

ANATOMICAL CORRELATES OF IMPROVEMENT AFTER LEUCOTOMY.*

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OUT of 95 leucotomy cases of which the brains and clinical records have been collected at this laboratory, 45 were cases with post-operative survival of over 5 months, and more than 20 of these showed some degree of clinical improvement. Such numbers now 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 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. Over 20 of the same 45 cases had a recorded post-operative change of personality, so that relationship of post-operative personality change to the leucotomy lesions can conveniently be investigated in the same group of cases. Only some general findings concerning the personality change will, however, be touched on in the present paper.

Apart from previous publications from this laboratory (Meyer and Beck, 1945; Meyer and McLardy, 1947; Meyer, McLardy and Beck, 1948; Meyer and McLardy, 1948) no study at all comparable involving post mortem determination of the actual lesions created, has appeared in the literature. Since some of the cases included in the group under review here have been described in part in previous publications it should be mentioned that minor discrepancies occur between the description of the same case in successive papers due to the continuous recheck of material and extension of histological investigation.

MATERIAL AND PROCEDURE.

Fifty cases were eliminated from the present study on account of post-operative survival of less than 5 months' duration, because such brief survival does not permit reliable evaluation of the clinical results and in practically all such cases undesirable physiological sequelae tend to obscure the picture of the mental state (see Meyer and McLardy, 1948). 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 months survival period, and a fifth because it was an isolated case of epileptic psychosis. This left 40 cases suitable for investigation of correlations between the lesions and clinical improvement (and personality change).

* This paper was to have been read by A. Meyer to the International Conference on Psychosurgery held in Lisbon from 3rd-7th August, 1948, but owing to unforeseen circumstances could not be presented in full.

For each of these 40 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 (see Diagrams 1*a* and *b*), segments of white matter (see Diagram 2) seen to be involved on macroscopic and microscopic inspection or shown to be damaged from histological study of retrograde cell changes and gliosis in the dorsomedial and anterior nuclei of the thalamus,* nature and duration of post-operative improvement if any,

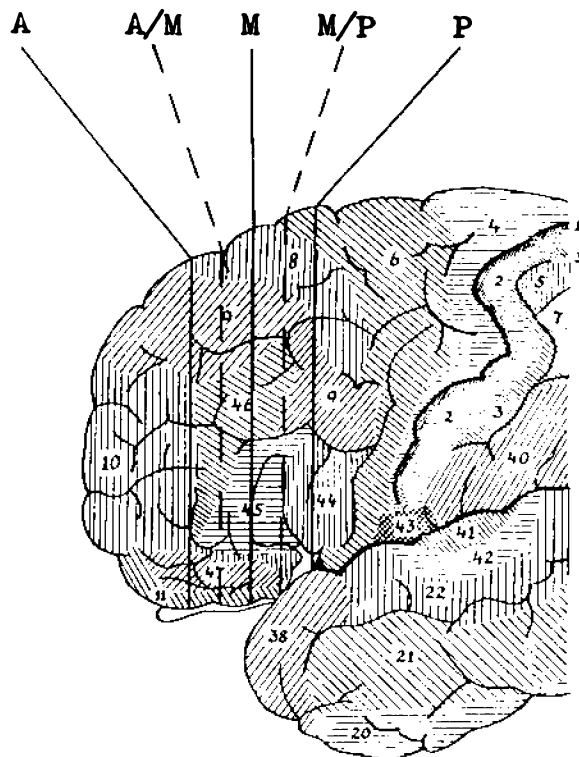


DIAGRAM 1*a*.—"M" is the normal plane of cut aimed at in the "blind" operation. The plane tabulated in each case is frequently a mean, for often the final lesion was cystic and frequently it was oblique to the coronal plane.

post-operative personality change (graded roughly for severity as indicated by plus and minus signs), 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 case records, most of which were compiled during the war years.

The cases were then divided into the three clinical groups of Predominantly Affective Conditions (Table I), Mixed mainly Paranoid Psychoses with

* This thalamic check was done especially in cases with small lesions situated posteriorly in or close to the anterior thalamic radiation, using the analysis of the cortical projection of especially the dorsomedial nucleus described and illustrated at the International Meeting arranged by the Nederlandsche Vereeniging voor Psychiatrie en Neurologie in 1947 (Meyer, McLardy and Beck, 1948), and since then elaborated by data (not yet published) from a total of 30 hemispheres.

onset after 35 years of age (Table II), and Schizophrenia with onset under 35 years of age (Table III). In each of these three tables the cases were divided into an upper "Improved Group" and a lower "Unimproved Group."

