CLINICO-ANATOMICAL STUDIES OF FRONTAL LOBE FUNCTION BASED ON LEUCOTOMY MATERIAL.*

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THE present paper is based upon the investigation of 95 brains of patients dying some time after leucotomy, and mainly, though not exclusively, upon the 45 cases in which the survival period was more than 5 months (up to 5 years). In a third of the total material and in about half of the 45 cases with survival longer than 5 months a full microscopical investigation has been carried out or is nearing completion. Eventually all the informative cases will have been so examined, but investigation by serial sections of considerable parts of the brain is a time-consuming undertaking. An unfortunately irremediable defect in our material is the unevenness and incompleteness of the clinical, physiological and psychological investigations of the patients. Obviously only limited correlation studies can be carried out on such material. Again, the number of fully recovered cases in our material is small, in fact only some four (Nos. 66, 71, 10 and 18) of the total could be classed as such. The reason for this is that fully recovered patients are likely to die from intercurrent disease outside mental hospitals, when it is difficult to procure a post-mortem.

The frontal cortex is customarily subdivided into a granular and an agranular portion. The main agranular cortex, called areas 6 and 4 by Brodmann (Fig. 5), constitutes the premotor and motor regions, which do not concern us directly in this paper. We are concerned with the prefrontal region or frontal association area, which has been subdivided by Brodmann into areas 8, 9, 10, 11, 12, 45, 46 and 47. All these are granular except perhaps part of 8 and of the posterior third of the ventral (orbital) surface, which are agranular. Walker (1940) has recently differentiated posterior parts from the rest of the orbital region in monkeys as areas 13 and 14, and the human homologues of these areas have been defined by Beck (unpublished), working in this laboratory. Fig. 1 has been kindly supplied by Mrs. Beck to illustrate the position of these areas in the human brain. These two regions are important because, as has been shown recently, they are concerned with autonomic function, and bilateral ablation of area 13 leads in monkeys to severe restlessness. Autonomic control seems also to be exercised by the anterior cingular region (area 24), which, though not part of the prefrontal region, may be involved in the usual cut. In front of it on the medial surface is area 32, which is part of the cingular belt, and apparently a nodal point of considerable physiological activity between cortex and subcortical basal ganglia.

The prefrontal region has many connections with other parts of the brain, and much of the work in our department is concerned with investigation into

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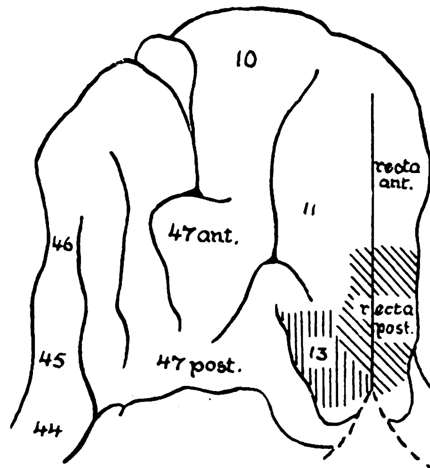

FIG. 1.—Position of Walker's area 13 in the human brain. Topographically area recta posterior roughly corresponds to area 14, but it is cytoarchitecturally not homologous.

their still very considerable obscurities. Such purely anatomical matters will not be dealt with here except to stress the important connection of the frontal lobe, firstly, with the thalamus, which relays most sensory impulses coming from the periphery, and secondly, through the thalamus, with the hypothalamus, which is known to be an important control station of metabolism and, in particular, of autonomic function (Fig. 2). It has actually been suggested recently

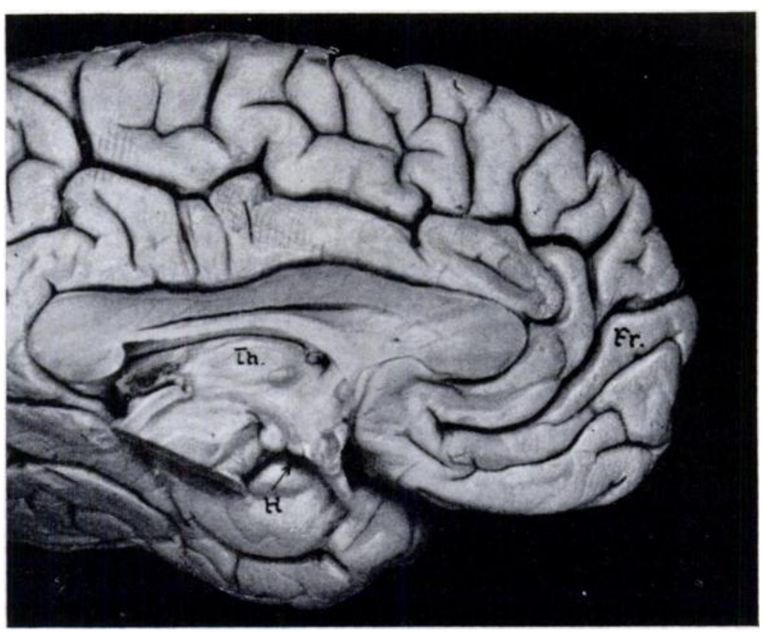

FIG. 2.—Medial aspect of a left hemisphere demonstrating the relationship of frontal lobe (*Fr.*) to thalamus (*Th.*) and hypothalamus (indicated by arrow from *H.*).

