POST-OPERATIVE SYNDROMES IN SELECTIVE PREFRONTAL SURGERY*

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The prefrontal region lies in front of the motor and premotor areas of the frontal lobe. In Brodmann's terminology this corresponds to areas 8, 9, 10, 45 and 46 on the convexity; 11, 47 and 13 on the orbital surface; 24, 32 and 12 on the mesial surface. When speaking of selective prefrontal surgery, we mean topectomy or cortical undercutting or partial leucotomy of one or several of these areas.

In a preceding paper (7) the difficulties of performing a really selective operation have been discussed; topectomy was advised in most cases for reasons of both safety and selectivity, but cortical undercutting was considered advantageous in patients over 60 years of age. In cortical undercutting an additional difficulty arises in that following even very slight changes in the position of the head variations of site occur. It is absolutely necessary to check the extent of any type of operation by X-ray study of such landmarks as clips or gelfoam with lipiodol. Thus, it was felt, a method has become available for evaluating statistically the possible correlations between anatomical lesions of areas variable in size and the clinical consequences of the operation.

Since the beginning of psychosurgery two theories have been developed to explain the action of the operation, which, generally speaking, might be called the quantitative and qualitative theory respectively. However, little concrete research had been done in this respect before publication of an important paper in 1949 by Meyer and McLardy (14). These authors arrived at the conclusion that "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." However, as the authors themselves admitted, their material was made up of patients submitted to extensive lobotomies who had been suffering from complex psychotic states; the conclusions might have been different if selective operations performed in simpler conditions, such as cases of intractable pain, anxiety neurosis or psychomotor agitation had been analysed (9, pp. 1550–1).

For a long time our own work has been directed towards demonstrating eventual differences of function corresponding to different prefrontal areas; such differentiation seemed likely in view of their relative individuality in structure and connections (5, 8 and 9). Recently the *long-term therapeutic results* have been analysed for a series of 100 selective prefrontal operations (7). In this paper we present the clinical differences between the *immediate post-*

* This paper, together with a previous one (7), contains essential parts of a lecture given at the Maudsley Hospital on 31 May, 1951.

operative syndromes following 134 topectomies and selective leucotomies in various locations. So far no special psychological investigations are available for publication. The present paper, therefore, is based on rather crude observations of obvious behaviour disturbances, such as confusion with disorientation in time and space, apathy, agitation, euphoria, depression and their customary emotional expressions and, finally, vesical and rectal incontinence.

Sometimes the post-operative syndrome is very slight or lasts a few hours only; such cases will be considered as normal. However, there is usually little difficulty in diagnosing it as a clinical entity when it lasts several days or, as is usual, one or two weeks, or even, as is more rare, six to eight weeks. It is not exceptional to see it appear one or two days after the operation and to reach its maximum about 10 days later, then to fade away progressively. In all our patients the post-operative syndromes were transitory, in contrast to what is so often observed after the posterior cuts of the classical lobotomies.

The total number of cases in the present study is 134, but not all lend themselves to a useful analysis. We have omitted three categories: (*a*) 8 early fatalities, (*b*) 8 mentally very backward individuals, (*c*) 10 unilateral operations not followed by any significant clinical change; these were unilateral topectomies or undercuttings, or unilateral lobotomies, with cuts always at least 2 to 3 cm. in front of the coronal suture.

Thus we were left with a series of 108 bilateral prefrontal operations, all in front of area 8, whatever their mesial or lateral extension; of this material 81 were topectomies, and 27 "leucotomies" (the distinction between a very rostral lobotomy and an apical cortical undercutting is not always easy).

A first conclusion stands out with little doubt: *there is a great difference in post-operative behaviour between the "convexity" and the "mesial" patients.* Of 76 operations involving the convexity and/or the orbital region, 40—more than half of them—were followed by a marked post-operative syndrome, whilst of 32 mesial operations, only 4 were followed by definite behaviour abnormalities. The difference seems significant and, we believe, constitutes a strong argument in favour of the qualitative theory. Presumably the extent of cortical resection or isolation as checked by radiography is on the average not very different in these two groups. That the mesial surface of the prefrontal lobe and its convexity do not have the same function with regard to behaviour is not entirely unexpected: one could not fail to observe, for instance, the striking disorder of behaviour following a bilateral prefrontal lobectomy for an olfactory meningioma, whereas, in marked contrast, the post-operative syndrome following removal of a glioma invading the anterior corpus callosum and the mesial walls of both frontal lobes is far less conspicuous (20).

