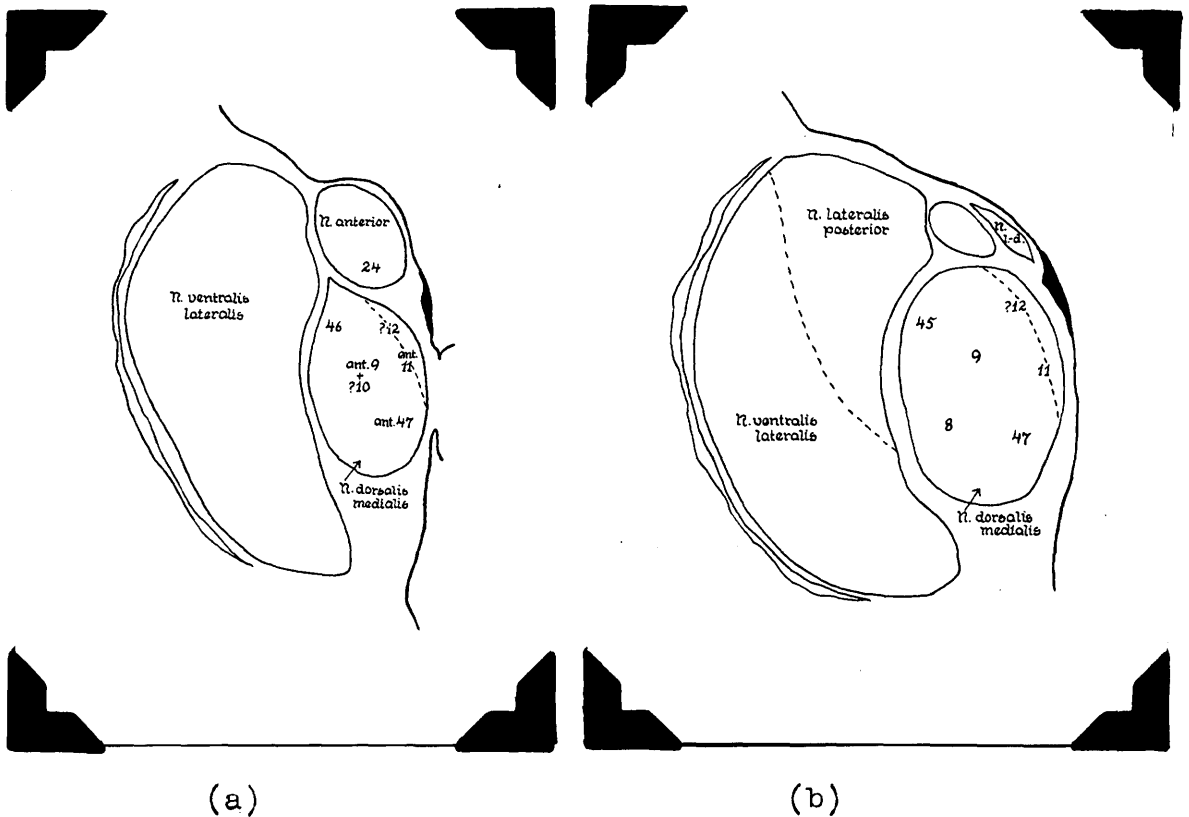


Fig. 12: (a) Anterior Coronal Level of Thalamus.  
 (b) Middle Coronal Level of Thalamus.

Once in possession of this scheme it is easy, though a time-consuming procedure, to deduce from serial sections of the thalamus just what prefrontal regions have been isolated in all cases where the extent of effect of the primary leucotomy lesion on the thalamic radiation is at all doubtful. Figure 13 demonstrates this method of indirect analysis of such a case.

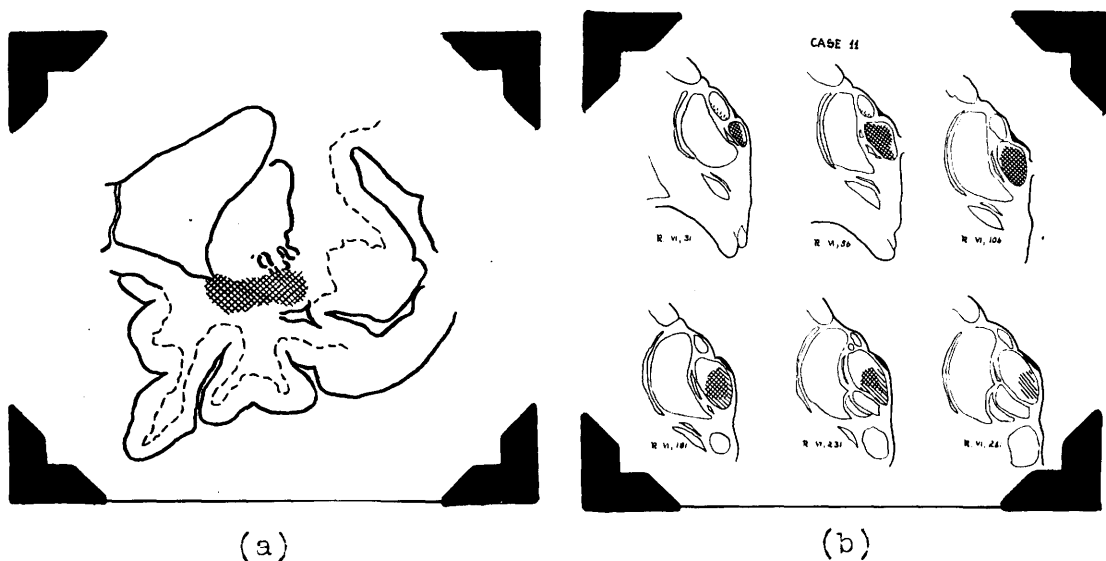


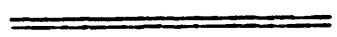
Fig. 13: (a) The circumscribed posterior leucotomy lesion in Case No. 11, left.  
 (b) The secondary degeneration in the dorsomedial nucleus of the left thalamus.

This is, of course, for any white matter lesion a more accurate method of determining the location and amount of cortex isolated than naked-eye inspection and judgement. Where, however, correlation has to be made with rather crude clinical observations its routine use is unwarranted.

#### Statistics.

It may conveniently be mentioned here that statistical formulae have not been applied to the data. The grossness of much of the clinical information, together with the small numbers of cases concerned, renders such procedure inadvisable, and liable to be actually misleading in consequence of, for instance, the approximate nature of the tabulated plane of cut. Instead,

whenever a suggestion of correlation has been found all the cases concerned have been checked back against the actual brain material, all the unstained sections and unsectioned remnants of which are preserved in permanent storage.





### SECTION III.

#### POSTERIOR CUTS.

Among other things, one might expect that bilateral "posterior" leucotomy cuts (i.e. cuts transgressing territory beyond the prefrontal regions) involving the dorsal premotor region would lead to signs of disturbed bladder function (Fulton, 1943); that those involving the posterior\* orbital or the anterior cingulate region might cause serious upset of autonomic functions in view of recent experimental studies by such workers as Fulton and his associates (1947a, b), McCulloch (1944) and Ward (1948); and that bilateral damage to the striatum might prove lethal in view of Freedman and his co-workers' (1947) demonstration that this is the case in animals. One would surmise further that if even the general expectation of undesirable physiological sequelae to posterior cuts is borne out, there might be opportunity to deduce from a detailed correlation study of leucotomy lesions and post-operative physical symptoms some precise principles of localisation of physiological function in parts of the human brain rostral to the precentral cortex.

To test such postulates the cases other than those dying from haemorrhage or infection were divided into those with

Footnote. \* The posterior orbital region for purposes of the present study is defined as that part of the orbital cortex lying behind the junction of the middle and posterior thirds of the distance between the centre of the olfactory trigone and the rostral tip of gyrus rectus.

bilateral involvement of a posterior region (striatum, Area 6, posterior third of the orbital region, external capsule, anterior cingular region), those with none of these regions involved in either hemisphere and therefore having truly "prefrontal" lesions, and those with unilateral involvement of one or more "posterior" region. Figures 14 to 16 and figure 7 (page 19) illustrate the extreme types of lesions concerned in this study.



Fig. 14: Damage confined within the prefrontal white matter in each hemisphere of Case No. 44.

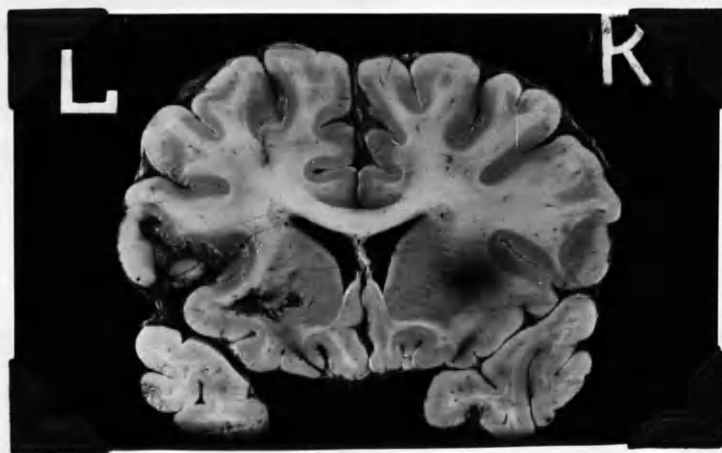


Fig. 15: Bilateral damage to the putamen in Case No. 58.



Fig. 16: Bilateral damage to the premotor cortex (Area 6) in Case No. 88.

To obtain maximum contrast the group of cases with bilateral posterior cuts have been tabulated in Table III (facing page 34) and those with purely prefrontal cuts in Table IV (page 34). The intermediate group with unilateral posterior lesions is not tabulated. In Table III the cases are further subdivided into those with bilateral damage of the striatum, posterior orbital region and/or dorsal premotor region (Part A), and those with bilateral involvement of only the anterior cingulate region and/or the external capsule (Part B).