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(Le Gros Clark, 1948) that the prefrontal region is in essence the projection area of the hypothalamus. The thalamic projection to the prefrontal region arises in the dorsomedial nucleus ; that to the anterior cingular region in the anterior nucleus. If the fibres of these projection systems are cut, retrograde degeneration ensues in these thalamic nuclei, and it is possible to infer from the location of the degeneration which parts of the frontal cortex have been cut off. Fig. 3, in which Brodmann's figures have been inserted in diagrams of the dorsomedial nucleus and the anterior nucleus of the thalamus, shows a rough scheme of the " point to point " projections arising from these nuclei. This diagram

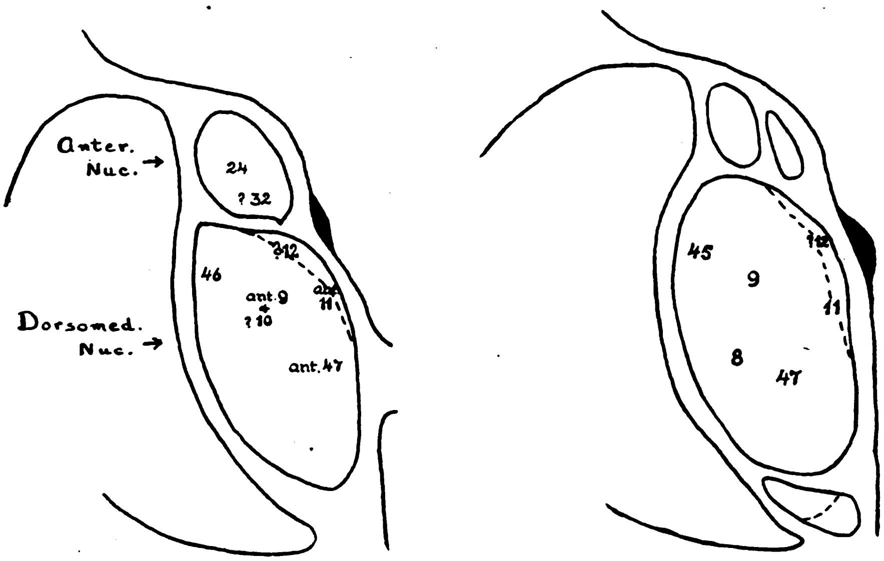

FIG. 3.—The numerals indicate the Brodmann areas of cortex to which the nerve cells in the various parts of the dorso-medial and anterior nuclei of the thalamus project.

is an elaboration of a similar one contained in a previous paper (Meyer, McLardy and Beck, 1948). It is based now on the study of 30 hemispheres, and will be published elsewhere in greater detail. It is provisionally included in this paper in order to demonstrate how a histological investigation of the thalamus can add considerably to the accuracy of estimation of the frontal lobe damage.

The variability of the leucotomy cuts, which was first demonstrated in 1945 (Meyer and Beck), is still an impressive finding in cases operated upon in 1946 and 1947 (Fig. 4). After making due allowance for the unrepresentative nature of our material, for differences of technique used by different neurosurgeons and, in a very few instances, for deliberate intention, it is difficult to escape from the conclusion that, to a large extent, this variability is a consequence of the blind operation based on superficial skull bearings only. The inaccuracy in placing the cut has led to modifications of the surgical technique and, particularly in the U.S.A., to an increasing use of open operations introduced under various names, such as topectomy, gyrectomy and areactomy, all designed to ablate circumscribed cortical areas.

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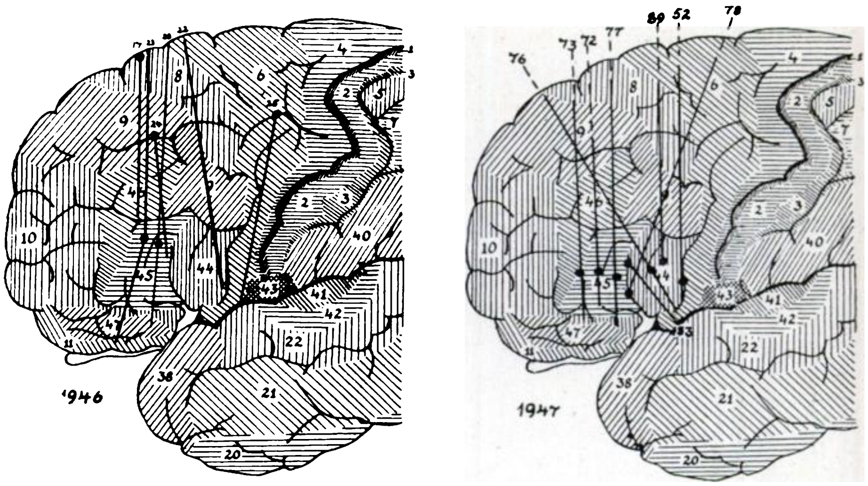

FIG. 4.—Illustrating largely unintentional variability in plane and direction of cuts.