A more detailed analysis of the post-operative syndrome is now possible according to the location of our selective resections:

1. *Convexity Operations.*

Our results are shown in Fig. 1, which is a diagram similar to the one already published (7) on the therapeutic effects. The numbered levels correspond to the *mean* lengths of some prefrontal areas, as measured by Beck, McLardy and Meyer (2): from $-5\cdot5$ to -4 = area 13; from -4 to -1 =

area 11; from − 1 to 4 = area 10; from 4 to 7 = area 9; (from 7 to 14 = areas 8 and 6). Level 0 corresponds to the foramen caecum, and the measurements of our resections or sections were taken near the midline on the post-operative X-rays (lateral view of the skull). We believe that the possible error of these measurements of lengths is nearly ½ centimeter.

The diagram is divided into three parts, A, B and C. If we leave out for the time being the orbital resections and the lobotomies, it will be seen that in part A nearly all the operations which had no sequelae of a significant post-operative syndrome involved most of area 10 and extended little into area 9. Now, even if one believes firmly in the qualitative theory, there remains the fact that a minimal amount of cerebral resection is necessary for the production of any clinical effect (probably 8 to 10 grammes on each side). It is for this reason that we should discard the five most lateral (area 46) resections in the diagram, as well as the three labelled "small-sized fragments." Even so, there are still 20 selective operations more or less confined to area 10 and belonging to class A.

Part B of the diagram is made up of the patients showing post-operatively the classical hypomanic frontal syndrome. Often these patients break into spontaneous loud singing. There may be some degree of mental confusion, but when vesical and rectal incontinence is observed it is usually due to indifference or even meant as a joke. If we leave out the lobotomies, it will be seen that most of these resections are definitely higher than in class A and probably include much of area 9. These findings, therefore, strongly suggest that the appearance of the prefrontal hypomanic syndrome is related to the suppression of area 9.

Alternative explanations would be:

(a) *A quantitative effect.*—This, it is believed, is not likely; a simple comparison between the lengths of operations A and B shows that there is certainly no prevalence of size on the B side; if anything it would be rather the reverse.

(b) *The pre-operative condition.*—This point needs careful discussion. Firstly it is necessary to limit the comparison to cases submitted to prefrontal operations roughly equivalent in extent. This leaves 20 cases in class A and 18 cases in class B. In A, 14 were classified as intractable pain, and 6 as psychoses; in B, 9 were pain cases and 9 psychoses. Many more cases are, therefore, necessary to draw statistically significant conclusions. The most typical hypomanic syndromes were seen in 4 cases of pain and 2 of psychoses, and it is our impression that the special post-operative syndrome is more closely related to the suppression of area 9 than to the pre-operative personality. Following Petrie's lead on lobotomies (16), our patients were tested pre-operatively and as soon as possible in the post-operative period (Rylander and his associate Mrs. Schalling actually perform tests during the operation itself). We have not yet collected a sufficient number of observations available for statistical analysis, but this line of investigation is likely to yield some useful information both on the role of the pre-operative personality and on the type of post-operative change.

Exceptions.—The first two cases in class B seem to disprove our point.

However, the first, though intended to be a cortical undercutting of areas 10 and 11, was in reality (7, Fig. 10) a rather deep section, likely to cut most of the fibres connecting area 9 and thalamus; the hypomanic post-operative syndrome therefore is in accord with the other class B cases. The second case was a topectomy limited to parts of 10 and 11, but was complicated by oedema of the brain developing during the operation.

Part C of the diagram contains a group of patients showing a post-operative syndrome of inertia, apathy and mental confusion; sphincteric incontinence is nearly always present, but seems to be related to the deep, stupor-like disturbance of consciousness. If lobotomies and orbital and lateral resections are omitted, there remains a group of 13 cases. A study of the lengths of incision yields a roughly equal distribution over areas 9 and 10. Furthermore there is no significant quantitative difference in length between class C and classes A and B (except in one case with large-sized fragments). However, in nearly all the C cases there were some general factors which might explain the post-operative changes. More than half of the cases in class C were over 55, against 15 per cent. in class A and 30 per cent. in class B. Moreover, the general condition of the patients should be taken into account: three were carcinomas, one a very deteriorated drug addict, four suffered from hypertension accentuated during operation; of these, two had fits during the night following the operation. Finally one case developed oedema of the brain. We are therefore led to assume that the post-operative syndrome of class C is not directly related to the actual prefrontal removal, but the result of a generalized effect, very likely involving hypothalamic disturbance (7).