	REGIONS INVOLVED					CLINICAL SEQUELAE				Intercurrent Cause of Death		
	Striatum	Poster. Orbital	Dorsal Premotor	Anterior Cingulate	External Capsule &/or Insula	General Restlessness	Vasomotor &/or Trophic	Persist. Incont.	Miscellaneous		Survival Period	
Part A.	L. R.	L. R.	L. R.	L. R.	L. R.							
3	+	+	-	-	-				N/U	2 mth.	-	-
11	+	+	-	-	-				.	5 mth.	-	-
16	+	+	-	-	-				. H	7 wk.	-	-
29	+	+	-	-	-				N	9 dy.	-	-
32	+	+	+	-	+				.	7 wk.	-	-
52	+	+	+	+	+				S	20 dy.	-	-
56	+	+	+	+	+				U	9 mth.	-	-
68	+	+	-	-	-				.	21 dy.	-	-
102	+	+	-	-	-				U/N	10 wk.	-	-
4	+	-	+	+	+				.	4 mth.	-	-
22	+	-	+	+	+				U	9 wk.	-	-
58	+	-	-	-	-				.	7 dy.	-	-
87	+	-	-	-	-				.	1 1/2 yr.	+	-
89	+	-	-	-	-				.	3 1/2 mth.	-	-
10	+	+	-	-	-				N	3 yr.	-	-
33	+	+	-	-	-				.	10 wk.	-	-
38	+	+	-	-	-				.	1 1/2 yr.	-	-
41	+	+	-	-	-				H	6 dy.	-	-
49	+	+	-	+	+				H	24 dy.	-	-
59	+	+	-	+	+				R	4 hr.	-	-
65	+	+	+	-	+				S	3 yr.	+	+
69	+	+	-	-	-				.	2 yr.	+	+
88	-	-	+	-	-				.	8 wk.	-	-
Part B.												
5	-	-	-	+	-				E	1 1/2 yr.	-	+
12	-	-	-	+	-				E	2 yr.	+	+
60	-	-	-	+	-				.	3 yr.	+	+
95	-	-	-	+	-				E	1 1/2 yr.	+	+
8	-	-	-	-	+				.	1 1/2 yr.	+	+
27	-	-	-	+	-				.	3 1/2 yr.	+	+
37	-	-	-	-	+				.	4 1/2 yr.	+	+
47	-	-	-	-	+				N	3 1/2 yr.	+	+

TABLE III: BILATERAL POSTERIOR CUTS.

Serial No.	REGIONS INVOLVED						CLINICAL SEQUELAE				Survival Period	Intercurrent Cause of Death		
	Striatum		Orbital		Dorsal Anterior Cingulate		External Capsule &/or Insula		General Restlessness	Vasomotor &/or Trophic			Persist. Incont.	Miscellaneous
	L. R.	L. R.	L. R.	L. R.	L. R.	L. R.	L. R.	L. R.						
9	-	-	-	-	-	-	-	-	-	-	-	-	1 3/4 yr.	+
14	-	-	-	-	-	-	-	-	-	-	-	-	8 mth.	-
18	-	-	-	-	-	-	-	-	-	-	-	-	1 1/4 yr.	+
19	-	-	-	-	-	-	-	-	-	-	-	-	6 mth.	+
26	-	-	-	-	-	-	-	-	-	-	-	E	3 3/4 yr.	+
31	-	-	-	-	-	-	-	-	-	-	-	-	1 1/4 yr.	+
34	-	-	-	-	-	-	-	-	-	-	-	-	2 yr.	-
35	-	-	-	-	-	-	-	-	-	-	-	-	1 yr.	-
44	-	-	-	-	-	-	-	-	-	-	-	-	3 3/4 yr.	+
46	-	-	-	-	-	-	-	-	-	-	-	-	9 mth.	+
62	-	-	-	-	-	-	-	-	-	-	-	-	2 1/4 yr.	+
63	-	-	-	-	-	-	-	-	-	-	-	-	1 1/4 yr.	+
66	-	-	-	-	-	-	-	-	-	-	-	-	9 mth.	+
67	-	-	-	-	-	-	-	-	-	-	-	-	2 yr.	+
74	-	-	-	-	-	-	-	-	-	-	-	N E	3 1/2 yr.	+
75	-	-	-	-	-	-	-	-	-	-	-	-	3 yr.	+
80	-	-	-	-	-	-	-	-	-	-	-	-	1 1/4 yr.	+
85	-	-	-	-	-	-	-	-	-	-	-	-	1 1/4 yr.	+
90	-	-	-	-	-	-	-	-	-	-	-	-	4 3/4 yr.	+
99	-	-	-	-	-	-	-	-	-	-	-	-	4 1/4 yr.	+

E = Epilepsy  
H = Hyperthermia  
N = Nutritional Deficiency  
R = Respiratory Inhibition  
S = Speech Defect  
U = Uraemia

TABLE I.V: PURELY PREFRONTAL CUTS.

On the right hand side of the Tables are recorded any untoward clinical sequelae reported to have followed the operation. The heading "Vasomotor and/or Trophic" has been used to cover such symptoms as cyanosis of extremities, oedema and blisters of the skin (often commencing as aseptic bullae). "Persisting Incontinence" applies only to urine and was tabulated as positive when of over 6 weeks duration. In the "Miscellaneous" column "E" has been used to denote Epilepsy developing for the first time after operation; "H" to mark the occurrence of Hyperpyrexia as a prominent sequel; "N" to indicate the development of signs of Nutritional Deficiency; "R" to denote marked respiratory disturbance; "S" to represent any recorded upset of Speech; and "U" to indicate the appearance of Uraemia. All neurological sequelae clearly referable to area 4 have been omitted. The penultimate column shows the post-operative survival period: the last column those cases in which death can be attributed definitely to an exogenous intercurrent illness.

## 1. Undesirable Physiological Sequelae.

A glance at Tables III and IV reveals that the most general proposition is borne out: namely that the group of cases with bilateral involvement of posterior regions has a relatively enormous incidence of undesirable physiological sequelae: 42 items in 31 cases as against 4 items in the 20 cases with purely prefrontal cuts.

Another conspicuous fact is that practically all cases displaying any of the sequelae except epilepsy, fall within Part A of Table III, i.e. possess bilateral damage to either the striatum, the posterior orbital region or the premotor region. No clear-cut relationship, however, is found when more detailed attempt is made to correlate these specific regions with specific sequelae. For instance, the five cases of bilateral striatal damage without posterior orbital lesion show no significant difference in incidence of general restlessness, vasomotor and trophic lesions or incontinence from the eight with bilateral posterior orbital damage but no striatal involvement. This is not surprising, for lesions in the region of the head of the caudate nucleus are extremely liable to damage fibres which are projecting to and from premotor and orbital cortex: indeed they must do so if, as Fulton, Livingstone and Davis (1947) have suggested is the case in monkeys, fibres projecting to Area 13 pass through the caudate nucleus, and as Rosett (1933) maintained projection fibres from premotor regions course



through the caudate nucleus.

An incidental conclusion which may be drawn from these broad correlates is that in man, as in animals, the mechanism concerned in the production of these clinical changes, so far as related to the orbital region, is confined to its posterior third. This is the region within which Ruch and Shenkin (1943) showed stimulation to produce hypermotility in monkeys, and Fulton and his associates (1947a, b) found bilateral ablation to produce elevation of skin temperature and motor hyperactivity. The latter workers considered their results to derive essentially from destruction of that part of the orbital cortex in the monkey brain which Walker (1940) distinguished cytoarchitecturally as Area 13. That in fact the medial half of this part of the human brain (Fig. 17) contains a region which is structurally homologous with Area 13 of monkeys, has been shown in cytoarchitectonic studies by E. Beck (in press) working in the Maudsley Laboratory.

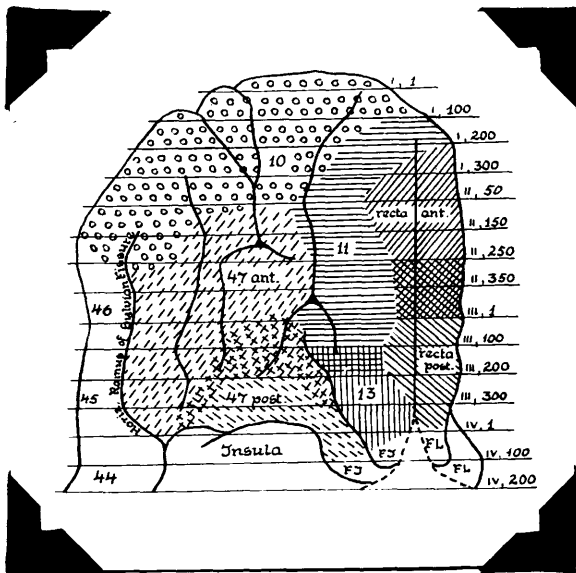


Fig. 17: Typical cytoarchitectural parcellation of the orbital aspect of a human frontal lobe: crossed hatching indicates transitional zones.

Although evidence is accumulating that the cingulate region has important autonomic functions (McCulloch, 1944; Smith, 1945; Kremer, 1947; Ward, 1948), the bilateral involvement of the anterior cingulate region in the present material shows no suggestive correlation with any of the autonomic sequelae listed. Hence damage to this area (the anterior third of Brodmann's Area 24) has apparently no causal connection with at least the rather gross types of clinical manifestations to which the present study is limited. There is, however, considerable evidence in the case records that, as Freeman and Watts (1942) suspected, its damage correlates with transient post-operative confusion.

That the four cases having bilateral posterior lesions confined to the external capsule (the bottom group of Part B of Table III) display no sequelae bar one instance of nutritional deficiency, indicates clearly that the essential anatomical substrate concerned in these undesirable clinical changes does not include the external capsule, (or, it may be added, the claustrum, extreme capsule, insular cortex, or uncinate fasciculus, which were bilaterally involved in at least three of these four cases).

The Restlessness in the present cases cannot, unfortunately, be equated with the restless pacing of experimental animals which Ruch and Shenkin regarded as the characteristic result of bilateral damage to Area 13 and which Richter and Hines (1938) and Mettler (1945) related to damage of the striatum, - for all the patients displaying it were largely confined to bed.

With regard to Vasomotor and Trophic Disturbances it is probably relevant to recall that Kennard (1935) created vasomotor changes in monkeys by ablation of the premotor area, and that in Ziegler and Osgood's (1945) leucotomy cases displaying vasomotor and trophic phenomena there seemed to be some relationship with posterior cuts, as determined by contrast radiography.

Persisting Incontinence of Urine is a very general symptom which, especially in psychotics, cannot be expected to correlate closely with damage to any circumscribed region, for although it is well known to be brought about by lesions of the dorsal part of the premotor region<sup>it</sup> can, for instance, be determined simply by the general deterioration in a patient's conduct. All but one of the cases exhibiting it in fact had lesions likely to affect fibres from the dorsal premotor region or showed post-operative mental deterioration.

The "Miscellaneous" Sequelae are too few to warrant full individual analysis at present. It is interesting, however, that of the nine cases developing Epilepsy none occurs in Part A of Table III. This accords with Dax, Reitman and Radley-Smith's (1948) finding of complete absence of post-operative epilepsy in a large series of cases with cuts confined to the posterior orbital region. Another curious point is that the four in which fits commenced within a few months of operation had on at least one side more anteriorly extending cuts than any of the other cases in the series. The damaged anterior regions

peculiar to these four cases lie definitely rostral to any of the sites which Russell (1947) has tentatively related to post-traumatic epilepsy. They remind one more of Pennybacker's (1945) series of cases of abscess of the anterior pole with epilepsy. It may be that one is dealing here with the same factor as responsible for the  $33\frac{1}{3}\%$  incidence of post-operative epilepsy in 9 psychiatric cases treated by bilateral polar lobectomy by Penfield (personal communication) and for the 10% with such a sequel in the first 35 cases of resection of areas 9 and 10 performed by Pool (personal communication).

