Involuntary movements following stereotactic operations for Parkinsonism with special reference to hemi-chorea (ballismus)

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When one examines stained sections of the thalamic area of the brain and sees the mass of fibres and cells in this area interconnecting almost every structure in the vicinity and receiving and sending millions of fibres to remote parts of the brain and spinal cord one marvels at the temerity of the early stereotactic surgeons who dared to place electrodes in this area and make massive destructive lesions. One might imagine that such lesions would have a profound effect on gait and motor control, on sensation and even mental function but, in practice, the clinical effects of such massive lesions are hardly detectable. Whether this reflects the high degree of adaptability in the brain or the relative unimportance of this area is difficult to determine. The main difficulty encountered by the surgeon probing this area is to produce any effect at all. All varieties of test procedures are used to determine the efficacy of lesions—stimulation, micro-electrode recording, 'trial lesions' with heat or cold—and yet, in some instances, no clinical effect can be produced.

Most of such lesions are made for the treatment of involuntary movements, particularly the tremor and rigidity of Parkinsonism. The results in general are excellent, yet these abnormal movements are presumed to be the result of cell and fibre destruction and it is a matter for great surprise that such lesions do not in themselves invoke involuntary movements. That we find such concepts difficult to understand may well reflect wrong thinking on our part concerning the organization of the nervous system. When we see a discrete tract of fibres, or a collection of cells of similar size and connexions, we tend to think that they must serve some single function. We may accept the idea that this function differs from time to time and may well depend on the state of other parts of the nervous system at that time. Our minds, however, are not sufficiently alive to the possibility that such a discrete system may well be serving several functions, often directly opposed to each other. Fibres which facilitate or inhibit certain function may well run

side by side and the physical destruction of both could well have no apparent clinical effect at all.

Involuntary movements are most often the result of infections, of degenerations of unknown cause, or of developmental anomalies. It is easy to conceive that such processes may affect only facilitatory or inhibitory fibres, but not both, and that the gross physical lesions made by the surgeon destroy both and cancel out the imbalance. Tremor and rigidity, ballismus and athetosis, are very rarely caused by discrete physical lesions such as tumour growth, though occasional cases are reported and this suggestion may well account for the fact that the surgeon destroying large areas of the globus pallidus, lateral thalamus, and adjacent structures relatively seldom induces involuntary movements or makes them worse.

Such complications do, however, occur, in a small proportion of cases, about 2.5% overall, and the situation of such lesions, together with the pre-existing state of the nervous system, seemed a worthwhile study and forms the basis of this paper.

INCIDENCE OF INVOLUNTARY MOVEMENTS FOLLOWING OPERATION

Personal contact with many neurosurgeons carrying out stereotactic operations has shown that all are familiar with this complication. Perusal of the series of cases reported in the literature does not show, however, that this is a universal experience. In many series this complication is not mentioned specifically though on the other hand no mention is made that such movements had never occurred following operation. In some cases in my own experience the movements have been very slight and short-lived and possibly only personal observation of every post-operative patient every day until the time of discharge from hospital has brought them to light.

For example, Taarnhøj, Arnois, and Donahue (1960) in 118 patients and Gillingham, Watson,

Donaldson, and Naughton (1960) in 60 patients do not mention this as a complication though in a later paper (Gillingham, Kalyanaraman, and Donaldson, 1964) they report one case in 344 patients with a unilateral operation and three cases in 83 bilateral operations. Spiegel and Wycis (1958) in 50 cases of Parkinsonism do not record an example but mention later in their paper that in cases of choreoathetosis the movements may be made worse by operation. The largest series of cases are those recorded by Cooper and he states (1961) that in his first 1,000 cases this complication occurred in 36 patients. The movements were all transitory and lasted from one day to five months. Only one example occurred in 500 operations on the globus pallidus, the others were related to thalamic lesions.

Of considerable interest are two recent series of operations in which a lesion has been deliberately made in the subthalamic area. A series of 58 patients reported by Andy, Jurko, and Sias (1963) resulted in ballismus in five. In three it stopped in a week and in the other two in two months. Their lesions were presumed to involve the field H of Forel, the zona incerta, and the pre-rubral field medial to the subthalamic nucleus. All lesions causing ballismus were lateral to 10.5 mm. from the midline but many similarly placed lesions did not result in ballismus. Spiegel, Wycis, Szekely, Adams, Flanagan, and Baird (1963) report 25 cases in which similar lesions were made but none developed ballismus.

Gros, Serrats, Adib-Yazdi, and Parker (1963) report 185 cases with transient athetosis in 11 and persistent ballismus in one. Dierssen, Bergmann, Gioino, and Cooper (1961) reported one case from Cooper's series in which a post-mortem study had been made.