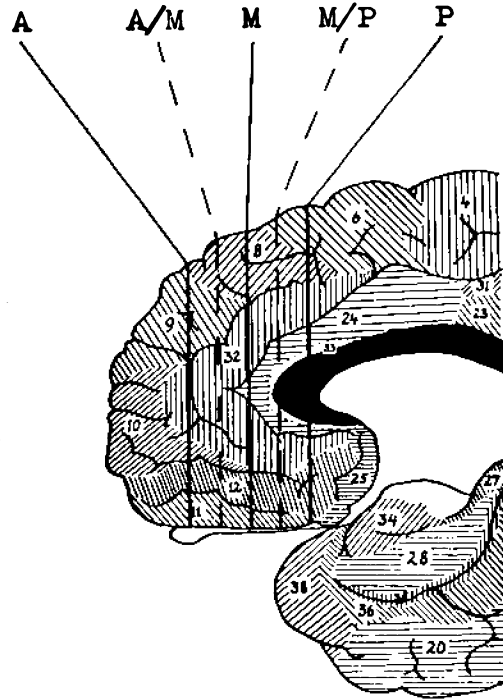


DIAGRAM 1b.—The same planes viewed from the mesial surface of the brain.

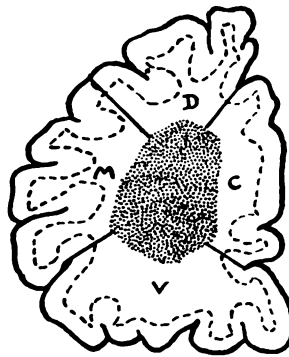


DIAGRAM 2.—D, dorsal segment ; M, middle segment ; V, ventral segment ; C, cingulate segment ; stippled area, central segment.

The improved cases are arranged roughly in order of grade of improvement. The unimproved cases are listed simply in serial order. The resultant distribution of cases is as follows :

| | Improved. | Unimproved. | Total. |
|--|-----------|-------------|--------|
| Predominantly Affective Conditions | 11 | 4 | 15 |
| Mixed, mainly Paranoid, Psychoses | 6 | 6 | 12 |
| Schizophrenias | 5 | 8 | 13 |
| | — | — | — |
| Total cases | 22 | 18 | 40 |

It should be emphasized that the quality of improvement which is being dealt with here is not representative of improvement after leucotomy in general. The present cases are not a "fair sample" because they are, with few exceptions, cases who never left or lost touch with the mental hospital in which they were treated. If only autopsy investigation could be obtained on a more substantial sample of much improved cases who have died at home or in a general hospital, important information could quickly be derived towards solving the pressing practical problem of the optimum lesions for the optimum result in each type of case. Failing such material, the present less well-improved cases can still be graded among themselves and differentiated from the unimproved in such a way as to reveal, more slowly and laboriously, at least tentative pointers towards any general principles involved.

ANALYSIS.

A preliminary survey of the cases reveals four general points of note :

1. The cases in Tables I and II consist essentially of involuntional illnesses.
2. Three of the Affective cases rank higher in improvement than any of the Mixed Psychoses, of which two in turn rank higher than any of the Schizophrenias, so that from the range of improvement as well as the number of improved cases in each of the groups one would expect any clinico-anatomical correlations to show up most clearly in the Affective Group, least clearly in the Schizophrenic Group.

3. 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 by the leucotome entry track.

4. The average total number of segments involved (7.9 out of a possible 10) in the whole 22 improved cases is much greater than in the whole 18 unimproved cases (4.6), involvement of individual segments being relatively highest for the central one.

One general point not demonstrated by the tables is that there was no difference in the quality of the histopathology of the leucotomy scars between the improved and unimproved groups as a whole, appearances in individual cases varying consistently 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.

* Except in enumerating the total number of segments involved, no account of unilateral damage of segments is taken in this paper because of the generally accepted principle that prefrontal lesions must be bilateral to produce physiological or psychological effects.