Speech. Of seven cases with bilateral severe damage to Area 44 the two cases indicated in Table III were the only ones with any recorded post-operative speech defect. No. 56 did not speak at all after her operation, No. 65 became monotonous and dull in his speech. This apparent inconsistency with orthodox modern views on the location and vulnerability of a "Broca's speech centre" would seem worthy of further investigation, for although certainly only a small amount of grey matter is destroyed even when the leucotome entry point is through Area 44, a large proportion of the uncinate and other association fibres of the area are damaged in most of these seven cases. One is reminded of Marie and Foix's (1917) and Weisenburg and McBride's (1935) views that "Broca's area" has very little to do with speech.

Area 8. It may be mentioned in passing that no persistent symptom referable to the eyes was recorded in any case in the

whole series although more than the seven cases with bilateral Area 6 involvement had appreciable bilateral damage to the white matter related to Area 8 (the frontal eye field).

Nutritional Deficiency took the form of pellagrous symptoms in three cases, Wernicke Syndrome in one case and vitamin C-like deficiency symptoms in a fifth. In view of the complexity of the whole problem of nutritional deficiency it would be idle to speculate whether the condition was primarily or only secondarily related to the lesions, but it is noteworthy that at least two of the cases failed to respond to prolonged treatment with multiple vitamins.

The three cases displaying Hyperpyrexia revealed no histological evidence of infection of the brain or meninges. They had in common only bilateral damage of the posterior orbital region.

It is impossible to say as yet whether the Uraemia which developed after operation in four cases might have had anything to do with the damage to the brain, but Cumings' (1942) findings of uraemia in cases of head injury, and the recent discoveries concerning autonomic control of kidney circulation (Trueta, 1946) suggest that it is a sequel worthy of attention in any future clinico-anatomical correlation studies.

The one case of Respiratory Inhibition with severe bilateral damage of the posterior orbital region (the case illustrated in Fig. 7) brings forcefully to mind that this was a site of the lesions which Smith (1938), Bailey and Sweet (1940) and Delgado,

Fulton and Livingstone (1947) found to produce respiratory inhibition in animals.

The fact that all cases with similar lesions did not display identical sequelae does not necessarily invalidate the broad correlation trends and experimental analogies which have been pointed out. Quite apart from the possibility of constitutional variation in the homeostatic mechanisms of different individuals, it may well be that grossly similar lesions differ in details which have not been distinguished, but which may determine differences in the nature of the upset of physiological balance. Actually, many other variables than these tabulated have been examined, - e.g. involvement of the ventricles, damage to the fasciculus subcallosus, affection of grey as well as merely white matter of Brodmann areas, - but without revealing any correlation trend.

## 2. Delayed Post-Operative Death.

A further striking point of contrast between Tables III and IV is that whereas neither bilateral damage to the external capsule alone nor bilateral damage to Area 24 alone (Table III, Part B) resulted in death any earlier, on the average, than purely prefrontal lesions, the survival period of the cases in Part A of Table III ( $7\frac{1}{2}$  months) is on the average very much lower than the average of those in Table IV ( $2\frac{3}{4}$  years). The cases in Part A are therefore essentially those responsible for the second cumulus of deaths noted in Table I at the outset.

Only one of the 14 cases with bilateral striatal damage and one of the 7 cases with bilateral premotor involvement survived over nine months. By contrast, four out of the eight cases with bilateral damage to the posterior orbital region alone survived over 1½ years. Closer analysis reveals that each of the other four cases (who all died within 2½ months) possessed the distinguishing feature of at least unilateral damage to "Area 13".

A closely parallel feature is that only three of the 23 cases in Part A of Table III died from an exogenous intercurrent disease, as against 7 of the 8 cases in Part B and 17 of the 20 cases in Table IV. Manifestly, therefore, posterior cuts, if they affect the striatum, postero-medial orbital region or dorsal premotor region, tend to determine relatively early death, i.e. "delayed post-operative death". Many of the gross physical sequelae actually recorded doubtless play either a primary or secondary lethal role. In view, however, of the increasingly clear experimental evidence (quoted above), as well as recent evidence from circumscribed cortical ablations in man (personal communication: Professor Freeman), that the anterior cingulate region and the posterior orbital region contain important stations of autonomic control, and of Heath, Freedman and Mettler's (1947) impression that the invariable death in felines after bilateral enucleation of striatal tissue is due to upset of metabolic function, it would seem that "loss of autonomic homeostasis" might be the most appropriate general aetiological term under which one might group all these delayed

deaths: a loss of power of adequate internal adaptation to everyday environmental variations.

On this basis one could conceive that the third cumulus of deaths remarked upon in Table I, (and which actually contains 13 of the 17 cases with<sup>a</sup> unilateral "posterior" cuts), may be due to lesser structural damage to these regions reducing homeostatic flexibility to a point where it can cope with "normal" environmental variations, but not with "abnormal stresses", such as benign infection, asthma and status epilepticus. However, a much more detailed physiological study of a much larger number of cases would be necessary to substantiate this speculative analogy with Cannon's (1932) sympathectomised animals when exposed to stress.

The absolute incidence of such delayed post-operative deaths in the general "leucotomised population" cannot be estimated with any accuracy from the available data, but the writer's impression is that it surpasses the 3% for direct post-operative deaths. The chief causes of the over-posterior cuts are probably the same as those suggested for haemorrhage in Section I. The precaution necessary to prevent them is therefore the same, namely open operation. The danger of such fatalities is, of course, again very much reduced in trans-orbital, and other, leucotomies aimed at only the rostral prefrontal white matter.



### Summary.

Bilateral lesions extending beyond the prefrontal regions, and especially into striatum, posterior orbital region or pre-motor region, cause undesirable post-operative physiological sequelae such as restlessness, vasomotor and trophic lesions and incontinence: not so those extending only into the anterior cingulate region or external capsule. No more specific localisation of function can be deduced, at least from the present material.

Epilepsy as a sequel is notably absent in postero-ventral cuts and notably frequent in unusually rostral lesions. Speech and eye movements are surprisingly undisturbed by severe bilateral damage to the white matter of Areas 44 and 8 respectively.

The fact that 74% of the cases with bilateral damage to striatum, Area 6 or posterior orbital region died within 5 months in the absence of intercurrent illness strongly suggests use of the term "delayed post-operative death" in such cases. This would seem most probably due, in general terms, to upset of homeostatic mechanisms to such an extent as to prevent adequate adjustment to "normal" variations in the environment. Many of the deaths between 5 months and 2½ years after operation may be due to lesser upset of the mechanisms being still enough to prevent adaptation to unusual stresses.

The over-posterior lesions responsible for the bulk of these undesirable sequelae and delayed post-operative deaths

are probably due to the same factors as were suggested in Section I to be responsible for fatal haemorrhage. The surest method of their prevention would seem therefore to be the same, namely open operation.

The results emphasise, it is hoped, the potentialities of such studies in elucidating the physiology of frontal parts of the human brain, the importance of concise physiological observations before and after operation, and the necessity of eventual systematic anatomical analysis of the lesions.



## SECTION IV.

### POST-OPERATIVE PERSONALITY CHANGE.

It has been postulated that the more posterior the leucotomy cuts the more severe the post-operative personality change (Freeman and Watts, 1942) and that purely prefrontal cuts do not (Hebb, 1945) or may not (Heath and Pool, 1948) cause any personality change; that the euphoric type of personality change has special relationship to damage of the orbital regions (Reitman, 1946); that cutting of the thalamo-prefrontal projection fibres is the essential factor in creating the personality change (Freeman and Watts, 1947); and that clinical improvement varies with, and may be dependent upon, the personality change (Frankl and Mayer-Gross, 1947).

The present study aims at testing the validity of the first three of these postulates in the light of post mortem investigation of the actual lesions, and to amplify any of them which prove to be true. The fourth proposition will be dealt with in Section V.

#### 1. Anatomical Correlates of Different Degrees of Personality Change.

After elimination of all cases with direct operative death or post-operative physiological sequelae obscuring the mental picture 38 cases were left (all of over 5 months survival) in which the clinical records allowed rough grading of the severity of the personality change as between ++, + and -.

Segments Involved.

	<u>Post-op.</u> <u>Pers.</u> <u>Chge.</u>	<u>Plane</u> <u>of</u> <u>Cut</u>		<u>Segments Involved.</u>						<u>Total</u> <u>Segs.</u>
		<u>Dorsal</u>	<u>Middle</u>	<u>Ventral</u>	<u>Central</u> <u>Core</u>	<u>Cingu-</u> <u>late</u>	<u>L. R.</u>	<u>L. R.</u>	<u>L. R.</u>	
<b>GROUP A (Severe):-</b>										
10	++	M	M	--	++	++	++	--	--	6
18	++	M	A/M	-+	++	++	++	++	++	9
57	++	M	M	+ -	++	++	++	++	+ -	8
62	++	A	A	- +	++	++	++	++	--	7
65	++	P	P	++	++	++	++	++	--	8
67	++	A/M	A/M	- +	++	++	++	++	--	7
69	++	M	M	+ -	++	++	++	++	--	7
71	++	M	P	- +	++	++	++	++	+ -	8
75	++	A	A/M	+ -	++	+ -	+ -	--	+ +	6
81	++	P	M/P	+ -	++	- +	++	--	--	6
86	++	A/M	A/M	++	++	+ -	++	--	--	7
95	++	M	P	+ -	++	+ -	++	++	++	8
<b>GROUP B (Moderate):-</b>										
9	+	M	M/P	+ -	++	--	+ -	--	--	4
19	+	M	M	--	++	++	++	--	--	6
20	+	A/M	A/M	- +	++	--	+ -	+ -	--	5
38	+	P	M	--	+ -	++	--	--	--	3
39	+	A/M	A/M	++	--	--	++	--	+ +	5
47	+	M/P	P	--	++	--	--	--	--	2
60	+	M	M	++	++	++	++	++	++	10
61	+	M	M	++	++	++	++	++	--	8
78	+	P	M/P	+ -	++	--	++	--	--	5
80	+	M	M	- +	++	- +	++	--	--	6
98	+	P	P	++	++	- +	++	++	+ -	8
<b>GROUP C (Negligible):-</b>										
8	?	P	P	--	--	--	--	--	--	0
14	?	M	M/P	--	++	- +	--	--	--	3
21	?	M	M	--	++	--	--	--	--	2
26	?	P	P	--	++	--	--	--	--	2
27	?	P	P	++	++	+ -	+ -	+ -	--	7
31	-	P	P	--	++	--	++	--	--	4
35	-	M	M	--	++	--	--	--	--	2
36	?	M/P	P	--	++	- -	--	--	--	2
37	?	M	P	- +	++	- +	- +	- +	--	6
46	?	M	M	- +	++	--	+ -	--	--	4
66	?	M	M	++	++	++	++	--	--	8
85	?	M	A	--	++	--	--	--	--	2
87	?	M	M	--	++	+ -	--	--	--	3
90	-	M	M	--	- +	--	++	--	--	3
99	-	A/M	A/M	++	--	--	++	--	--	4

**TABLE V:** Analysis of the Leucotomy Lesions in 38 cases where the clinical notes recorded reliably the Post-Operative Personality Change.