In conclusion, this analysis of the convexity operations strongly suggests that *post-operative appearance of the typical hypomanic syndrome has a relation to the removal or the exclusion of area* 9.

Figs. 2 and 3 are taken from especially instructive cases. In Fig. 2 a topectomy of area 10 with no post-operative syndrome (except a very slight apathy) is contrasted with a topectomy of part of 10 and the greater part of 9 with a marked post-operative hypomanic syndrome which began at the end of the resection. In Fig. 3 two successive operations on the same patient are shown: first an undercutting of part of 10 and 9, followed by euphoria, incontinence and mild confusion, all clearing up in a few weeks. As the patient was not relieved of her pain, an undercutting of 10 and part of 11 was performed several months later, with no post-operative disturbance, but a good therapeutic result. This case shows conclusively that the post-operative syndrome cannot be due only to a quantitative factor (a comparison of the two cases of fig. 2 leads to the same conclusion).

2. *Orbital Operations.*

These may also be discussed with the help of the diagram, Fig. 1: only four resections or sections limited to the orbital region (areas 11, 13, part of 47, area recta anterior and posterior—as described by Beck (1)) were available. Two belong to class A, and two to class C. It is our definite impression that orbital resection tends to produce apathy and incontinence, particularly when it extends slightly on to the mesial side, into "area 12." In addition we have five operations involving the convexity and the orbital surface almost equally ; here again apathy seems a predominant feature, slight in A, very marked in C. Lobotomies with orbital involvement are discussed below. As a whole, the orbital post-operative syndrome is less conspicuous than that of the convexity

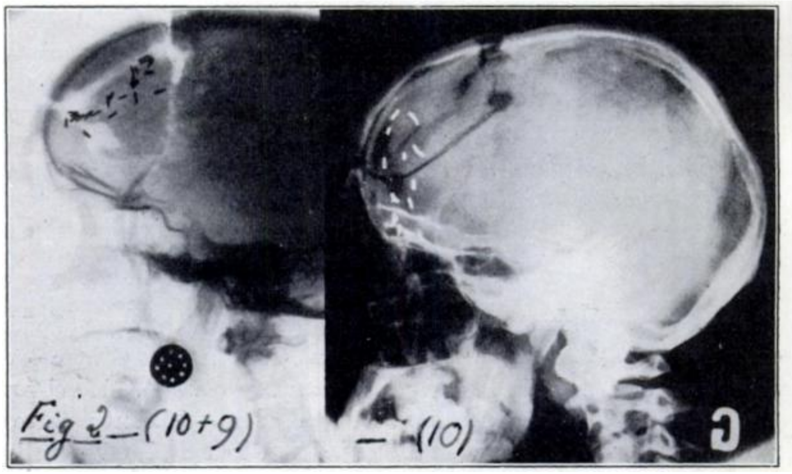

FIG. 2.

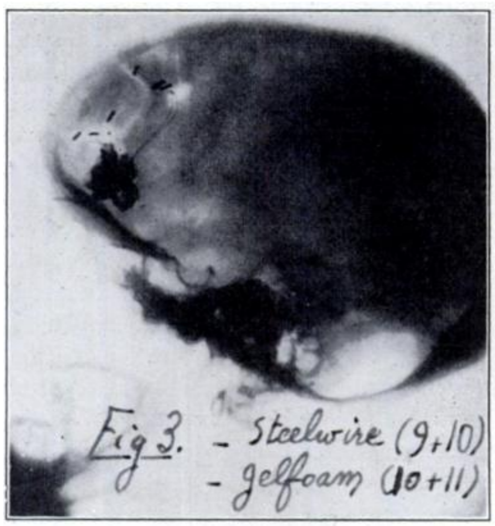

FIG. 3.

but it should be pointed out that the orbital resections did not extend far into area 47. We have never yet observed either restlessness or autonomic disturbances.

3. *Lateral Operations.*

Five cases of this group belong to class A (Fig. 1), one involving the junction of 8 and 9, two areas 10 and 45 and two areas 10 and 46. In class B we have no case. There were two in class C, but they were carcinomas in a very poor

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general condition. Our lobotomies, being as a rule very rostral, spare most of the fibre connections with the lateral prefrontal areas ; for this reason they cannot yield much information on the post-operative syndrome, which apparently is not very marked. Here again area 47 was not involved.