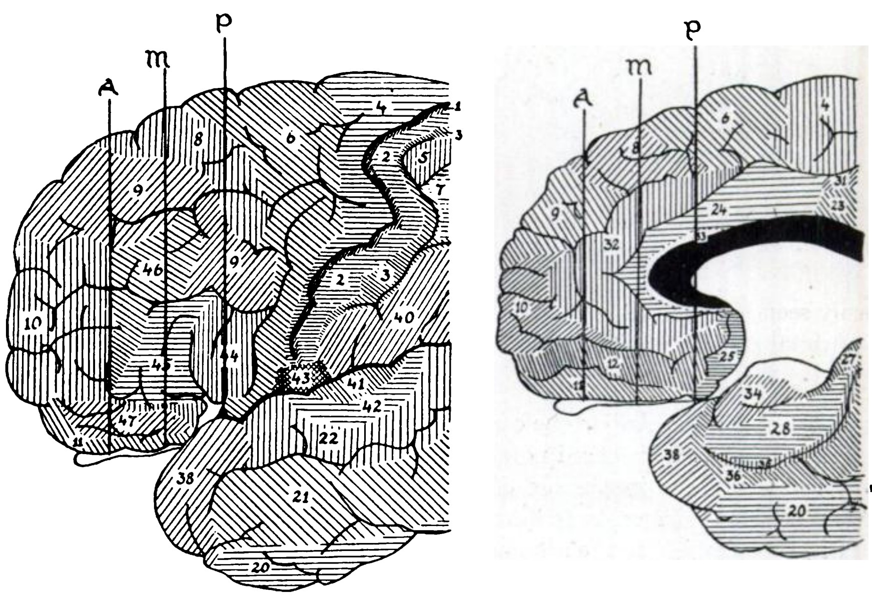

FIG. 5.—Demonstrating the position of Anterior (*A.*), Middle (*M.*) and posterior (*P.*) planes of the cut in relation to Brodmann's cortical areas.

For purposes of classification our cases have been divided into those with cuts in anterior, middle and posterior planes (Fig. 5). In addition to the wide variation in the antero-posterior position, there are also very considerable differences in the extent of the cut in the transverse plane. We have therefore divided the coronal surface for purposes of analysis into five segments : Dorsal, middle, ventral or orbital, medial or cingulate, and central (Fig. 6). Figs. 7, 8 and 9 illustrate such differences in the cut in actual cases.

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The variety of the cuts in such leucotomy material gives an opportunity of studying the clinical and anatomical effects of very different frontal lesions indeed. Thus, clinico-pathological correlations can be derived which, in a steadily growing series of cases such as ours, are bound in time to yield results of considerable importance. In an earlier paper the present authors (Meyer and McLardy, 1948) compared the clinical symptomatology in a group of cases in which the surgical lesions were confined to the prefrontal region (i.e. our A and M planes) with another group with bilateral posterior cuts. Tables I and II represent an amplification and modification of the previously published tables. In each of the tables are listed *inter alia* the cause of death (whether intercurrent or otherwise), the survival time and some gross undesirable symptoms, such as restlessness, vasomotor and trophic lesions, persisting incontinence of urine, nutritional deficiency and respiratory disturbance. It is

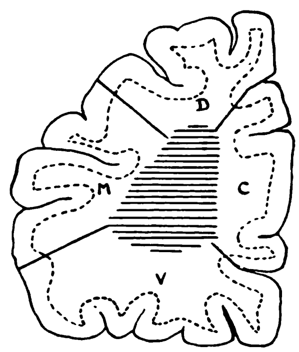

FIG. 6.—*D* = dorsal segment; *M.* = middle segment; *V.* = ventral segment; *C.* = cingulate segment; shaded area = central segment.

easily seen how few of these undesirable symptoms occur in cases with strictly prefrontal cuts, as compared with those with bilateral posterior cuts. Moreover, the survival time of the patients with posterior cuts is on the average less than half of that of those with prefrontal cuts. Again, most of the patients with posterior cuts die from delayed effects of the operation rather than from intercurrent disease, which is the usual cause of death in the prefrontal group. There is probably a multiplicity of reasons why patients with cuts in the posterior plane should do badly. It will be remembered for instance that such cuts may involve the posterior orbital region, the cingular region and the premotor area—all regions known to be concerned with the control of autonomic function. In addition, the anterior portion of the corpus striatum is liable to be involved, and it is known from animal experiments (Heath, Freedman and Mettler, 1947) that bilateral operations on the basal ganglia are dangerous to life.