They have been tabulated in Groups A, B and C of Table V (facing) according to their grading. Opposite each case is plotted the dimensions of the leucotomy cuts as determined by the methods described in Section II.

If only because of the unevenness of the clinical data, no close parallelism between degree of personality change and extent of damage in individual cases could be expected. When, however, the groups of cases are studied as a whole a striking difference becomes apparent in the number of segments involved between the cases with severest personality change (Table V, Group A) and those with inconspicuous change (Group C). The average in the former is 7.3 segments, in the latter 3.5 segments, and in the intermediate group (Group B) 5.7 segments. This would indicate clearly that the degree of personality change varies directly with the amount of prefrontal cortex isolated from its connections, by association or projection fibres, with more posterior regions.

At a glance it would appear paradoxical that the average plane of the cuts is slightly more anterior the severer the personality change. Closer scrutiny shows, however, that this is due to the fact that in this particular series those cases with posterior cuts happen to have, on the whole, relatively circumscribed lesions largely sparing the anterior thalamic radiation. Such cases indicate clearly that it is ~~to~~ the thalamic connections of the prefrontal cortex to which the foregoing quantitative principle essentially applies.

(Contents face page 51)

... (non) ...  
... (non) ...

... (non) ...  
... (non) ...

... (non) ...  
... (non) ...

... (non) ...  
... (non) ...

... (non) ...  
... (non) ...

50

50

50

50

50

... (non) ...

50

50

50

50

50

<u>Post-operative Personality Change</u>	<u>Average Plane of Cuts</u>	<u>Segments of White Matter Involved in the Leucotomy Lesions</u>					<u>Ave. Total Segs.</u>
		Bilateral Dorsal Segment	Bilateral Middle Segment	Bilateral Ventral Segment	Bilateral Central Segment	Bilateral Cingulate Segment	
A. ++ (12 cases)	M	17%	100%	67%	92%	17%	7.3
B. + (11 cases)	Slightly posterior to M	36%	82%	36%	64%	9%	5.7
C. - (15 cases)	Between M and M/P	20%	80%	7%	27%	0%	3.5

TABLE VI: Summarised Analysis of Table V in Terms of Bilateral

Involvement of Segments.

Analysis of the individual segments\* (Table VI) shows the middle segment to be about equally frequently, and the dorsal and cingulate segments to be about equally seldom, involved in each of the groups. The central and ventral segments show very appreciable, progressive, increasing involvement from the group with insignificant to the group with severe personality change.

Since the central segment collects most fibres converging from the prefrontal cortex to form the anterior thalamic radiation, its behaviour in this analysis, considering the quantitative principle which has just been deduced, is not surprising if Freeman and Watts' (1947) theory of the "thalamic" rationale of the personality change be accepted. Its behaviour becomes, in fact, strong evidence in favour of such a rationale. Further, since at the average plane of the cuts in the cases with positive personality change (Plane "M") the central segment contains thalamic fibres connecting mainly with areas 10, 46 and anterior 9, 32, 11, 12 and 47, it follows that these rostral areas are strongly concerned in the causation of personality change.

The behaviour of the ventral segment, by similar argument, accentuates the importance of the orbital members of these areas, (viz. ventral area 10 and anterior areas 11, 12 and 47) relative to the rest. A further point which can be deduced from the present material is that the importance of the orbital region in

Footnote. \* Heed is paid only to bilateral involvement in view of the generally accepted principle that prefrontal lesions must be bilateral to produce physiological or psychological effects.



the causation of personality change is certainly not confined to its posterior agranular part (containing "area 13"), the part which is believed to be directly concerned with autonomic function (see Section III).

It is of no small interest that this tentative analysis pointing to some degree of localisation of the substrate responsible for personality change is in full agreement with recent reports (Heath and Pool, 1948; Freeman, 1948b) of absence of any appreciable degree of personality change after ablation or isolation (by transorbital leucotomy) of mainly dorsal parts of these rostral areas. That the impression should have grown that personality change is greater the more posterior the cuts is probably due to the fact that more posterior cuts can more easily ensure complete section of ventral as well as central segment fibres as they diverge from the anterior limb of the internal capsule (c.f. Fig. 13). That posterior cuts may not do so is singularly well demonstrated by some of the cases under review which fall into Groups B and C of Table V. This fact, as already noted, ~~incidentally~~ furnishes further negative evidence in favour of Freeman and Watts' concept of the rationale of personality change.

There is abundant evidence in Table V that personality change of even severe degree does occur in cases with purely prefrontal lesions. Recently Hebb (1945) has questioned the occurrence of a frontal lobe deficit syndrome in any condition except where lesions may extend beyond the frontal association

areas or where there may be irritative effects of actively growing tumour, progressive atrophy, haemorrhagic cysts or scars. He extends his criticism to leucotomy, maintaining that if personality change appears after leucotomy, it is due more to pathological complications than to the actual severance of the connections of the frontal lobes. It cannot be denied that within the first few months of the operation this may be the case, but it is difficult to credit the possibility of such an aetiology in cases with longer survival and relatively circumscribed lesions (such as illustrated in Figure 14) which are macroscopically and histologically inactive. No untoward histopathological changes were in fact discovered in or beyond the leucotomy lesions in any of the cases in Table V. The histopathological appearances in individual cases varied consistently simply in accordance with the length of time since operation.

## 2. Anatomical Correlates of Different Kinds of Personality Change.

The history of the frontal lobe syndrome shows that damage to the orbital region has for long been regarded as a specially frequent cause of personality change of the euphoric type associated with "Witzelsucht" (Welt, 1887; Schuster, 1902; Berger, 1923; Kleist, 1934, 1937; Spatz, 1937; Rylander, 1939). Kleist, as a result of his studies of head injuries from the first world war, also related damage to dorsal parts of the prefrontal region to an akinetic type of personality change and

more recently Freeman and Watts (1948) and Dax, Reitman and Radley-Smith (1948) have associated leucotomy damage in this region to the apathetic type of post-operative personality change. Our analysis so far supports neither of these suggestions of relative exclusiveness regarding the location of the substrate of different types of change. Several cases with the euphoric type of personality change had bilateral ventral damage, but others with typical fatuous euphoria had cuts which excluded these regions. Conversely, though several cases with the akinetic type of personality change had bilateral dorsal cuts, many others with such a personality change had no such involvement. In other words, the analysis of this leucotomy material so far fails to indicate the existence of any atomistic localisation of "mental faculties" within the frontal lobe, even in its simplified form as expressed by Freeman and Watts (1948) and Dax, Reitman and Radley-Smith (1948).

Unfortunately the clinical data bearing on premorbid personality were too inadequate to permit any attempt at evaluation of this factor in determination of the post-operative personality change. Fortunately such studies do not depend on pathological follow-up. Negative anatomical findings such as just described should, however, stimulate fresh clinical research in this important sphere.

The absence of frequent involvement of the anterior cingulate region in the cases with positive personality change in Table V is of some special interest in that it tends to

corroborate the recent American finding that focal ablation of the cingulate gyrus fails to produce personality change (Freeman: personal communication). It therefore likewise does not support Ward's (1948) view that area 24 may be concerned with the mechanism of fear and therefore worth interfering with in psychiatric patients. It should be emphasised that detailed analysis of the material shows these remarks to apply to area 24 only and not to area 32 (part of the so-called cingular belt) which rather behaves, in its correlation trends, like the rest of the prefrontal cortex.

### 3. "Anatomical Basis" of the Personality Change.

There has been much recent controversy about the fibre systems involved in the mechanism of personality change. Freeman and Watts now (1947) lay main emphasis on the thalamo-prefrontal connections, but other workers (Reitman, 1946; Mettler, 1947; Carrillo, 1947; Russell, 1948; Yahn et al, 1948) take a less exclusive view. The clinico-anatomical correlates discussed in Part 1 of the present Section, as already pointed out, both positively and negatively strongly support Freeman and Watts' view. Furthermore, preliminary reports on thalamotomy recently introduced by Spiegel and his associates (1947) indicate that direct bilateral lesions confined within the dorsomedial nucleus of the thalamus cause at least the reduction in emotional reactivity which is so common a component of the personality change after ordinary leucotomy. Cases in the present series, in which

the cuts were behind the frontal lobes, tend to confirm this observation. For instance, Fig. 13 (page 28) illustrates a case in which the thalamo-prefrontal projection was severed bilaterally in the ventral part of the anterior limb of the internal capsule and led to a very considerable retrograde degeneration in almost all parts of both dorsomedial nuclei, accompanied by very considerable personality change of the apathetic type, (as well as improvement of the patient's agitated depression).

#### Summary.

In so far as more posterior lesions are more liable to cut a larger proportion of the thalamo-prefrontal fibres (especially orbital ones) as they diverge from the internal capsule, they are more liable to cause more severe degrees of personality change than more anterior cuts, but severe personality change is by no means limited to cases with posterior cuts. Bilateral lesions confined to the prefrontal region are capable of causing severe personality change persisting for long after the process of active repair and irritation has become quiescent. Hebb's contention that substantial bilateral destruction of prefrontal regions can occur without personality change is therefore untenable.

The severity of the change seems to depend mainly on the quantity of prefrontal cortex isolated from its afferent connections from the dorsomedial nucleus of the thalamus. Isolation

of anterior parts of the orbital areas 47 and 11 is apparently much more important than of dorsal regions such as the anterior parts of areas 9 and 8. Areas 13 and 24 seem to be causally unconcerned. Heath and Pool's report of insignificant personality change after circumscribed dorsal cuts is therefore consistent with the present analysis.

There is no evidence of any correlation between the type of personality change and the position of the lesions which might substantiate any at all atomistic theory of localisation of functions within the prefrontal regions.

Segmental analysis as well as some cases with circumscribed posterior lesions tend to confirm the theory that the personality change depends largely on section of the thalamo-prefrontal connections.