TABLE I.—*Predominantly*

| Serial No. | Sex. | Nature of mental illness. | Pre-op. duration of illness, yrs. | Previous physical therapy. | Age at operation. | Plane of cut. | | Segments involved. | | | |
|------------|------|--|-----------------------------------|----------------------------|-------------------|---------------|-------|--------------------|----|------|----|
| | | | | | | L. | R. | Dors. | | Mid. | |
| | | | | | | | | L. | R. | L. | R. |
| 66 | F. | Affective psychosis with depression, compulsive thoughts, impulsive outbursts and many hysterical features | 2 | None | 25 | M. | M. | + | + | + | + |
| 71 | M. | Depression with delusions of poverty and ruin | 7 | None | 63 | M. | P. | - | + | + | + |
| 18 | M. | Recurrent depression with hypochondriacal delusions and depersonalization. | 7 | None | 66 | M. | A./M. | - | + | + | + |
| 10 | F. | Impulsive psychopathy with hysterical features including outbursts of rage | 4+ | E.C.T. Cardz. Insul. | 25 | M. | M. | - | - | + | + |
| 44 | F. | Recurrent agitated depression with hypomanic swings | 3 | Phren. E.C.T. | 43 | A. | A. | + | + | + | + |
| 9 | M. | Depression with hypochondriacal delusions and depersonalization | 4 | None | 37 | M. | M./P. | + | - | + | + |
| 39 | M. | Depression with hypochondriacal delusions and strong hysterical features. | 3+ | None | 64 | A./M. | A./M. | + | + | - | - |
| 86 | F. | Manic-depressive with strong hysterical features and mild hypochondriasis | 16 | E.C.T. | 68 | A./M. | A./M. | + | + | + | + |
| 62 | F. | Agitated depression with deterioration | 3 | None | 67 | A. | A. | - | + | + | + |
| 67 | M. | Agitated depression with paranoid delusions and auditory hallucinations during excited phases | 7 | None | 65 | A./M. | A./M. | - | + | + | + |
| 78 | F. | Manic-depressive with mild paranoid ideas | 6 | Insul. | 35 | P. | M./P. | + | - | + | + |
| 35 | F. | Agitated depression with vague nihilistic and persecutory delusions | 2 | E.C.T. Insul. | 63 | M. | M. | - | - | + | + |
| 46 | M. | Recurrent depression with tense feelings of suppressed aggression | 3+ | Cardz. E.C.T. | 50 | M. | M. | - | + | + | + |
| 47 | F. | Recurrent depression with hypochondriacal features | 2+ | E.C.T. | 42 | M./P. | P. | - | - | + | + |
| 87 | M. | Agitated depression with delusions of unworthiness | 3 | None | 64 | M. | M. | - | - | + | + |

Affective Conditions.

| Segments involved. | | | | | | Post-operative improvement. | Post-operative persity. change. | Survival period. yrs. | Cause of death. |
|--------------------|----|-------|----|-------|----|--|---------------------------------|-----------------------|------------------------|
| Vent. | | Cent. | | Cing. | | | | | |
| L. | R. | L. | R. | L. | R. | | | | |
| + | + | + | + | - | - | Cheerful and free from mental symptoms throughout survival. Discharged to sanatorium after 6 weeks | - | 4 | Phthisis. |
| + | + | + | + | + | - | Discharged home cheerful and sl. overactive. Started new job. Sudden relapse during attack of carbuncles | ++ | 1½ | CO Suicide. |
| + | + | + | + | + | + | Became cheerful and lost anxiety about delusional ailments | ++ | 1½ | Coronary thrombosis. |
| + | + | + | + | - | - | Milder, less frequent and shorter outbursts. Discharged home after 1 yr. 8 months. | ++ | 3 | Septicaemia. |
| - | - | + | + | + | + | Ten months normal mood, then relapsed and developed paranoid delus. and aud. hallucinations | + | 3½ | Phthisis. |
| - | - | + | - | - | - | Six months' disappearance of delns. and much diminished deprsn., then complete relapse with aud. hallucns. | + | 1½ | Status asthmaticus |
| - | - | + | + | - | + | Eight months less worried about delus., then relapse with progressive detern. | + | 1 | Purulent bronchitis. |
| + | - | + | + | - | - | Evening out of mood swings and less tendency to worry | ++ | 11 m. | ? Uraemia. |
| + | + | + | + | - | - | Lost all resistiveness and agitation; slightly less depressed | ++ | 2½ | Carcinoma of uterus. |
| + | + | + | + | - | - | Less depressed; noisy outbursts greatly reduced in frequency and duration | ++ | 2 | Carcinoma of pancreas. |
| - | - | + | + | - | - | More even in mood until death | + | 5½ m. | Phthisis. |
| - | - | - | - | - | - | None | - | 1 | ? |
| - | - | + | - | - | - | Normal mood for three weeks, then complete relapse | ? | ¾ | CO Suicide. |
| - | - | - | - | - | - | One month very cheerful then relapsed rapidly and detertd. during termnal yr. | + | 3½ | Carcinoma of cervix. |
| + | - | - | - | - | - | One month less depressed and agitated, then complete relapse | ? | 1½ | Lung abscess. |