The last column of Tables I and II contains data relating to personality change. From the available notes it is not always easy to assess at all accurately the degree and quality of the personality change in these psychotic patients, none of whom was personally known to the authors; hence the considerable number of question marks. Notwithstanding this, there is ample evidence

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TABLE I.—*Purely Prefrontal Cuts.*

Serial number.	Regions involved. Posterior orbital. L.	Posterior orbital. R.	Striatum. L.	Striatum. R.	Dorsal premotor area. L.	Dorsal premotor area. R.	Ext. caps. and/or insula. L.	Ext. caps. and/or insula. R.	Anterior cingulate. L.	Anterior cingulate. R.	Anterior orbital. L.	Anterior orbital. R.	Clinical sequelae. General restlessness.	Vasomotor and/or trophic.	Persistent incontinence	Miscellaneous	Survival period.	Intercurrent cause of death.	Post-operative personality change.
5	—	—	—	—	—	—	—	—	+	+	+	+	—	—	—	E	1½ yr.	—	+
9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1¾ ,,	+	+
12	—	—	—	—	—	—	—	—	+	+	+	—	—	—	+	E	2 ,,	+	+
14	—	—	—	—	—	—	—	—	—	—	—	+	—	—	—	—	8 mth.	—	?
18	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—	1¼ yr.	+	++
19	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—	6 mth.	+	+
26	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	E	3¾ yr.	+	?
31	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1¼ ,,	+	?
34	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—	2 ,,	—	?
35	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1 ,,	—	?
39	—	—	—	—	—	—	—	—	—	+	—	—	—	—	—	—	1 ,,	+	+
44	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	3¾ ,,	+	+
46	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	9 mth.	+	?
62	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—	2¼ yr.	+	++
63	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—	1¾ ..	+	+
66	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	R	9 mth.	+	?
67	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—	2 yr..	+	++
74	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	N	3½ ,,	+	+
75	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—	E	3 ,,	+	++
80	—	—	—	—	—	—	—	—	—	—	—	+	—	—	—	—	1¼ ,,	+	+
85	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1¼ ,,	+	?
90	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	E	4¾ ,,	+	?
													Total 8 items.				Average 2 yr.		Total 17+

E = Epilepsy; R = respiratory inhibition; N = nutritional deficiency.

TABLE II.—*Bilateral Posterior Cuts.*

Serial number.	Regions involved. Posterior orbital. L.	Posterior orbital. R.	Striatum. L.	Striatum. R.	Dorsal premotor area. L.	Dorsal premotor area. R.	Ext. caps. and/or insula. L.	Ext. caps. and/or insula. R.	Anterior cingulate. L.	Anterior cingulate. R.	Anterior orbital. L.	Anterior orbital. R.	Clinical sequelae. General restlessness.	Vasomotor and/or trophic.	Persistent incontinence.	Miscellaneous.	Survival period.	Intercurrent cause of death.	Post-operative personality change.
3	+	+	+	+	—	—	—	—	—	—	—	—	—	—	+	N/U	2 mth.	—	+
11	+	+	+	+	—	—	—	—	—	—	+	—	—	—	+	—	5 ,,	—	++
16	+	+	+	+	—	—	—	—	—	—	—	—	—	—	—	—	7 wk.	—	+
29	+	+	+	+	—	—	—	—	—	—	—	—	—	—	—	H	9 dy.	—	..
32	+	+	+	+	+	+	+	+	—	—	—	—	—	—	—	N	7 wk.	—	+
52	+	+	+	+	+	+	+	—	—	—	—	—	+	—	—	—	20 dy.	—	+
56	+	+	+	+	+	+	+	+	+	+	—	—	—	+	+	—	9 mth.	—	+
68	+	+	+	+	—	—	—	—	—	—	—	—	—	—	—	U	21 dy.	—	+
10	+	+	—	—	—	—	—	—	—	—	—	—	—	+	—	N	3 yr.	—	++
33	+	+	+	—	—	—	—	—	—	—	—	—	+	+	+	—	10 wk.	—	++
38	+	+	—	—	—	—	—	—	—	—	+	+	+	—	+	—	1½ yr.	—	+
41	+	+	—	—	—	—	—	—	—	—	—	—	—	—	—	H	6 dy.	—	..
49	+	+	+	—	—	—	—	—	+	—	—	+	+	—	—	H	24 ,,	—	+
59	+	+	—	—	—	—	—	—	+	+	—	—	—	—	—	R	4 hr.	—	..
65	+	+	—	—	+	+	+	+	—	—	—	—	—	—	—	(R)	3 yr.	+	++
69	+	+	—	—	—	—	—	—	—	—	—	—	+	—	—	—	2 ,,	+	++
4	—	—	+	+	+	+	+	+	+	+	—	—	+	+	+	U/N	4 mth.	—	++
20	—	—	+	+	—	—	—	—	+	—	—	—	—	+	+	—	2¼ yr.	+	+
22	+	—	+	+	+	+	+	+	—	+	—	—	—	+	—	—	9 wk.	—	+
27	+	—	+	+	—	—	+	+	+	—	—	—	—	—	—	—	3¾ yr.	+	?
58	—	—	+	+	—	—	+	—	—	—	—	—	+	—	—	U	7 dy.	—	..
87	+	—	+	+	—	—	—	—	—	—	—	—	—	—	—	—	1½ yr.	+	?
89	—	—	+	+	—	—	+	+	—	—	—	—	—	+	—	—	3½ mth.	—	+
88	—	—	—	—	+	+	—	—	+	—	—	+	—	+	+	—	8 wk.	—	?
													Total 36 items.				Average 10 mth.		Total 23+

N = Nutritional deficiency; U = uraemia; H = hyperthermia; R = respiratory inhibition.