All these results should be regarded as tentative and liable to considerable modification in the light of greater numbers of cases and of improved clinical observations. Meantime they perhaps indicate something of the contribution to psychiatric practice and theory latent in clinico-anatomical analysis of such leucotomy material.

---

---

## SECTION V.

### ANATOMICAL CORRELATES of CLINICAL IMPROVEMENT and RELAPSE.

Out of the 101 cases 48 had post-operative survival of over 5 months, and more than half of these showed some degree of clinical improvement. Such numbers make worth while an attempt to ascertain whether or not any attribute common to the lesions is a prerequisite to clinical improvement; whether or not the degree of improvement, other things being equal, tends to vary with any qualitative or quantitative feature of the lesions; and whether or not any such relationship between lesions and improvement which is revealed holds good in equal degree for each of the main types of functional psychosis. Some of even the best improved cases relapsed after an interval of several months. Relationship of the lesions to relapse may therefore be studied at the same time in a smaller subgroup of cases.

All cases with post-operative survival of less than 5 months duration were eliminated from the present study because such brief survival does not permit reliable evaluation of the clinical results and in practically all such cases undesirable physiological sequelae, such as described in Section III, tend to obscure the picture of the mental state. A further three cases were rejected on account of inadequacy of either the clinical data or the brain material, a fourth on account of

severe neurological sequelae obscuring any changes in the mental state throughout a nine month's survival period, and a fifth because it was an isolated case of epileptic psychosis. This left 43 cases suitable for investigation of correlations between the lesions and clinical improvement or non-improvement.

For each of these 43 cases the following data were tabulated, - serial number, sex, nature of illness, pre-operative duration of illness, previous physical therapy, age at operation, plane of left and right cuts, segments of white matter involved, nature and duration of post-operative improvement if any, post-operative personality change (graded as described in Section IV), survival period and cause of death. Premorbid personality had perforce to be omitted on account of the inadequacy of its reporting in the majority of cases records.

The cases were then divided into the three clinical groups of Predominantly Affective Conditions (Table VII), Mixed mainly Paranoid Psychoses with onset after 35 years of age (Table VIII), and Schizophrenia with onset under 35 years of age (Table IX). (Tables VII to IX are contained in the Appendix, pages 81 to 83.) In each of these three tables the cases were divided into an upper "Improved Group" and a lower "Unimproved Group". The improved cases are arranged roughly in order of grade of improvement\*. The unimproved cases are listed simply in serial order.

Footnote.\* It should be emphasised again that the quality of improvement which is being dealt with here is not representative of improvement after leucotomy in general.



The resultant distribution of cases is as follows:-

	Improved	Unimproved	Total
Predominantly Affective Conditions	11	4	15
Mixed, mainly Paranoid, Psychoses	6	7	13
Schizophrenias	7	8	15
	—	—	—
Total cases	24	19	43

### Analysis.

A preliminary survey of the cases reveals five general points of note:-

1. Very few of the improved cases could, as judged by pre-operative data, be called cases with good prognostic potentiality in terms of Freeman's (1948a, b) criteria.

2. There is no coronal segment which is always bilaterally\* involved whenever improvement occurs. The central segment comes closest to being so, if due allowance is made for the fact that a plus in the column for the middle segment often implies only very limited damage in the leucotome entry track.

3. The average total number of segments involved (7.7 out of a possible 10) in the whole 24 improved cases is much greater than in the whole 19 unimproved cases (4.8), involvement of individual segments being relatively highest for the central one.

Footnote. \* Except in enumerating the total number of segments involved no account of unilateral damage is taken in this section for the same reason as stated in Section IV.

... ..

...	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...

(Contents face page 62)

...	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...

...	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	...	...	...	...

...

Ave. Age at Onset yrs. Ave. Duration yrs. Ave. Pre-op. Plane of Cuts Pre-Plane of Cuts Ave. Total No. of Segments Involved. (out of possible 10) % Bilat. Dorsal Segment % Bilat. Middle Segment % Bilat. Ventral Segment % Bilat. Central Segment % Bilat. Cing. Segment

1. Predominantly Affective Conditions.

A. <u>Improved</u> (11 cases)	45	5½+	A/M-M	6.7	36%	91%	55%	91%	18%
B. <u>Unimproved</u> (4 cases)	52½	2½+	M	2.8	0%	100%	0%	0%	0%

2. Mixed, mainly Paranoid, Psychoses.

A. <u>Improved</u> (6 cases)	43	6	M	5.7	17%	83%	33%	50%	0%
B. <u>Unimproved</u> (7 cases)	49½	5½	M	4.7	14%	86%	29%	29%	14%

3. Schizophrenias.

A. <u>Improved</u> (7 cases) (1 chronic deteriorated)	-23	4+	M	8.0	86%	86%	71%	100%	29%
B. <u>Unimproved</u> (8 cases) (All chronic, 6 deteriorated)	-28	15+	M	5.8	25%	100%	38%	75%	25%

TABLE X - Summary of data contained in Tables VII to IX (in the Appendix).

4. In general, equally extensive cuts in cases of equal prognostic potentiality produce greater improvement the more posterior their level.

5. There is no segment which is consistently spared wherever relapse occurs.

One general point not demonstrated by the tables is that there was no difference in the quality of the histo-pathology of the leucotomy scars between the improved and unimproved groups as a whole, appearances in individual cases varying consistently, as already stated in Section IV, in accordance with the length of time since operation. Another point is that general histological investigation of the unimproved cases showed no evidence of independent organic cerebral conditions which might have militated against improvement.

Any further gross comparison of the whole 24 improved cases with the whole 19 unimproved cases is unprofitable in view of the divergencies in findings between the different clinical types of cases. Further analysis has therefore been carried out by clinical groups. Table X, derived from data contained in Tables VII to IX, summarises some of the main features.

#### 1. Predominantly Affective Conditions. (Table VII).

On the clinical side the only conspicuous difference between the improved 11 and the unimproved 4 is that a much larger proportion of the former, including the three best improved, had not had the benefit of previous physical therapy.

On the anatomical side the most striking difference between the improved and the unimproved is the much higher average total number of segments involved in the former (6.7) than in the latter (2.8). If one discounts the middle segment for the reason given above, this higher frequency is seen to hold for bilateral involvement of each of the segments, but in different degrees. It is most marked in the central segment, somewhat less in the ventral, still less in the dorsal and least in the cingulate segment, where in fact the damage is only twice bilateral (and actually on both sides in each case involves only Area 32 and not Area 24).

Within the improved group a noteworthy feature is that on the whole the better improved have more posterior and fuller cuts. Another feature is that the four best improved have bilateral involvement of the ventral segment.

The cases in the unimproved group would indicate that bilateral superficial damage to the white matter (and cortex) of either Area 45 (Nos. 35, 46 and 87) or the insula (No. 47) is insufficient to cause more than transitory improvement in what are generally agreed to be favourable types of cases for leucotomy.

Two fully cured cases (Nos. 71 and 44) and two partially cured cases (Nos. 9 and 39) relapsed fully after an interval of over six months. In No. 71 the relapse was sudden and back to the pre-operative symptomatology. In the other three it was more gradual and to a worse symptomatic picture. No uninvolved

segment was common to all four.

2. Mixed, Mainly Paranoid, Psychoses with onset over the age of 35.  
(Table VIII)

No suggestive trend is discernible in the incidence of any of the clinical data of recognised prognostic value. The only anatomical differences of any note between the improved 6 and the unimproved 7 is the slightly higher average total number of segments involved and the appreciably higher frequency of bilateral involvement of the central segment in the former.

Within the improved group there is again, as in the Affectives, a tendency for the better improved to have more posterior and fuller cuts. Two of the three best improved cases have bilateral involvement of the ventral segment.

No. 26 in the unimproved group would seem to indicate that bilateral interruption of substantial numbers of fibres coursing through the external capsule is insufficient to cause more than transitory improvement in a prognostically favourable type of case.

Two fully cured cases (Nos. 64 and 14) and two partially cured cases (Nos. 75 and 90) relapsed fully after an interval of over four months. In all the relapse was fairly gradual. Nos. 64 and 75 resumed their pre-operative symptomatology, Nos. 14 and 90 became worse. No uninvolved segment is common to all four cases.

### 3. Schizophrenia with onset under the age of 35. (Table IX).

In this group there is a major clinical difference between the improved 7 and the unimproved 8, in that the latter contain wholly chronic and mostly deteriorated cases while the former contain only one such. This renders it of dubious value to observe that the improved cases have in general a more extensive isolation of prefrontal cortex when the plane of the cuts and their extent are considered together, or to note that of the individual segments the one with outstandingly higher frequency of bilateral involvement in the improved group is the dorsal segment. In the four cases with bilateral involvement of the cingulate segment the damage extended into Area 24 on each side in all except case No. 94.

Within the improved group the most striking feature is that the grading varies almost directly with the pre-operative duration of the illness and the age of the patient at its onset. A less conspicuous but possibly very important feature is that full "M" plane cuts are followed by only moderate improvement in cases of only moderate prognosis, whereas less complete even more anterior cuts are followed by full recovery in cases of the best prognosis.

Two fully recovered cases (Nos. 99 and 57) and four partially cured cases (Nos. 94, 98, 60 and 63) relapsed fully after an interval of from  $2\frac{1}{2}$  months to  $3\frac{1}{2}$  years. In Nos. 99 and 63 the relapse was sudden. In all six it took the form of return to

the pre-operative symptomatology. No particular segment was uninvolved in all six, and indeed no segment whatsoever was spared in Nos. 94 and 60.

### Discussion.

Although the difference is outstanding only in the Affective group, there is in each of the clinical groups an appreciably higher average total number of segments involved in the improved cases than in the unimproved ones. In the Affective and Mixed groups this principle likewise applies between the best improved and the less well improved cases, and in addition the best improved have on the average more posteriorly placed cuts. On the whole, in these two groups equally extensive cuts are associated with the greater improvement the more posterior\* their level. When it is recalled that most of the improved cases were of only moderate, or poor, prognostic potentiality, (the only cases with under 2 years duration of illness being among the schizophrenias), all these facts seem to point clearly to a general quantitative principle, namely that in poor clinical material improvement varies directly with the total amount of prefrontal cortex isolated from its long fibre connections. This would imply that many of these

Footnote. \*It should be borne in mind that, by the method of selection, practically all cases with bilateral involvement of premotor or posterior orbital cortex or the basal ganglia have been excluded from this study.



particular cases might have profited by more posterior, fuller cuts, and conversely that, in cases selected for their favourable prognosis, more rostral and more circumscribed lesions than any in the present series (except No. 99), may isolate just the optimum amount of cortex for maximum improvement.