In my own series involuntary movements have appeared in 10 cases in a series of 200. In all but one they have been mild and transitory. The overall incidence amongst reported cases with thalamic or subthalamic lesions would appear to be a little over 2%.

TYPES OF INVOLUNTARY MOVEMENTS FOLLOWING STEREOTACTIC SURGERY

The nomenclature of involuntary movements is still in a very unsatisfactory state and one can never be quite certain just what an author means by terms such as ballismus, chorea, athetosis, etc. Careful study of the individual patient, usually with the aid of slow-motion film, enables one to give a clear description of his movements but it is seldom possible to give them an exact definition in more general terms and, hence, the use of multiple terms such as choreoathetosis has become common. We owe to Denny-

Brown (1962) the best attempt to define such movements in physiological terms and his definition of athetosis and dystonia are supreme examples of acute observation combined with clear thinking and lucid description. Athetosis he considers to result from the release of two conflicting postures, a 'fluctuation in posture superimposed on a persistent attitude'. The swing is usually from hyperextension of fingers and wrist and pronation of the forearm to full flexion of the fingers and wrist and supination of the forearm. Athetosis refers to the swings of movement and not to the posture, for which he uses the term dystonia.

Chorea is more difficult of definition and the one may merge into the other. In chorea there is a continual flow of movement without the irregular alternation of posture that characterizes athetosis. There is no underlying posture. Denny-Brown states, however, that 'in a more coarse form the movements become identical with those of athetosis' and later that 'the movements as such, in terms of parts involved and variability in amplitude, are the same. The more rapid performance of choreic movements is but a relative criterion'.

TREMOR AT REST This is the typical tremor of Parkinsonism and needs no further definition. In no case was this type of tremor initiated in patients whom it had been absent before operation. This appears to be a universal, though surprising, experience. It will also be recalled that it has proved very difficult to produce such tremor in animal experiments, even in the monkey. In some reported cases tremor appears to have been aggravated after surgery, usually in the post-encephalitic cases. No such aggravation was experienced in this series.

INTENTION TREMOR In this series 24% of patients had intention tremor before operation; in some it was severe and disabling. In most it was abolished by thalamic lesions but in two, not included in the incidence figures, it was thought to be slightly worse after operation. This type of tremor is easy to demonstrate and only too apparent to the patient but most difficult to quantitate. In both cases the worsening was transitory and they will not be considered further here.

ATHETOSIS This occurred in two cases. In each it affected the forearm, wrist, and fingers, and consisted of a writhing movement with flexion and extension of the fingers and wrist, and pronation-supination of the forearm. They exemplified well the alternation of posture so well described by Denny-Brown (1962). The movements were always the same, occurred in spasms, and were often absent

when the patients were at rest or their attention was occupied elsewhere. They lasted less than 48 hours and follow-up over several years has not shown any recurrence.

CHOREA (BALLISMUS) Terminology in this type of movement is difficult and many authors have concerned themselves with the distinction between chorea and ballismus: some consider them identical. In most cases the movements are persistent, completely irregular and faster than those of athetosis. One factor which may be agreed upon is a continual flow of movement. In some cases, mentioned below, the movements were at first quite slight and intermittent. In one case they affected the distal joints and were, at first, so mild that they were mistaken for simple fidgeting. They gradually spread up the arm, however, and by the time the shoulder was affected were wild flinging movements with rotation at the shoulder which would be recognized immediately as ballismus.

They appear at first sight to be quite irregular and to have none of that regular alternation of posture which characterizes athetosis. And yet if one watches such patients over a period of time, in life or on film, it becomes apparent that many grotesque postures are adopted and these recur again and again, though in quite random fashion.

In some the movements affected the distal joints, were quite irregular, exhibited a continual flow of movement, and could easily be classed as chorea. In others, the movements were affecting the proximal joints, were therefore of wide amplitude and exhibited rotation at the shoulder, and therefore could be classified as ballismus. In others, the initial chorea became converted in the course of time to typical ballismic movements and it is this fact that suggests the close relationship between the two. Denny-Brown (1962) would distinguish ballismus absolutely from chorea on the grounds that the essential feature of the former is the rotary character of the movements, especially external rotation at the shoulder, and affection of proximal joints. He admits, however, that they may 'in time develop a flowing quality which could be termed choreic, but its characteristics are still those of mid-brain disorder'. I find this distinction difficult to accept and record below one case at least in which chorea appeared to develop into ballismus.