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that personality change, of both the euphoric and the apathetic type, does occur in cases with prefrontal lesions only. Recently Hebb (1945) has submitted the evidence for the existence of a frontal lobe deficit syndrome to severe criticism. This evidence is mainly based upon experience with tumours, head injuries, certain presenile degenerations and frontal lobe extirpations in man and animals. According to Hebb, in none of these conditions can the possibilities be excluded that either the lesions themselves extended beyond the frontal association area, or that the effects were caused by the irritation of actively growing tumour or progressive atrophy or haemorrhagic cysts and scars which causes the behavioural change rather than the loss of normal frontal tissue. Hebb extends his criticism also 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

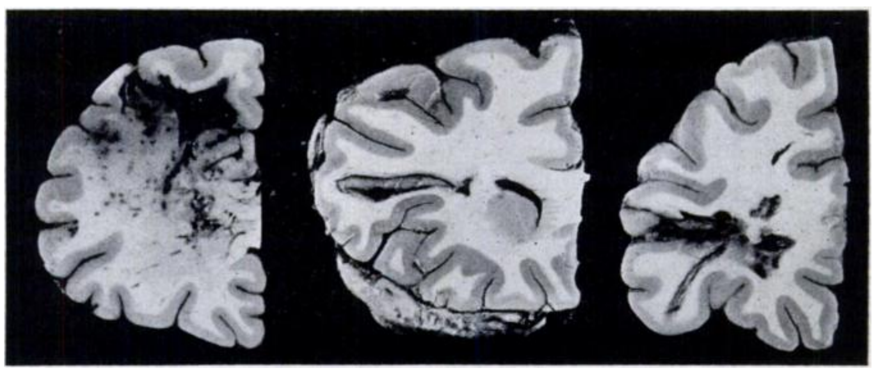

FIG. 7.—Different cases demonstrating cuts predominantly in (*a*) the dorsal, (*b*) the middle and (*c*) the ventral segment.

be denied that in leucotomy cases with short survival this point is of considerable importance. For instance, the group with posterior cuts collected in Table II contains a considerable number of cases with short survival, such as represented in Fig. 8, where this may well be one explanation for the severity of the personality change. On the other hand, the example illustrated in Fig. 9 demonstrates the usual appearance in cases with longer survival, the surgical lesion being relatively limited and macroscopically (and also histologically) inactive. It is difficult to believe that such pathological lesions cause much irritation over wide distances.

In view of Hebb's criticisms cases with survival of less than five months have been excluded in Tables III and IV, in which the remainder have been graded roughly according to severity of personality change indicated in terms of plus or minus. For each case there has been plotted the dimensions of the surgical cuts as defined by their mean plane in the antero-posterior direction and the segments involved in the transverse direction. All cases in Table III showed definite personality change, whilst in the cases collected in Table IV down to the dividing line the personality change was either questionable or

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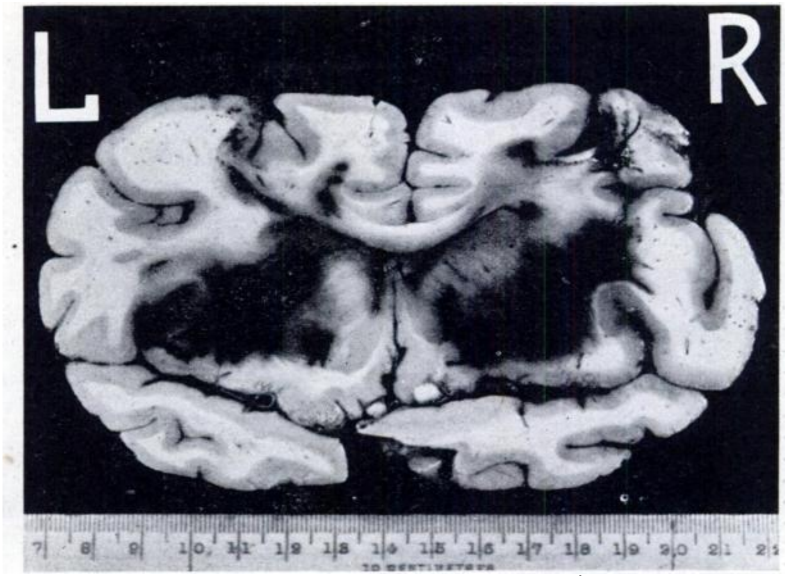

FIG. 8.—Fresh bilateral posterior cuts with haemorrhagic lesions involving the basal ganglia.