At the same time the figures point to the fibres which run in the central segment as being those whose cutting matters most of all, at least in affective and mixed paranoid conditions. This is not surprising since, if as is generally believed the rationale of the operation is concerned with the cutting of the anterior thalamic radiation, it simply reflects the quantitative principle, for thalamic fibres to and from all other segments tend to collect in this central region. A more remarkable feature is that in cuts at the commonest plane found in the best improved five cases (Nos. 66, 71, 18, 99 and 57) in this series, namely plane M-A/M, this central segment must contain long fibres connecting with only rostrally situated areas of prefrontal cortex. This would tend to substantiate recent American clinical findings such as the preliminary report by Heath and Pool (1948) of substantial improvement in two psychotic cases after cortical resection limited to dorsal parts of areas 10, 46 and 9, and Freeman's (1948b) report of a high rate of favourable response in over a hundred cases after transorbital lobotomy which he considers isolates essentially these same

relatively small portions of cortex. Whether this simply means that in more suitable, especially earlier, cases than in the majority of the present series cutting off these polar regions represents the optimum quantity of isolation of prefrontal cortex, or whether a more specific "qualitative" factor comes in, remains as yet to be decided.

Heath and Pool and Freeman, as mentioned, attribute special therapeutic significance to particularly the dorsal aspect of the rostral region. The present analysis, of admittedly still limited material, would tend to put emphasis rather on its orbital aspect so far as Affective and Mixed Psychoses are concerned, for the five best improved such cases (Nos. 66, 71, 18, 10 and 65) for instance, have all bilateral involvement of the ventral segment. Nevertheless, within the present series there are several instances of considerable improvement where the bulk of the orbital white matter was completely spared, and Freeman and Watts (1947) described a case of involutional melancholia where spectacular improvement followed lesions which almost entirely spared the orbital regions.

The findings in the Schizophrenias of early onset are somewhat more in accord with the experience of the American workers, for here there is strongest correlation of improvement with involvement of the dorsal segment at a fairly rostral plane. Whether one is observing here the hint of a different selective, operative requirement in different extreme types of psychosis is extremely doubtful. It may well be a chance

finding within the present limited number of relevant cases. Analysis of larger numbers of circumscribed differently located cortical ablations or undercuttings in controlled series of cases could quickly resolve this most important practical question.

A further point of interest regarding specific locations is the negative one that finer anatomical analysis, not recorded in the tables, shows that in no instance within the whole series of 24 improved cases did the ventral lesion encroach upon "Area 13".

The few instances of bilateral involvement of Area 24 suggest that it is only this part of the cingulate segment which entirely fails to correlate with improvement. This again (c.f. Section IV) seems to disagree with Ward's (1948) suggestion that "some of the (beneficial) results of prefrontal leucotomy may be due to section of fibres leaving this area", but tallies with recent American experience (W. Freeman: personal communication) which tends to show that bilateral circumscribed ablation of area 24 has no ameliorative effect. Whether bilateral damage to area 24 militates against improvement and might explain the unusually poor response to full cuts in a strongly obsessional patient such as Case 60, must remain conjectural until more such material has been investigated.

The clinical factors which have been remarked upon, and others not recorded, no doubt play a large part in determining the improvement (or its absence) in this series and may be the most important determinants in a few of the cases. Unfortunately

so little detail is known of the premorbid personality in the majority of the cases that it is futile to search for any correlation with improvement. No valid comment based on this material can therefore be made on Stengel's (1948) impression that improvement depends materially on the maturity of the premorbid personality.

It is a striking fact that the anatomical correlates of clinical improvement in especially the Affectives are precisely the same as those arrived at for post-operative personality change in Section IV, except that the latter is perhaps related still more strongly to bilateral damage to the ventral segment. Hence one would expect, and there is, in this group a relatively high correlation of personality change with improvement. This of course does not necessarily imply that the personality change causes the improvement, although in fact, such a tentative conclusion was come to by Frankl and Mayer-Gross (1947) from clinical observations. Whether the positive correlation with involvement of the ventral segment is significantly higher for personality change than for improvement in affective conditions is too fine a point to be determined from the unsystematic clinical observations available in this series of cases. Close attention will continue to be paid to this important practical matter in further studies.

Such a case as No. 94 where, after practically complete bilateral isolation of the prefrontal regions of cortex from their long fibre connections (Fig. 18), all the pathological

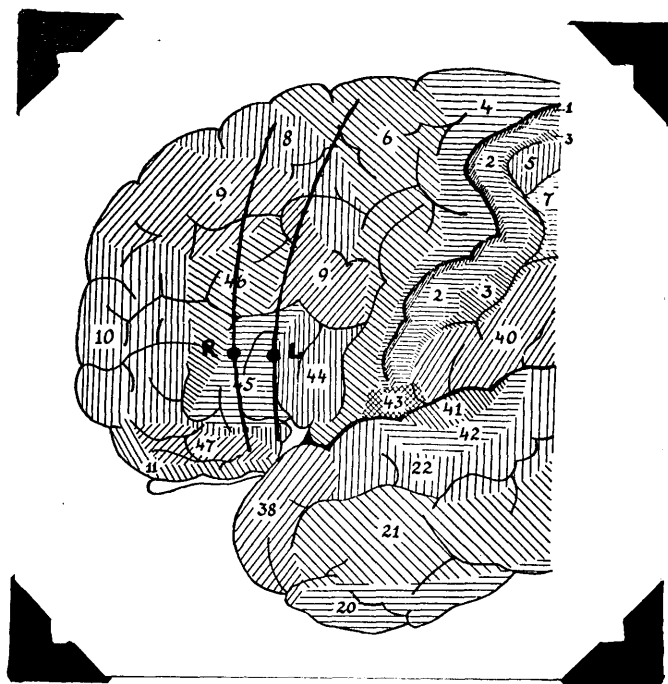


Fig. 18

symptoms disappeared for an appreciable period and then returned in identical form and intensity, is a particularly convincing instance of the non-permanency of improvement after leucotomy. Other cases, with from 6 to 8 of the possible 10 segments cut, show that depressive, maniacal, obsessional and catatonic symptoms may fare no better than delusions and hallucinations. All may actually become worse after relapse. This appears to be the first time that Relapse has been checked at post mortem against the amount of prefrontal cortex actually isolated. The findings seem to speak against any concept of selective localisation of the cuts for different types of symptom or psychosis (c.f. Dax and Radley-Smith, 1946; Carrillo, 1947). They would suggest that the quantitative principle of proportioning

the cuts in accordance with the severity of the illness may hold good because of some such general rationale as that temporary upset of homeostatic balance causes or permits modification of behaviour for the better, - if not quite "a new framework of personality in which the patient's mental life has to be reconstructed" (Mayer-Gross, 1948). If this is the correct interpretation of the facts it makes careful post-operative rehabilitation imperative, as stressed by Berliner and his associates (1945).

These instances of relapse do not necessarily refute Freeman and Watts' (1942) thesis that "without the frontal lobes there could be no functional psychoses", for firstly leucotomy is very different from lobectomy, and secondly as Cobb (1943) and Russell (1947) have emphasised, the essential importance of the prefrontal regions may be confined to the formative years. The alternative possibilities remain open either that the remainder of an adult brain can manifest all forms of psychotic symptomatology after the prefrontal "lobes" have been cut off, or that if the prefrontal cortex is left in situ the effective energy in due course finds its way back to it by pathways other than via the cells of the dorsomedial nucleus and their axons (or other long fibre systems). Follow-up study of the permanence of improvement in such cases as these treated by Peyton and his associates (1948) by bilateral lobectomy would settle this issue. Meantime the present findings must be taken into account in any hypothesis concerning

"compensatory capacity" of residual parts of the brain (c.f. Golla, 1943; Yahn, et al; 1948) or concerning the mechanism of functional psychoses.

#### SUMMARY.

(1) There is strong evidence that, in at least predominantly affective conditions, improvement varies, among cases of equally moderate or poor prognostic potentiality, directly with the amount of prefrontal cortex isolated from its white matter.

(2) There is no segment of white matter the bilateral involvement of which is indispensable to improvement, but the central segment comes near to being such a region. If the theory is correct that cutting of the thalamo-prefrontal fibres is the essential operative, this may simply be an expression of the foregoing quantitative principle, and would support recent evidence of good results in cases selected for their prognostic potentiality, after circumscribed ablation or (transorbital) leucotomy limited mainly to circumscribed rostral prefrontal regions.

(3) As far as selective localisation of lesions is concerned, the present analysis tends to point to greater importance of the orbital aspect than of the dorsal aspect of the rostral regions in at least affective and mixed psychoses. Any hint of a differential rationale should be tested at earliest by selective ablation or undercutting on carefully controlled series

of cases.

(4) There is no evidence that bilateral involvement of area 24 or of the agranular part of the posterior orbital region contributes to improvement: on the contrary it may militate against improvement.

(5) The anatomical correlates of post-operative personality change would appear to be roughly the same as those of post-operative improvement especially in affective psychoses, with perhaps some additional emphasis, in the former, on isolation of orbital cortex.

(6) Isolation of practically the whole of the prefrontal cortex in both hemispheres from its long fibre systems does not prevent fully recovered cases of any of the main types of functional psychosis, or psychotic symptom, from relapsing completely within a few months of the operation.

---

---



### GENERAL CONCLUSIONS.

The more particular conclusions, and those of more academic import, have been summarised at the end of each Section. The most general practical conclusions may be reviewed as follows:-

1. There is strong evidence that the amount of prefrontal cortex isolated should, for optimum improvement with minimum personality change, be varied according to the prognostic potentiality of the individual case, whatever its diagnostic type.

2. To minimise both direct and delayed post-operative deaths the substantial bilateral leucotomy cut required in cases of poor or moderate prognosis should be made under the fullest possible visual control.

3. In rostral circumscribed lesions for cases of good prognosis there is minimum risk of the haemorrhage and damage of extra-prefrontal structures responsible respectively for the bulk of direct and delayed post-operative deaths, so that the arguments for an open operation are not so strong; but the unavoidable inaccuracy of blind cuts precludes valid use of such cases for deduction of detailed clinico-anatomical principles without post-mortem follow-up.

4. There is little evidence to support any theory regarding the value of specific cuts for specific psychotic syndromes or symptoms.

5. Post-operative personality change and clinical improvement, in at least affective and mixed psychoses, display such similar anatomical correlates that with appropriate cuts the personality change is bound to be the greater the graver the illness.

6. Epilepsy may be a particularly high post-operative risk after rostral lesions, whereas Area 44 (the region of Broca's "speech centre") and the frontal eye field may apparently be damaged bilaterally with relative impunity in more posterior lesions.

7. All and any psychotic symptoms can recur after fairly lengthy disappearance following almost complete bilateral leucotomies. Adequate rehabilitation with periodic review may be the most reliable safeguard against such relapse.