4. *Mesial Operations.*

This group, with 32 patients, is our second largest. Unfortunately it is not yet possible to establish tentative correlations with cortical structures, since there are no precise data on the limits and variations of areas 12, 32, 24 and 25. This uncertainty is particularly true of 32 and 12 ; area 24 is easier to recognize "macroscopically" since rostrally it envelops the genu of the corpus callosum, which as a rule is a sufficiently clear landmark during operation (9).

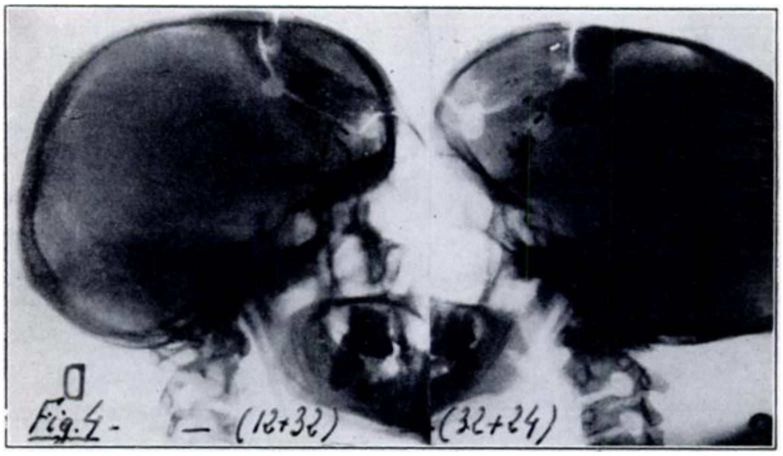

FIG. 4.

For purely practical reasons these cases have been divided into three groups, according to the mean level of the resection above the orbital roof on lateral X-ray view. Generally speaking the length and orientation of these mesial topectomies is about the same : 3 to 4 cm. on each side (1 cm. deep, 2 cm. high), directed obliquely upwards and backwards. *No obvious autonomic disturbances* have so far been observed.

The upper group (roughly corresponding to area 24) is made up of resections centred about 2 to 3 cm. above the orbital roof. We have five such cases (all topectomies), none of which was followed by a clinically significant post-operative syndrome.

The middle group (24 and 32) is centred about 2 cm. above the orbital roof. We have sixteen such cases with only one (cortical undercutting in a patient aet. 65) showing a marked syndrome of apathy, slight confusion, and incontinence. In about four cases there was slight agitation lasting 2–3 days.

In the lower group the operation extends up to 1 cm. above the orbital roof. We have eleven such cases (five topectomies, six undercuttings). In four there was marked apathy, with mental confusion and incontinence of urine

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lasting from two to six weeks (ages, 28, 57, 48, 25 respectively; two were topectomies and two undercuttings).

It is therefore suggested that confusion with apathy and incontinence are sequelae most often when cortical destruction extends downwards and forwards on to the mesial prefrontal surface, involving Brodmann's area 12. This indirectly confirms our impression obtained from the few orbital operations of our material, as pointed out above. Fig. 5 demonstrates the two types of mesial resection, with and without post-operative syndrome.

5. *Lobotomies.*

Only eight bilateral lobotomies are available for this paper, all belonging to the anterior or rostral type. They are represented in the diagram of Fig. 1. Three are in class B, all showing a hypomanic syndrome accompanied by

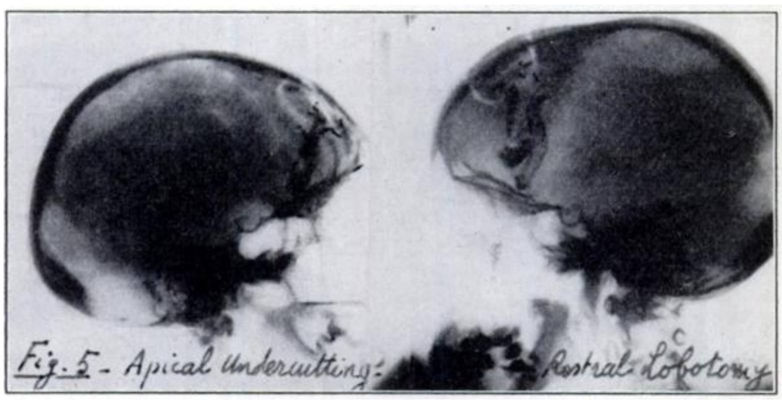

FIG. 5.

urinary incontinence. It is at least suggestive that their upper limit is definitely above that of the four belonging to class A. Only one is in class C with apathy and no incontinence (patient aet. 63).