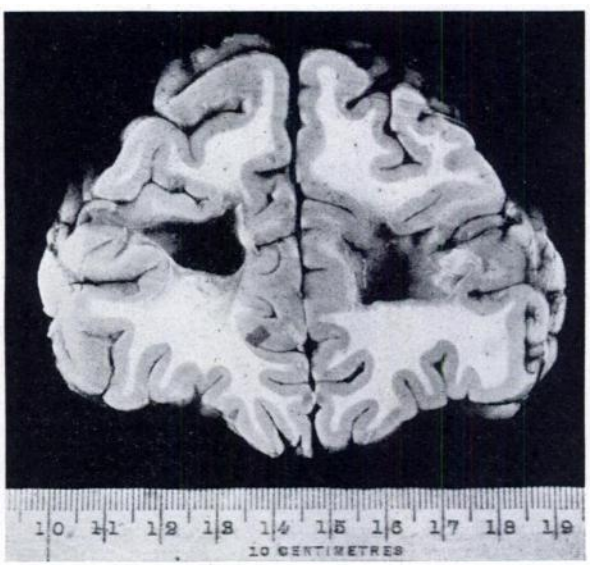

FIG. 9.—Old circumscribed bilateral leucotomy lesions in a fairly anterior plane and practically confined to the central white matter.

negative. There is a striking difference in the number of segments involved between the cases with positive personality change on the one hand and those with negative or questionable change on the other. The average in the former is 7·2 segments in the more severe group and 5·5 in the less severe. In the latter

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it is 3·4. The average plane of the cuts is not appreciably different in the two groups. In view especially of the unevenness of the clinical data no close parallelism between degree of personality change and extent of damage in

TABLE III.—*Correlation of the Severity of Personality Change with the Extent of Prefrontal Damage; Cases with ++ and + Degree of Personality Change.*

Serial number.	Post-operative personality change.	Plane of cut. L.	Plane of cut. R.	Segments involved. Dorsal. L.	Dorsal. R.	Middle. L.	Middle. R.	Ventral. L.	Ventral. R.	Central. L.	Central. R.	Cingulate. L.	Cingulate. R.	Total segments.	
10	+ +	M	M	—	—	+	+	+	+	+	+	—	—	6	
18	+ +	M	A/M	—	+	+	+	+	+	+	+	+	+	9	
57	+ +	M	M	+	—	+	+	+	+	+	+	+	—	8	
62	+ +	A	A	—	+	+	+	+	+	+	+	—	—	7	Average
65	+ +	P	P	+	+	+	+	+	+	+	+	—	—	8	7·2
67	+ +	A/M	A/M	—	+	+	+	+	+	+	+	—	—	7	segments.
69	+ +	M	M	+	—	+	+	+	+	+	+	—	—	7	M plane.
71	+ +	M	P	—	+	+	+	+	+	+	+	+	—	8	
75	+ +	A	A/M	+	—	+	+	+	—	+	—	—	+	6	
81	+ +	P	M/P	+	—	+	+	—	+	+	+	—	—	6	
86	+ +	A/M	A/M	+	+	+	+	+	—	+	+	—	—	7	
9	+	M	M/P	+	—	+	+	—	—	+	—	—	—	4	
19	+	M	M	—	—	+	+	+	+	+	+	—	—	6	Average
20	+	A/M	A/M	—	+	+	+	—	—	+	—	+	—	5	5·5
38	+	P	M	—	—	+	—	+	+	—	—	—	—	3	segments.
39	+	A/M	A/M	+	+	—	—	—	—	+	+	—	+	5	Plane sl.
47	+	M/P	P	—	—	+	+	—	—	—	—	—	—	2	posterior
60	+	M	M	+	+	+	+	+	+	+	+	+	+	10	to M.
61	+	M	M	+	+	+	+	+	+	+	+	—	—	8	
78	+	P	M/P	+	—	+	+	—	—	+	+	—	—	5	
80	+	M	M	+	+	+	+	—	+	+	+	—	—	7	

TABLE IV.—*Correlation of the Severity of Personality Change with the Extent of Prefrontal Damage; Cases with No and ? Personality Change (above) and Seven Paradoxical Cases (below).*

Serial number.	Post-operative personality change.	Plane of cut. L.	Plane of cut. R.	Segments involved. Dorsal. L.	Dorsal. R.	Middle. L.	Middle. R.	Ventral. L.	Ventral. R.	Central. L.	Central. R.	Cingulate. L.	Cingulate. R.	Total segments.	
8	?	P	P	—	—	—	—	—	—	—	—	—	—	0	
14	?	M	M/P	—	—	+	+	—	+	—	—	—	—	3	
21	?	M	M	—	—	+	+	—	—	—	—	—	—	2	
26	?	P	P	—	—	+	+	—	—	—	—	—	—	2	Average
27	?	P	P	+	+	+	+	+	—	+	—	+	—	7	3·4
31	—	P	P	—	—	+	+	—	—	+	+	—	—	4	segments.
35	—	M	M	—	—	+	+	—	—	—	—	—	—	2	Plane
36	?	M/P	P	—	—	+	+	—	—	—	—	—	—	2	halfway
37	?	M	P	—	+	+	+	—	+	—	+	—	+	6	between
46	?	M	M	—	+	+	+	—	—	+	—	—	—	4	M and
66	?	M	M	+	+	+	+	+	+	+	+	—	—	8	M/P.
85	?	M	A	—	—	+	+	—	—	—	—	—	—	2	
87	?	M	M	—	—	+	+	+	—	—	—	—	—	3	
90	—	M	M	—	—	—	+	—	—	+	+	—	—	3	
5	?	A	A	+	+	+	+	+	+	+	+	+	+	10	Average 8·3
12	?	A	A	+	+	+	+	+	—	+	+	+	+	9	segments.
44	?	A	A	+	+	+	+	—	—	+	+	—	+	7	Plane
74	?	A	A/M	—	—	+	+	+	+	+	+	—	—	6	halfway
63	?	A/M	M	+	+	+	+	+	+	+	+	—	—	8	between
64	?	A/M	M	+	—	+	+	+	+	+	+	+	—	8	A and
94	?	M/P	M	+	+	+	+	+	+	+	+	+	+	10	A/M.