These conclusions, though based on a still limited material and hence in many respects tentative, would seem to indicate something of the potential wealth of useful knowledge to be derived from more systematic pre-, trans- and post-operative observations on leucotomy cases than are as yet commonly made in this country. However that may be, these present studies have certainly been undertaken with conviction in such potentialities: a conviction based on premises which have been succinctly expressed in a recent Lancet Leader (1948) inspired by Fulton: "Further knowledge can be gained, and three developments are worth encouraging. Firstly, all frontal-lobe material should be

preserved for full histological and anatomical study post mortem. Secondly, pre- and post-operative study, especially of autonomic function, should be undertaken in every leucotomy case, however unpromising the material appears. And thirdly, we should try to replace blunderbuss leucotomy by a more accurate and limited cortical excision. There is no doubt that operations at present practised on the frontal lobe sometimes produce a profound change in personality, aside from their therapeutic effect, and we are scarcely measuring up to our responsibility unless we do everything we can to make our therapy benefit the patient without harming his personality." - or, it might have been added, "without prejudicing his expectation of life."

---

---

REFERENCES.

- ALEXANDER, G.L. (1943) J. Ment. Sci., 89, 187.
- BAILEY, P. and SWEET, W.H. (1940) J. Neurophysiol., 3, 276.
- BECK, E., "A Cytoarchitectural Investigation into the Boundaries of Cortical Areas 13 and 14 in the Human Brain", (J. Anat., Lond.: in press).
- BERGER, H. (1923) Arch. f. Psychiat., 69, 1.
- BERLINER, B., BEVERIDGE, R.L., MAYER-GROSS, W. and MOORE, J.N.P. (1945) Lancet, 2, 325.
- BOARD of CONTROL (1947) H.M. Stationery Office, London. "Pre-Frontal Leucotomy in 1000 Cases",
- CANNON, W.B. (1932) "The Wisdom of the Body", New York.
- CARRILLO, R. (1947) Arch. Sec. Sal. Pub., Argentina, 2, II.
- CLARK, W.E. Le Gros (1932) Brain, 55, 406.
- CLARK, W.E. Le Gros and BOGGON, R.H. (1933) J. Anat., Lond., 67, 215.
- CLARK, W.E. Le Gros and BOGGON, R.H. (1935) Phil. Trans. Roy. Soc., B. 224, 317.
- COBB, S. (1943) "Borderlands of Psychiatry", Harvard Univ. Press.
- CUMINGS, J.N. (1942) J. Neurol. Psychiat., 5, 40.
- DAX, E.C. and RADLEY-SMITH, E.J. (1943) J. Ment. Sci., 89, 182.
- DAX, E.C., REITMAN, F. and RADLEY-SMITH, E.J. (1948) Abstract in Digest Neurol. Psychiat., 16, 533.
- FLEMING, G.W.T.H. (1944) J. Ment. Sci., 90, 486.
- FRANKL, L. and MAYER-GROSS, W. (1947) Lancet, 2, 820.
- FREEDMAN, D.A., HEATH, R.G. and METTLER, F.A. (1947) Fed. Proc., 6, 126.
- FREEMAN, W. (1948a) Med. Ann. Dist. Columbia, 17, 257.
- FREEMAN, W. (1948b) Lancet, 2, 371.
- FREEMAN, W. and WATTS, J.W. (1942) "Psychosurgery", Baltimore.
- FREEMAN, W. and WATTS, J.W. (1947) J. Comp. Neurol., 86, 65.
- FREEMAN, W. and WATTS, J.W. (1948) Digest Neurol. Psychiat., 16, 62.

- FULTON, J.F. (1943) "Physiology of the Nervous System", Oxford Univ. Press.
- FULTON, J.F., LIVINGSTONE, R.B. and DAVIS, G.D. (1947a) Fed. Proc., 6, 108.
- FULTON, J.F., LIVINGSTONE, R.B. and DELGADO, J.M.R. (1947b) Fed. Proc., 6, 96.
- GOLLA, F.L. (1943) J. Ment. Sci., 89, 189.
- HEATH, R.G. and POOL, J.L. (1948) J. Nerv. Ment. Dis., 107, 411.
- HEBB, D.O. (1945) Arch. Neurol. Psychiat., Chicago, 54, 10.
- JOHNSON, H.C., WALKER, A.E., CASE, T.J. and KOLLROSS, J.J. (1946) Arch. Neurol. Psychiat., 56, 184.
- KENNARD, M.A. (1935) Arch. Neurol. Psychiat., 33, 537.
- KLEIST, K. (1934) "Handbuch der ärztlichen Erfahrungen im Weltkriege", Leipzig, 4.
- KLEIST, K. (1937) Zeitschr. ges. Neurol. Psychiat., 158, 159.
- KREMER, W.F. (1947) J. Neurophysiol., 10, 371.
- LANCET LEADER (1948) 1, 994.
- LYERLY, J.G. (1944) South Med. Surg., 106, 124.
- McCULLOCH, W.S. (1944) Physiol. Rev., 24, 390.
- MARIE, P. and FOIX, Ch. (1917) Rev. Neurol., 31, 53.
- MAYER-GROSS, W. (1948) Folia Psychiat., Neurol., Neurochir., Neerland, Congresnummer, p. 31.
- METTLER, F.A. (1945) J. Neuropath. & Exper. Neurol., 4, 99.
- METTLER, F.A. (1947) J. Comp. Neurol., 86, 119.
- MEYER, A. and BECK, E. (1945) J. Ment. Sci., 91, 411.
- MEYER, A., BECK, E. and McLARDY, T. (1947) Brain, 70, 18.
- MEYER, A. and McLARDY, T. (1947) Proc. Roy. Soc. Med., 90, 141.
- MEYER, A. and McLARDY, T. (1948) J. Ment. Sci., 94, 555.
- MEYER, A., McLARDY, T. and BECK, E. (1948) Folia Psychiat., Neurol., Neurochir., Neerland, Congresnummer, p. 45.

APPENDIX

TABLE VII

- PENNYBACKER, J. (1945) Proc. Roy. Soc. Med., 38, 431.
- PEYTON, W.T., NORAN, H.H. and MILLER, E.W. (1948) Amer. J. Psychiat., 104, 513.
- POPPEN, J.L. (1948) Digest Neurol. Psychiat., 17, 403.
- REITMAN, F. (1946) Amer. J. Psychiat., 103, 238.
- RICHTER, C.P. and HINES, M. (1938) Brain, 61, 1.
- ROSETT, J. (1933) Arch. Neurol. Psychiat., Chicago, 30, 1248.
- RUCH, T.C. and SHENKIN, H.A. (1943) J. Neurophysiol., 6, 349.
- RUSSELL, W.R. (1947) Brain, 70, 225.
- RUSSELL, W.R. (1948) Lancet, 1, 356.
- RYLANDER, G. (1939) Acta Psychiat. Neurol., Suppl. 20.
- SCHUSTER, P. (1902) "Psychische Störungen bei Hirntumoren,"  
Stuttgart.
- SMITH, W.K. (1938) J. Neurophysiol., 1, 55.
- SMITH, W.K. (1945) J. Neurophysiol., 8, 241.
- SPATZ, H. (1937) Zeitschr. ges. Neurol. Psychiat., 158, 208.
- SPIEGEL, A.E., WYCIS, H.T., MARKS, M. and LEE, A.J. (1947)  
Science, 106, 349.
- STENGEL, E. (1948) Lancet, 2, 257.
- TRUETA, J. et al (1946) Lancet, 2, 237.
- WARD, A.A. (1948) J. Neurophysiol., 11, 13.
- WALKER, A.E. (1938) "The Primate Thalamus", Chicago.
- WALKER, A.E. (1940) J. Comp. Neurol., 73, 59.
- WEISENBURG, T. and McBRIDE, K.E. (1935) "Aphasia", Oxford  
Univ. Press.
- WELT, L. (1887) Deut. Arch. f. Klin. Med., 42, 339.
- YAHN, M., PIMENTA, A.M. and SETTE, A. (1948) Abstract in  
Digest Neurol. Psychiat., 16, 618.
- ZIEGLER, L.H. and OSGOOD, C.W. (1945) Arch. Neurol. Psychiat.,  
53, 262.

Serial No.	Sex	Nature of Mental Illness	Pre-op. Duration of Illness yrs.	Previous Physical Therapy	Age at Opern.	Plane of Cut		Segments Involved						Post-operative Improvement	Post-operative Perslty. Chng. Yrs.	Survival Period Yrs.	Cause of Death		
						L	R	Dors. L	Mid. R	Vent. L	Core R	Cing. L	Cing. R						
66	F	Affective psychosis with depression, compulsive thoughts impulsive outbursts & many hysterical features.	2	none	25	M	M	+	+	+	+	+	+	-	-	Cheerful & free from mental symptoms throughout survival. Discharged to sanatorium after 6 weeks.	+	9 m.	Phthisis
71	M	Depression with delusions of poverty and ruin.	7	none	63	M	P	-	+	+	+	+	+	+	-	Discharged home cheerful & sl. overactive. Started new job. Sudden relapse during attack of carbuncles.	++	1 3/4	CO Suicide
18	M	Recurrent depression with hypochondriacal delusions & depersonalisation.	7	none	66	M	A/M	-	+	+	+	+	+	+	+	Became cheerful & lost anxiety about delusional ailments.	++	1 1/2	Coronary Thrombosis
10	F	Impulsive psychopathy with hysterical features including outbursts of rage.	4+	E.C.T. Cardz. Insul.	25	M	M	-	-	+	+	+	+	-	-	Milder, less frequent & shorter outbursts. Discharged home after 1yr.8m.	++	3	Septicaemia
44	F	Recurrent agitated depression with hypomanic swings.	3	Phren. E.C.T.	43	A	A	+	+	+	+	-	-	+	+	10 mths. normal mood, then relapsed & developed paranoid delus. & aud. hallus.	+	3 3/4	Phthisis
9	M	Depression with hypochondriacal delusions & depersonalisation.	4	none	37	M	M/P	+	-	+	+	-	-	+	-	6 m. disappearance of delns. & much diminished deprsn. then complete relapse with aud. hallucns.	+	1 3/4	Status Asthmaticus
39	M	Depression with hypochondriacal delusions & strong hysterical features.	3+	none	64	A/M	A/M	+	+	-	-	-	-	+	+	8 mths. less worried about delus., then relapse with progressive detertn.	+	1	Purulent Bronchitis
86	F	Manic-depressive with strong hysterical features & mild hypochondriasis.	16	E.C.T.	68	A/M	A/M	+	+	+	+	+	-	+	-	Evening out of mood swings & less tendency to worry.	++	11m.	? Uraemia
62	F	Agitated depression with deterioration.	3	none	67	A	A	-	+	+	+	+	+	-	-	Lost all resistiveness & agitation: slightly less depressed.	++	2 1/2	Carcinoma of Uterus
67	M	Agitated depression with paranoid delusions & auditory hallucinations during excited phases.	7	none	65	A/M	A/M	-	+	+	+	+	+	-	-	Less depressed: noisy outbursts greatly reduced in frequency & duration.	++	2	Carcinoma of Pancreas
78	F	Manic-depressive with mild paranoid ideas.	6	Insul.	35	P	M/P	+	-	+	+	-	-	+	-	More even in mood until death.	+	5 1/2 m.	Phthisis
35	F	Agitated depression with vague nihilistic & persecutory delusions.	2	E.C.T. Insul.	63	M	M	-	-	+	+	-	-	-	-	None	-	1	?
46	M	Recurrent depression with tense feelings of suppressed aggression.	3+	Cardz. E.C.T.	50	M	M	-	+	+	+	-	-	+	-	Normal mood for 3 weeks, then complete relapse.	-	9m.	CO Suicide
47	F	Recurrent depression with hypochondriacal features.	2+	E.C.T.	42	M/P	P	-	-	+	+	-	-	-	-	1 m. very cheerful, then relapsed rapidly & detertd. during termnl yr.	+	3 1/2	Carcinoma of Cervix
87	M	Agitated depression with delusions of unworthiness.	3	none	64	M	M	-	-	+	+	+	-	-	-	1 m. less depressed & agitated, then complete relapse.	-	1 1/2	Lung Abscess

TABLE VII : P R E D O M I N A N T L Y A F F E C T I V E C O N D I T I O N S.