TABLE II.—*Mixed, Mainly Paranoid, Psychoses*

| Serial No. | Sex. | Nature of mental illness. | Pre-op. duration of illness. yrs. | Previous physical therapy. | Age at operation. | Plane of cut. | | Segments involved. | | | |
|------------|------|---|-----------------------------------|----------------------------|-------------------|---------------|-------|--------------------|----|------|----|
| | | | | | | L. | R. | Dors. | | Mid. | |
| | | | | | | | | L. | R. | L. | R. |
| 65 | M. | Paranoid psychosis with visual and auditory hallucinations and outbursts of violence; no deterioration | 5 | E.C.T. | 56 | P. | P. | + | + | + | + |
| 37 | F. | Paranoid psychosis with aud. hallucs., grandiose delusions and violent outbursts; gross deterioration | 13 | None | 62 | M. | P. | - | + | + | + |
| 64 | F. | Paranoid psychosis with outbursts of maniacal excitement; no deterioration | 3 | Cardz. | 44 | A./M. | M. | + | - | + | + |
| 14 | M. | Paranoid psychosis with visual and auditory hallucs. and manic-depressive swings; no deterioration | 9 | E.C.T. | 54 | M. | M./P. | - | - | + | + |
| 75 | F. | Paranoid psychosis; negativistic, suspicious, autistic; no deterioration | 2 | Insul. | 39 | A. | A./M. | + | - | + | + |
| 90 | M. | Paranoid psychosis; no deterioration | 3½ | E.C.T. Insul. | 37 | M. | M. | - | - | | + |
| 20 | F. | Paranoid psychosis with some alternating stupor and excitement; no deterioration | 5 | E.C.T. | 47 | A./M. | A./M. | + | - | + | + |
| 21 | M. | Paranoid psychosis with hallucinosis and manic-depressive features; no deterioration | 13 | None | 61 | M. | M. | - | - | + | + |
| 26 | F. | Paranoid psychosis with hallucs. and impulsive outbursts; no deterioration | 1 | E.C.T. | 44 | P. | P. | - | - | + | + |
| 27 | F. | Paraphrenia (delusions of reference, aud. hallucs., violent outbursts and grandiose features; no deterioration) | 2 | None | 54 | P. | P.* | + | + | + | + |
| 38 | F. | Paranoid psychosis with some alternating stupor and excitement; no deterioration | 10 | None | 68 | P. | M. | - | - | + | - |
| 74 | F. | Paranoid psychosis with impulsive outbursts and manic depressive features; no deterioration | 4½ | None | 54 | A. | A./M. | - | - | + | + |

with Onset Over the Age of 35.