In Fig. 5, lobotomy with a very typical hypomanic syndrome is contrasted with an apical undercutting with no post-operative syndrome whatsoever (ages 37 and 42 respectively). The main anatomical difference between the two seems to be the exclusion of area 9 in the case of the lobotomy; we believe that this is a corroboration of our findings in the topectomies of areas 10 and 9. In these two cases there is little, if any, difference with regard to orbital involvement, although there must be a difference with regard to lateral extension. However, on the frontal views which are not shown the lateral extension seems the same in both cases. The explanation is that we try to avoid cutting very far laterally in our lobotomies for fear of involving the anterior ascending branches of the Sylvian blood-vessels.

DISCUSSION.

This study of the post-operative syndrome suggests differences of function within the prefrontal region. This, we believe, would have been less clear if

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our material had consisted predominantly of complex psychoses, as is the case in the majority of publications on the surgery of mental disease. Most of our material consists of cases of intractable pain and of chronic neuroses. As has been explained previously (9), even if one adheres to a qualitative theory, it is necessary, in order to achieve a good result in a complex psychosis, to remove several areas, which—on the surface—looks like a quantitative effect. In our cases *analysis of therapeutic results* gives additional reasons in support of the qualitative theory of prefrontal activity. They have been published in various papers since 1948 (5, 6, 8, 9). The following is a summary of our results :

I. *Intractable pain :*

Bilateral operations :

Areas 9 and 10	30 good results	6 doubtful	9 failures
Lobotomies	3 ,, ,,	..	
11–13, 24–32, 45–46	0 ,, ,,	2 ,,	5 ,,

Unilateral operations :

9–10	1 ,, ,,	..	4 ,,
Lobotomies	1 ,, ,,	..	2 ,,

II. *Agitation and violence* (often with *epilepsy*) :—

All *bilateral :*

24–32	16 good results	..	7 ,,
9–10	5 ,, ,,	..	10 ,,

III. *Other Psychoses and Neuroses :—*

	17 good results	...	8 ,,

This table calls for some remarks : Group I contains cases ranging from purely organic pain to so-called psychalgias (6). The usual reasons for failure seem to be a resection not extending far enough over both areas 9 and 10, but this should not be interpreted as supporting a quantitative factor (as long as the minimal amount (2 × 12 grammes) is excised). Some failures cannot be explained by the operation of purely anatomical factors ; the search for psychological factors is imperative (7).

Group II is specially noteworthy for the relationship between generalized epilepsy and behaviour disorders (9) ; when the latter improved or disappeared we often saw a strikingly beneficial effect on the fits, though no cortical focus was found in the electroencephalogram or corticogram of the convexity or the mesiofrontal region (10). Group III is a heterogeneous group in which obsessions and phobias seemed greatly improved by the mesial operation ; in severe psychoses more extensive prefrontal exclusions are often necessary.

The therapeutic results supply some additional data in favour of a qualitative theory although, on the whole, this evidence is less convincing than the results of the present study of post-operative syndromes. The question arises whether eventually there is a *correlation between ultimate results and immediate syndrome*. So far our material is not in favour of any such correspondence neither in cases of intractable pain nor in schizophrenias. In Figs. 2, 3, 4, 5 all the operations not followed by a significant syndrome finally yielded good results whereas the others were failures, but, of course, the reverse is often also true. For practical reasons, however, the appearance of a hypomanic post-operative syndrome in cases of intractable pain is a good sign, since (if what we propose here is confirmed) it proves the exclusion of a large part of area 9; by cutting down to the level of the foramen caecum or 1 cm. below, most of area 10 is very likely to be excluded: thus, what appears to be the best surgical intervention in intractable pain can be performed with some precision.