**APPENDIX****TABLE VIII**

Serial No	Sex	Nature of Mental Illness	Pre-operative Duration of Illness yrs.	Previous Physical Therapy	Age at Operation	Plane of Cut		Segments Involved				Post-operative Improvement	Post-operative Personality Change	Survival Period yrs.	Cause of Death				
						L	R	Dors.		Mid.						Vent.		Core Cing.	
								L	R	L	R					L	R	L	R
65	M	Paranoid psychosis with visual & auditory hallucinations & outbursts of violence: no deterioration.	5	E.C.T.	56	P	P	+	+	+	+	-	-	More tractable & employed more usefully throughout survival. Hallucinations became inconspicuous. Granted parole.	++	3	Lobar Pneumonia		
37	F	Paranoid psychosis with aud. hallucs., grandiose delusions & violent outbursts: gross deterioration.	13	none	62	M	P	-	+	+	-	+	-	One year less aggressive. Lucid intervals (with E.C.T.) and cleaner until death.	-	4 $\frac{1}{4}$	Lobar Pneumonia		
64	F	Paranoid psychosis with outbursts of maniacal excitement: no deterioration.	3	Cardz.	44	A/M	M	+	-	+	+	+	-	Quiet & well-conducted with no evidence of delusions for 9 months, then complete relapse.	+	2	Chronic Nephritis		
14	M	Paranoid psychosis with visual & auditory hallucs. & manic-depressive swings: no deterioration.	9	E.C.T.	54	M	M/P	-	-	+	-	-	-	4 months normal mood & loss of hallucinations, then complete relapse with profound depression.	-	8m.	?		
75	F	Paranoid psychosis: negativistic, suspicious, autistic: no deterioration.	2	Insul.	39	A	A/M	+	-	+	-	-	+	2 months more sociable: 9 months less hostile, then relapsed into pre-operative state.	++	3	Phthisis		
90	M	Paranoid psychosis: no deterioration.	3 $\frac{1}{2}$	E.C.T. Insul.	37	M	M	-	-	-	+	+	-	Slightly less evidence of delusions of persecution for 2 years, then became worse, with aggressive outbursts & auditory hallucs.	-	4 $\frac{3}{4}$	Duodenal Ulcer		
20	F	Paranoid psychosis with some alternating stupor & excitement: no deterioration.	5	E.C.T.	47	A/M	A/M	+	-	+	-	+	-	Co-operative & brighter for 3 weeks, then gradually relapsed & deteriorated.	+	2 $\frac{1}{4}$	Lung Gangrene		
21	M	Paranoid psychosis with hallucinosis & manic-depressive features: no deterioration.	13	none	61	M	M	-	-	-	-	-	-	2 months slight improvement, then full relapse.	-	1 $\frac{3}{4}$	Cardio-vasc. Degeneration		
26	F	Paranoid psychosis with hallucs., & impulsive outbursts: no deterioration.	1	E.C.T.	44	P	P	-	-	-	-	-	-	6 weeks quiet & friendly, then complete relapse.	-	3 $\frac{3}{4}$	Pneumonia		
27	F	Paraphrenia (delusions of reference, aud. hallucs. violent outbursts & grandiose features: no deterioration).	2	none	54	P	P	+	+	+	-	+	-	4 months very slightly less aggressive, then relapsed & deteriorated.	-	3 $\frac{3}{4}$	Circ. Failure		
38	F	Paranoid psychosis with some alternating stupor & excitement: no deterioration.	10	none	68	P	M	-	-	+	+	-	-	None	+	1 $\frac{1}{2}$	?		
74	F	Paranoid psychosis with impulsive outbursts & manic depressive features: no deterioration.	4 $\frac{1}{2}$	none	54	A	A/M	-	-	+	+	+	-	1 month moderately well conducted, then relapsed & slowly deteriorated.	+	3 $\frac{1}{2}$	Carcinoma of Oesophagus		
95	M	Paranoid psychosis with auditory hallucs., hypochondr. delusions and depression.	2 $\frac{1}{2}$	Insul.	55	M	P	+	-	+	+	+	+	Loss of depression and hypochond. delus., but increase in audit. hallucs. and onset of delusions of identity.	++	1 $\frac{1}{4}$	Status Epilepticus		

TABLE VIII : MIXED, MAINLY PARANOID, PSYCHOSES WITH ONSET OVER 35 YEARS OF AGE.

Serial No.	Sex	Nature of Mental Illness	Pre-op. Duration of Illness yrs.	Previous Physical Therapy	Age at Operation		Plane of Cut		Post-operative Improvement								Post-operative Personality Change	Survival Period yrs.	Cause of Death
					L	R	Dors. L R	Mid. Vent. Core Cing.				+	-	+	-				
								L	R	L	R					L			
99 57	M	Paranoid schizoph. with delus. of effeminacy, feelings of inadequacy and intense agitation. Paranoid schizophrenia with hysterical features: no deterioration.	1	none Cardz.	23 23	M M	M M	+ +	+ +	- +	- +	- +	- +	- +	all symptoms Discharged 5 wks. after operatn. Absence of delus. of persecutn. while living & working away from home for 1 yr. Then almost complete relapse. More amenable, less disturbed by his delusions & occupied making toys throughout survival.	+ +	4 1/2 2 1/2	Suicide Hypoglycaemic Coma	
61	F	Paranoid schizophrenia: impulsive, unemployable: no deterioration.	7	Insul. E.C.T.	37	M	M	+ +	+ +	+ +	+ +	- -	- -	- -	4 1/2 mth. clear of delus., 6 mth. relapse, 9 mth. moderate recovery, then severe relapse until death 10 m. later. Discharged during remissions. Slightly less evidence of compulsive ideas for 4 months then complete relapse.	+ +	1 1/4	Sub. bacter. Endocarditis	
94	F	Paranoid schizophrenia with delusions of reference & auditory hallucinations: violent; hysterical element: no deterioration.	2 3/4	Narcos. Insul. E.C.T.	22	M/P	M	+ +	+ +	+ +	+ +	+ +	+ +	+ +	4 1/2 mth. clear of delus., 6 mth. relapse, 9 mth. moderate recovery, then severe relapse until death 10 m. later. Discharged during remissions. Slightly less evidence of compulsive ideas for 4 months then complete relapse.	+ +	2 1/2	Bronchopneu- monia	
60	F	Schizophrenia with delusions of sinfulness & prominent obsessional symptoms: slight deterioration.	4+	Insul. E.C.T.	24	M	M	+ +	+ +	+ +	+ +	+ +	+ +	+ +	2 1/2 mth. well behaved, showing sense of humour & occupied in handicrafts, then relapsed completely.	+ +	3 1/2	Electro- narcosis	
63	F	Catatonic schizophrenia with delusions of persecution & auditory hallucinations during excited periods: considerable deterioration.	20	none	47	A/M	M	+ +	+ +	+ +	+ +	- -	- -	- -	4 mth. quiescent, then onset of fits and complete relapse.	+ +	1 3/4	Chronic Phthisis	
98	M	Catatonic schizophrenia with rapidly alternating phases.	4+	none	23	P	P	+ +	+ +	- +	+ +	+ +	- -	- -	4 mth. quiescent, then onset of fits and complete relapse.	+ +	1	?	
5	M	Catatonic schizophrenia with grandiose & persecutory delus. & aud. hallus. during excited phases: deteriorated.	20	none	43	A	A	+ +	+ +	+ +	+ +	+ +	+ +	+ +	None.	+ +	1 1/2	Status Epilepticus	
12	M	Catatonic schizophrenia with grandiose delus. & aud. hallus. during excitement: severely deteriorated.	12	Cardz.	32	A	A	+ +	+ +	+ +	+ +	+ +	+ +	+ +	None	+ +	2	Phthisis	
19	M	Catatonic schizophrenia with many delusions & auditory hallucinations: deteriorated.	21	none	51	M	M	- -	- -	- -	- -	- -	- -	- -	None	+ +	6m.	? Uraemia	
31	M	Paranoid schizophrenia with aud. hallus.: autistic, mildly depressed: no detertn.	25	none	50	P	P	- -	- -	- -	- -	- -	- -	- -	More reserved and shy than ever.	- -	1 1/4	Myocard. Degeneratio	
36	F	Schizophrenia with violent outbursts: severely deterioratd.	3+	?	35	M/P	P	- -	- -	- -	- -	- -	- -	- -	None	- -	2	?	
69	F	Schizophrenia with delus. of reference, auditory hallus. & catatonic features: severely deteriorated.	11	none	37	M	M	+ -	+ -	+ -	+ -	- -	- -	- -	None	+ +	2	Phthisis	
81	F	Hebephrenic schizophrenia: inaccessible for last 3 years: deteriorated.	18	none	47	P	M/P	+ -	+ -	+ -	+ -	- -	- -	- -	None.	++ ++	1 1/2	Myocard. Degenerati	
85	F	Hebephrenic schizophrenia: no deterioration.	9	E.C.T.	30	M	A	- -	- -	- -	- -	- -	- -	- -	None	- -	1 1/4	Second Leucotomy	

TABLE IX : SCHIZOPHRENIA WITH ONSET UNDER 35 YEARS OF AGE.