| Segments involved. | | | | | | Post-operative improvement. | Post-operative perstly. change. | Survival period. yrs. | Cause of death. |
|--------------------|----|-------|----|-------|----|--|------------------------------------|--------------------------|----------------------------|
| Vent. | | Cent. | | Cing. | | | | | |
| L. | R. | L. | R. | L. | R. | | | | |
| + | + | + | + | - | - | More tractable and employed more usefully throughout survival. Hallucinations became inconspicuous. Granted parole | ++ | 3 | Lobar pneumonia. |
| - | + | - | + | - | + | One year less aggressive. Lucid intervals (with E.C.T.) and cleaner until death. | ? | 4½ | Lobar pneumonia. |
| + | + | + | + | + | - | Quiet and well-conducted with no evidence of delusions for 9 months, then complete relapse | + | 2 | Chronic nephritis. |
| - | + | - | - | - | - | Four months normal mood and loss of hallucinations, then complete relapse with profound depression | ? | 8 m. | ? |
| + | - | + | - | - | + | Two months more sociable; 9 months less hostile, then relapsed into pre-operative state | ++ | 3 | Phthisis. |
| - | - | + | + | - | - | Slightly less evidence of delusions of persecution for 2 years, then became worse, with aggressive outbursts and auditory hallucens. | - | 4½ | Duodenal ulcer. |
| - | - | + | - | + | - | Co-operative and brighter for 3 weeks, then gradually relapsed and deteriorated | + | 2½ | Lung Gangrene. |
| - | - | - | - | - | - | Two months slight improvement, then full relapse | ? | 1½ | Cardio-vasc. degeneration. |
| - | - | - | - | - | - | Six weeks quiet and friendly, then complete relapse | ? | 3½ | Pneumonia. |
| + | - | + | - | + | - | Four months very slightly less aggressive, then relapsed and deteriorated. | ? | 3½ | Circ. failure. |
| + | + | - | - | - | - | None | + | 1½ | ? |
| + | + | + | + | - | - | One month moderately well conducted, then relapsed and slowly deteriorated | + | 3½ | Carcinoma of oesophagus. |

TABLE III.—*Schizophrenia With*

| Serial No. | Sex. | Nature of mental illness. | Pre-op. duration of illness, yrs. | Previous physical therapy | Age at operation. | Plane of cut. | | Segments involved, | | | |
|------------|------|--|---|---------------------------------|-------------------|---------------|-------|--------------------|----|------|----|
| | | | | | | L. | R. | Dors. | | Mid. | |
| | | | | | | | | L. | R. | L. | R. |
| 57 | M. | Paranoid schizophrenia with hysterical features; no deterioration | 1 | Cardz. | 23 | M. | M. | + | - | + | + |
| 61 | F. | Paranoid schizophrenia: impulsive; unemployable; no deterioration | 7 | Insul. E.C.T. | 37 | M. | M. | + | + | + | + |
| 94 | F. | Paranoid schizophrenia with delusions of reference and auditory hallucinations; violent; hysterical element; no deterioration | 2½ | Narcos. Insul. E.C.T. | 22 | M./P. | M. | + | + | + | + |
| 60 | F. | Schizophrenia with delusions of sinfulness and prominent obsessional symptoms; slight deterioration | 4+ | Insul. E.C.T. | 24 | M. | M. | + | + | + | + |
| 63 | F. | Catatonic schizophrenia with delusions of persecution and auditory hallucinations during excited periods; considerable deterioration | 20 | None | 47 | A./M. | M. | + | + | + | + |
| 5 | M. | Catatonic schizophrenia with grandiose and persecutory delus. and aud. hallucs. during excited phases; deteriorated | 20 | None | 43 | A. | A. | + | + | + | + |
| 12 | M. | Catatonic schizophrenia with grandiose delus. and aud. halluc. during excitement; severely deteriorated | 12 | Cardz. | 32 | A. | A. | + | + | + | + |
| 19 | M. | Catatonic schizophrenia with many delusions and aud. hallucs., deteriorated | 21 | None | 51 | M. | M. | - | - | + | + |
| 31 | M. | Paranoid schizophrenia with aud. hallucs.; autistic, mildly depressed; no deterioration | 25 | None | 50 | P. | P. | - | - | + | + |
| 36 | F. | Schizophrenia with violent outbursts; severely deteriorated | 3+ | ? | 35 | M./P. | P. | - | - | + | + |
| 69 | F. | Schizophrenia with delus. of reference, auditory halluc. and catatonic features; severely deteriorated | 11 | None | 37 | M. | M. | + | - | + | + |
| 81 | F. | Hebephrenic schizophrenia; inaccessible for last 3 years; deteriorated | 18 | None | 47 | P. | M./P. | + | - | + | + |
| 85 | F. | Hebephrenic schizophrenia; no deterioration | 9 | E.C.T. | 30 | M. | A. | - | - | + | + |

Onset Under the Age of 35.