The search for selective prefrontal surgery aimed at causing more specific and or less deteriorative changes is a relatively recent one. Cunningham Dax in 1943 started partial lobotomies which he has developed since (4), but for the most part he has dealt with complex psychoses and the anatomical definition of the operations does not appear to be simple. Penfield (15) reported the first gyrectomies: even at that time he emphasized the probable importance of the study of the post-operative syndrome, and went as far as to ascribe psychomotor akinesia with incontinence and severe intellectual disorders to the bilateral removal of the anterior part of areas 6 and 8. Since we never perform a prefrontal operation situated more than 9 cm. above the foramen caecum we have no such cases in our series. Pool (3), who with Mettler originated topectomy, has demonstrated the effect of resection of areas 9, 10 and 46, on "anxiety." More recently, in still unpublished observations, Rylander on patients operated by Sjoquist (17, 18) has studied the immediate post-operative syndrome with great precision, his conclusion being that a convexity undercutting is often followed by a hypomanic syndrome, which is usually absent after orbital undercutting. Scoville, who originated the excellent technique of cortical undercutting, was not in favour of the qualitative theory in his first publications, but recently appears to have observed different personality changes following qualitatively different prefrontal undercuttings: unfortunately so far only an abstract of his paper (19) is available, which deals for the most part with permanent effects. His findings on these changes are more pronounced after a convexity operation than after one on the orbital region. The convexity operation is advised for pain with anxiety (*souffrânce* in our terminology (8)): the results of the mesial operation seem to be more promising than judged previously, thus confirming our findings; the orbital operation, of which we have little experience, is advised for relatively mild psychoneuroses.

On the other hand, recent careful psychological work on lobotomies is not in favour of qualitative action (16); the comparison is made, however, between standard and rostral lobotomies. Both these operations are performed along transverse planes, whilst topectomies and undercuttings follow more closely the curvature of the lobe, thus resulting in an entirely different extent of the excluded areas. It is possible that a psychological analysis of this kind applied to our types of selective surgery might yield somewhat different results;

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psychological work along these lines is actually in progress, as mentioned above.

Thus it can be seen that the tendency of modern research on the prefrontal lobes is in accord with our present observations. The hypomanic syndrome appears to be related to operations on the convexity and not to interventions on the mesial or the orbital cortex, thus confirming Rylander's findings. We venture to go a little further by attributing it to area 9 rather than to area 10. A possible explanation might be the release of the anterior hypothalamus, the mechanical irritation of which often produces an acute hypomanic syndrome in the course of the removal of a pituitary tumour. In that respect a case of area 10 topectomy with no post-operative syndrome (death from shock on the 11th day after a routine blood transfusion) showed that there were no degenerating efferent fibres from area 10 to the hypothalamus, in contrast to what happens after more posterior lesions in the orbital and dorsal prefrontal regions (Beck, Meyer and Le Beau, in press). Further anatomical work after similar selective operations will be of considerable value for any further physiological analysis of the prefronto-hypothalamic and prefronto-thalamic systems.

As the post-operative syndromes are largely transitory the question of *stimulation rather than exclusion* is raised. Corticography was performed on several of our patients. In all cases but one, areas adjacent to the resected tissues showed, as would be expected, slow waves of the delta type. This does not lend any support for the assumption of possible stimulation of these regions. The one case which showed a very transitory ($\frac{1}{2}$ hour) epileptic focus was a case of generalized epilepsy with behaviour disorder, in whom a small subarachnoid haemorrhage involving area 9 on one side was the site of quickly subsiding spikes and sharp waves. This particular patient had no significant post-operative change after bilateral resection of areas 24 and 32.

Finally one may well ask what kind of light the knowledge of post-operative syndromes casts on mental function. This is mainly a question of theory: firstly one has to correlate, if possible, specific mental changes with the ablation of distinct prefrontal areas; then to express these changes in measurable variables. At least for the time being, factorial analysis seems to us the most promising method for the selection of psychological elements which in all likelihood will be quite different from the old classifications (5); the eventual correlation of such elements to different brain areas would be a definite advance.

Conclusions.

A study of the immediate post-operative syndromes in 134 patients submitted to selective prefrontal surgery leads to the following conclusions:

(1) A convexity resection (areas 9 and 10) is more often followed by a marked syndrome than an orbital resection (areas 11 and 13), and much more often than a mesial resection (areas 24 and 32).

(2) Resection of area 9 seems to release a hypomanic syndrome, while resection of area 10 usually is not followed by obvious behavioural disturbances.

(3) Perhaps resection of "area 12" is responsible for the appearance of marked apathy with incontinence.

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