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TABLE V.—*Personality Change Correlated with Improvement and Extent of Prefrontal Damage in Different Clinical Types of Cases.*

	Average age at onset (yrs.).	Average pre-operative duration (yrs.).	Average plane of cuts.	Average total number of segments involved (out of possible 10).	Percent. bilateral dorsal segment.	Percent. bilateral middle segment.	Percent. bilateral ventral segment.	Percent. bilateral central segment	Percent. bilateral cingulate segment.	Average personality change.
1. *Predominantly affective conditions.*										
A. *Improved* (11 cases)	45	5½+	A/M–M	6·7	36%	91%	55%	91%	18%	1·5+
B. *Unimproved* (4 cases)	52½	2½+	M	2·8	0%	100%	0%	0%	0%	0·3+
2. *Mixed, mainly paranoid, psychoses.*										
A. *Improved* (6 cases)	43	6	M	5·7	17%	83%	33%	50%	0%	0·8+
B. *Unimproved* (6 cases)	49	6	M	4·2	17%	83%	33%	17%	0%	0·5+
3. *Schizophrenias.*										
A. *Improved* (5 cases) (1 chronic, deteriorated)	–23½	7+	M	8·8	80%	100%	100%	100%	40%	1·2+
B. *Unimproved* (8 cases) (All chronic, 6 deteriorated)	–28	15+	M	5·8	25%	100%	38%	75%	25%	0·8+

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individual cases can be expected. At the bottom of Table IV seven cases have been collected which show the apparent paradox of a doubtful personality change with a high number of segments involved. However, in four of these cases the plane of the cut was very anterior, while in the remainder the pre- and post-operative symptomatology of the psychosis was such as to preclude any accurate estimate of the personality change. It is therefore fair that these seven should not be included in the general tables.

Closer analysis of the individual segments shows only the middle segment equally involved in each group. This is not surprising, as the leucotome usually enters the brain in this sector. All the other segments show an increased involvement between the group with negative and the group with positive personality change, but interestingly this is much more marked in the central and ventral segments than in the dorsal and cingulate segments. For the central and ventral segments this parallelism is apparent also between the group with "+" and the group with "++" personality change.

The central segment collects most fibres converging from the prefrontal cortex to form the anterior thalamic radiation. Its prominence in this analysis is, therefore, considering the role which the thalamic connections are believed to play in the rationale of personality change, not surprising, and could be expressed as based upon a quantitative principle. Since, however, the more anterior the plane of the cut the progressively higher a proportion of fibres of the central segment connect with cortex near the pole—i.e. with areas 10, 46 and anterior 9, 11, 12 and 47 in the commonest cut (through area 45) in this series—it follows that these rostral areas are also concerned in the causation of personality change. This is worth noting in view of recent reports (Heath and Pool, 1948 ; Freeman 1948) which deny an appreciable degree of personality change after ablation or isolation of these rostral areas. The explanation for this discrepancy may be, firstly, that involvement of rostral parts alone causes an amount of personality change of no appreciable practical importance or, secondly, that the cortical ablation and transorbital leucotomy are confined largely to dorsal parts, whereas from our analysis the orbital aspect may have greater importance for personality change than the dorsal aspect.

The history of the frontal lobe syndrome shows that damage to the orbital region has for long been regarded as a particularly frequent cause of personality change, especially of the euphoric type associated with " Witzelsucht " (Welt, 1887 ; Schuster, 1902 ; Berger, 1923 ; Kleist, 1934, 1937 ; Spatz, 1937 ; Rylander, 1939 ; Reitman, 1946 ; and others). Kleist and, more recently, Freeman and Watts (1948), and Dax, Reitman and Radley-Smith (1948), have, in addition, associated damage to dorsal parts of the prefrontal region with the akinetic type of personality change. Our analysis so far supports neither of these contentions in their exclusiveness of location and of type 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, although several cases with the apathetic (akinetic) type of personality change had bilateral dorsal cuts, many others with such a personality change had no involvement whatever of the dorsal segments. In other words, as in our earlier reports (Meyer and McLardy, 1947 ; Meyer, McLardy and Beck, 1948), we still fail to confirm the existence of atomistic localization of mental faculties within the frontal lobe suggested by Kleist (1934, 1937), even in its simplified form as expressed by Freeman and Watts (1948) and Dax, Reitman and Radley-Smith (1948).

An additional point in this connection which can be deduced from our material is that any importance of the orbital region in the causation of personality change is certainly not confined to its posterior agranular part (containing area 13), which is particularly concerned with autonomic function.