| Segments involved. | | | Post-operative improvement. | Post-operative personality change. | Survival period. yrs. | Cause of death. |
|--------------------|----------------|----------------|--|---------------------------------------|--------------------------|----------------------------|
| Vent. L. R. | Cent. L. R. | Cing. L. R. | | | | |
| + | + | + - | Discharged 5 weeks after operatn. Absence of delus. of persecn. while living and working away from home for 1 yr. Then almost complete relapse | ++ | 2½ | Hypoglycaemic coma. |
| + | + | - - | More amenable, less disturbed by his delusions and occupied making toys throughout survival | + | 1½ | Sub. bacter. endocarditis. |
| + | + | + | Four and a half months clear of delus., 6 months' relapse; 9 months moderate recovery, then severe relapse until death 10 months later. Discharged during remissions | + | 2½ | Broncho-pneumonia. |
| + | + | + | Slightly less evidence of compulsive ideas for 4 months then complete relapse | + | 3½ | Electro-narcosis. |
| + | + | - - | Two and a half months well behaved, showing sense of humour and occupied in handicrafts, then relapsed completely | + | 1½ | Chronic phthisis. |
| + | + | + | None | + | 1½ | Status epilepticus. |
| + | - | + | None | + | 2 | Phthisis. |
| + | + | - - | None | + | ½ | ? Uraemia. |
| - - | + | - - | More reserved and shy than ever | - | 1½ | Myocard. degeneration. |
| - - | - - | - - | None | ? | 2 | ? |
| + | + | - - | None | + | 2 | Phthisis. |
| - + | + | - - | None | ++ | 1½ | Myocard. degeneration. |
| - - | - - | - - | None | ? | 1½ | Second leucotomy. |

Any further gross comparison of the whole 22 improved cases with the whole 18 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.

Predominantly Affective Conditions. (TABLE I).

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 the better improved have, on the whole, 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 case for leucotomy.

Mixed, Mainly Paranoid, Psychoses with Onset Over the Age of 35.
(TABLE II).

No suggestive trend is discernible in the incidence of any of the clinical data of recognized prognostic value. The only anatomical differences of note between the improved 6 and the unimproved 6 is the slightly higher average total number of segments involved and the very 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 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.

Schizophrenia with Onset Under the Age of 35. (TABLE III).

In this group there is a major clinical difference between the improved 5 and the unimproved 8, in that the latter contain wholly chronic and mostly deteriorated cases while the former contain only one such. This, together with the low grade of improvement, renders it of very 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 those with notably higher frequency of bilateral involvement in the improved group are the ventral and dorsal segments. 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.

Personality Change.

A feature not very readily appreciated from Tables I-III is that there is a strong suggestion of relationship between the severity of post-operative personality change and certain of the segmental data listed. A separate analysis of all cases where the recording of the personality change can be accepted as probably reliable is summarized in Table IV* and shows clearly

TABLE IV.—*Summarized Analysis of the Lesions in Relation to Different Grades of Post-operative Personality Change.*

| Post-operative personality change. | Segments of white matter involved in the leucotomy lesions. | | | | | Average total segs. |
|------------------------------------|---|------------------|-------------------|-------------------|-------------------|---------------------|
| | Bilat. dors. seg. | Bilat. mid. seg. | Bilat. vent. seg. | Bilat. cent. seg. | Bilat. cing. seg. | |
| ++ (11 cases) | 19% | 100% | 73% | 91% | 9% | 7.2 |
| + (10 cases) | 40% | 80% | 40% | 60% | 10% | 5.5 |
| - (14 cases) | 14% | 86% | 7% | 21% | 0% | 3.4 |

that the severity of the change tends to vary directly with the total number of segments involved, and particularly with bilateral involvement of the central and ventral segments. The more detailed analysis of anatomical correlates of personality change is described and discussed by the present writers in a separate paper (Meyer and McLardy, in press).

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 obtains between the best improved and the less well improved cases, and in addition the best improved have, on the average, more posteriorly† placed cuts. When cognizance is taken of the fact that most of the improved cases had only very moderate prognostic potentialities, all these findings seem to point clearly to one general principle, namely that clinical improvement in such circumstances varies directly with the total amount of prefrontal cortex isolated from its connections.

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 would still be in conformity with a

* The case of epileptic psychosis is included in this Table.

† 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.

quantitative principle, since thalamic fibres to and from all other segments tend to collect in this central region. Its full involvement in a posterior plane will sever most fibres coursing between the thalamus and prefrontal cortex. In progressively more anterior cuts the fibres travelling in it will become progressively more only those connecting with regions near to the frontal pole (areas 10, 46 and anterior parts of areas 9, 11, 12, 47 and 32). In cuts at a middle plane (i.e. the commonest plane of cut in the best improved cases in this series) such rostrally connected fibres will already constitute a high proportion of the fibres in the central segment. This is of considerable interest in the light of recent American clinical reports such as the preliminary one by Heath and Pool (1948) where substantial improvement occurred in two psychotic cases after cortical resection limited to dorsal parts of areas 10, 46 and 9, and Freeman's (1948*b*) report of a high rate of favourable response in over a hundred cases (including early schizophrenics) after transorbital lobotomy which he considers isolates essentially these same regions of cortex. Whether this simply means that in more suitable, especially earlier, cases than most of the present series, cutting off the poles happens to represent the optimum amount of isolation of prefrontal cortex, or whether a more specific factor comes in, cannot as yet be decided.

Heath and Pool and Freeman, as mentioned, attribute special therapeutic significance particularly to 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. The five best improved cases (Nos. 66, 71, 18, 10 and 65) in the whole series, 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) describe a case of involutional melancholia where spectacular improvement followed lesions which almost entirely spared the orbital regions.

A further point of interest is the negative one that finer anatomical analysis, not recorded in the tables, shows that in no instance within the whole series of 40 cases did the ventral lesion encroach upon the agranular cortex in the postero-medial part of the orbital region (Beck, in press) which probably contains cortex homologous to the monkey's area 13, which is known to be closely related to autonomic function.

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 disaccords with Ward's (1948) suggestion, derived from work on animals, that ablation of area 24 might benefit psychotic patients, and so tallies with recent American experience (W. Freeman: personal communication) which tends to show that bilateral circumscribed ablation of area 24 has no ameliorative effect, and actually severe physiological consequences. Whether the bilateral damage to area 24 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 doubtless others not recorded, no doubt also play their part in improvement (and its absence)

in this series and may be the most important prognostic factors in a few of the cases. So little detail is known of the premorbid personality in the majority of the cases that it is futile to search for any relationship 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.

The post-operative personality change in this series of cases would appear to have the same anatomical correlates as has the clinical improvement, except that it is perhaps related still more strongly to bilateral damage to the ventral segment. Hence one would expect, and there is, in the series a 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 is too fine a point to be determined from the unsystematic clinical observations available in this series of cases, but certainly it has for long been held that the orbital region is peculiarly related to at least the euphoric type of personality change. Close attention will continue to be paid to this important practical matter in further studies.

The most general result that comes out of the present study is therefore that the gross amount of isolation of *prefrontal* cortex from its white matter is an important correlate of clinical improvement (and personality change) after prefrontal leucotomy. This result, it should be emphasized, is derived from, as a whole, poor clinical material. In cases of better prognostic potentiality than in the majority of the present series more circumscribed and more rostral lesions may well constitute the optimum amount of damage. Heath and Pool's and Freeman's results seem to confirm that in fact such is the case. These authors suggest further that a principle of selective localization applies to such minimal lesions. They emphasize importance of dorsal parts of the rostral cortex. The tentative results of the present analysis would point rather to the ventral parts of the rostral cortex being the more important, at least in affective and mixed psychoses. From the descriptions and illustrations given in Freeman's papers (1948*a, b*) one gains the impression that, contrary to his own emphasis, transorbital leucotomy actually cuts more ventral than dorsal fibres.

SUMMARY.

(1) There is strong evidence that, in at least predominantly affective conditions and mixed mainly paranoid psychoses, improvement varies, among cases of equally moderate prognostic potentiality, directly with the amount of prefrontal cortex isolated from its white matter. The same tendency was observed in the schizophrenias, but owing to their low level of improvement and the lack of suitable unimproved cases for contrast no reliable trends could be derived from those in the present series.

(2) No evidence is found of any segment of white matter the bilateral involvement of which is indispensable to improvement. The central segment

comes nearest to being such a region. This may still be simply an expression of the general quantitative principle. Since, however, at the commonest level of effective leucotomy cuts in this series the central segment contains a high proportion of fibres connecting with the more rostral regions of prefrontal cortex, the finding does not contradict recent evidence, derived from selected cases with better prognostic potentiality than most of the present series, of good results after circumscribed resection or (transorbital) leucotomy—with the qualification that the present analysis points to rather greater importance of the orbital than of the dorsal aspect of the rostral regions of the cortex.

(3) 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 seems if anything to militate against improvement.

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

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