The absence of frequent involvement of the anterior cingulate region in Table III, especially the " ++ " group, is of considerable interest. It does not bear out the views of Ward (1948), who suspected area 24 to be concerned with the mechanism of fear, and therefore recommended its physiological investigation in psychiatric patients. Recent American experience with focal ablation of the cingulate gyrus (Freeman—personal communication) apparently likewise does not support Ward's view. It should be emphasized that detailed analysis of our 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.

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 (Mettler, 1947; Ritchie Russell, 1948; Reitman, 1946) take a less exclusive view. Preliminary reports on thalamotomy, recently introduced by Spiegel and his associates (1947), indicate that bilateral lesions in the dorsomedial nucleus have a marked influence upon personality and improvement, a result which would favour the view that the mechanism of the personality change depends very largely upon the thalamo-prefrontal projection. Cases in our material in which the cuts were behind the frontal lobes confirm this observation. For instance, Fig. 10 demonstrates 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 considerable personality change and improvement of the patient's agitated depression. This supplies another explanation of why posterior cuts sometimes cause very severe personality change, the whole of the thalamo-prefrontal projection being easily severed at this level by a circumscribed cut.

The problem of improvement will not be touched upon at length in this paper, which does not deal with therapeutic aspects. The anatomical correlates of improvement will be the subject of a separate paper by the present writers. Since, however, improvement has recently been linked by Frankl and Mayer-Gross (1947) with the personality change, it is relevant to note that the existence of some such association is borne out in our analysis. In Table V the cases with over five months' survival are presented under the three headings of predominantly affective conditions, mixed mainly paranoid psychoses, and schizophrenias, each of these groups being divided into an improved and an unimproved subgroup. It is easily seen that in each of the groups the improved cases tend to have a distinctly higher average number of segments involved, the emphasis being, as with personality change, on the central and to a lesser degree orbital segments. This tendency is still noticeable if the best improved cases are compared with the less well improved cases. As the

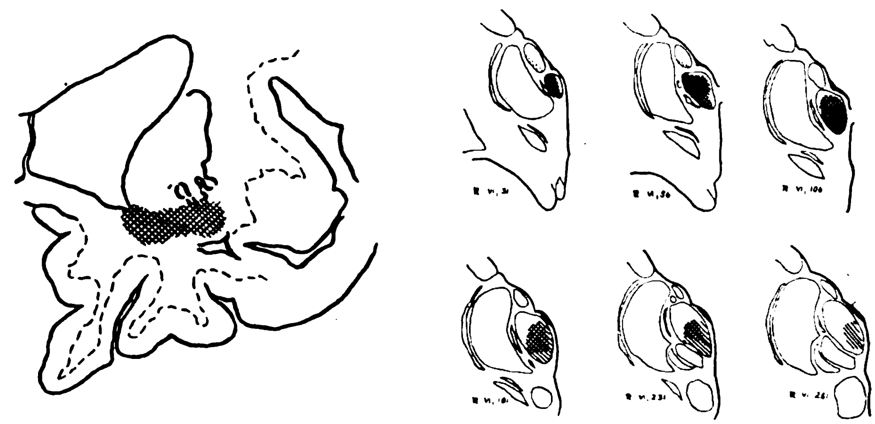

FIG. 10.—Leucotomy lesion (circumscribed posterior cut) in the ventral part of the internal capsule (*a*), severing the great majority of the thalamo-prefrontal projection fibres, as evidenced by (*b*) the almost total retrograde degeneration of the dorso-medial nucleus.

last column of the table indicates, this tendency runs roughly parallel with the severity of personality change, thus confirming Frankl and Mayer-Gross's clinical impression.

CONCLUSIONS.

A few points stand out with relative clarity. Bilateral lesions confined to the prefrontal region are capable of causing personality change persisting for long after the process of active repair and irritation has become quiescent. This controverts most of the criticisms raised by Hebb against the evidence for a frontal lobe syndrome. The persistent personality change caused by posterior (extra-prefrontal) cuts may be severe, but this is due, our material would indicate, to the cutting of the thalamo-prefrontal projection in its course nearer to the thalamus. These observations also tend to emphasize the importance of the thalamo-prefrontal projection with regard to the anatomical mechanism concerned in the personality change (and probably in improvement), and also to confirm the recent preliminary findings after thalamotomy.

Cases with posterior cuts almost consistently manifest undesirable symptoms of an autonomic or other nature. Some of these appear to have a definite relation to the posterior orbital, cingular and premotor regions, all of which are known to be concerned with autonomic functions.

No confirmation could be obtained of the more detailed and extravagant claims as to localization of mental faculties within the frontal lobe, such as the well-known scheme of Kleist (1934, 1937) suggests. Whatever tendency there may be for any degree of localization is, so far, overshadowed by a quantitative relationship between the degree of personality change and the amount of prefrontal cortex cut off. As personality change and improvement seem to be positively correlated, this quantitative principle would appear to apply also, to some extent at least, to the mechanism of improvement. The anterior cingular region (area 24) appears to play little part in determining personality change.

All these results should be regarded as tentative and liable to considerable modifications in the light of greater numbers of cases and of improved clinical observations. Their publication at the present juncture seems desirable, however, in order to emphasize the importance and potentialities of this type of clinico-anatomical analysis, and thus to stimulate the greatest possible use of this unique human material.

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