The arguments have been clouded in some degree by a consideration of hemiballismus occurring spontaneously from vascular disease of the subthalamic nucleus or elsewhere. The movements are violent, affect the proximal joints, are continuous and irregular and affect one side of the body. To deny the term to similar movements which are less

violent because they involve the distal joints, are not continuous or involve only one limb, is simply semantic pedantry. Many cases have been described in which the initial movements were mild and affected only one limb or part of a limb and yet developed subsequently into the characteristic picture of hemiballismus (Martin, 1927; Kelman, 1945; Russell Meyers, Sweeney, and Schwidde, 1949; Bedwell, 1960). There can be little doubt that the term hemiballismus has been used to denote a special disease entity in which the mode of onset, course, and pathology are as important as the type of movement. The position was admirably summed up by Martin and Alcock in 1934 who wrote: 'There may be some advantage in employing the special term hemiballismus for such an unusual and remarkable symptom, but if it is employed it should, in our opinion, be used to denote a special intensity of chorea and not a special form of it.' Lea-Plaza and Uiberall (1945) considered that there was a case for considering ballismus as a special clinical syndrome rather than a special form of movement.

Russell Meyers *et al.* (1949) put forward somewhat more concrete evidence for considering that hemiballismus was distinct from athetosis and chorea. They were reporting cases in which ballismus had been alleviated or cured by subpial resection of fibres in the pre-motor cortex. These operations had been largely successful. They stated that similar operations undertaken in cases of chorea and athetosis had not been successful. It is not clear, of course, just what they meant by these terms and it is interesting to note that H. A. Riley in the discussion on their paper said that he did not think that their cases were ballismus at all. The movements affected the face, which was not the case in ballismus, and he would consider that they were largely choreic with a minor athetoid element! To what confusion can terminology lead one.

My conclusions would be that minor degrees of athetosis do constitute a clinical entity, as defined by Denny-Brown. Where there is a 'continued flow of movement' and regular alternations of posture are not apparent then the term chorea should be used. Athetosis may develop into chorea when the movements become continual and many different postures are alternated in a random manner.

The severity and amplitude is largely related to the joints involved and the wide flinging movements of ballismus may be related simply to this fact. From personal observation I would state that the flowing movements of chorea may develop a rotary movement at the proximal joints and hence become by definition, ballismus. It is also an impression that the sudden flinging movements, so characteristic of ballismus, may be myoclonic jerks superimposed

on chorea but this would necessitate more exact investigation to prove.

In this series five patients developed chorea immediately after operation and in a further two cases it developed at a considerable time interval after operation.

MYOCLONUS Two patients suffered from typical flexion jerks of myoclonus. In one these were mild and affected the arm only, in the other they were prolonged and affected both arms. Both recovered completely. Denny-Brown (1962) has described these as occurring spontaneously in several forms of extrapyramidal disorder and has studied their physiological nature.

RHYTHMIC BLINKING Two patients suffered from rhythmic lid closure. In one there was an initial phase of complete lid closure for several weeks, but even during this time rhythmic closure movements were occurring all the time. Later the lids were opened but forced blinking continued for some time after. In the other patient there was rhythmic blinking at about two per second for a period of a week or so. These movements correspond to the segmental dystonia of Denny-Brown and are evidently closely related to the oculogyric crises seen in the post-encephalitic Parkinson patient. The essential difference, however, appeared to be that these were movements and not postures. The regular alternation seen may bear the same relationship to dystonia as athetosis.

MATERIALS AND METHODS

These complications occurred in a series of 200 operations for Parkinsonism. All cases were classified under this heading and the majority were in middle-aged people without apparent known aetiology. In 9% the aetiology was thought to be some form of encephalitis. In such cases either the condition had followed an illness identifiable as encephalitis lethargica, or there were other features indicative of this aetiology, the chief amongst these being the presence of oculogyric crises or tics, disturbances of ocular movement or pupillary reaction, or an onset in childhood or very early adult life.

Pre-operative assessment was carried out in hospital after drugs had been withdrawn. This included a numerical assessment of the patient's abilities modified from the scheme of Schwab and England (1958), a numerical assessment of the degree of tremor and rigidity in each limb, trunk, head and neck, a numerical assessment of akinesia, speech disturbance, mental change, and neurological findings. A careful psychiatric assessment was carried out by Dr. Warburton and will be the subject of a further report. Routine scalp E.E.G. records were made pre-operatively and post-operatively and the degree of cerebral atrophy was assessed at the time of operation

from the depth of the subarachnoid space, intracranial tension, and lateral ventricular size.

The method of operation was the same in every case though the exact site and size of the lesions varied a little from case to case as will be seen below. The Hughes stereotactic instrument was used throughout (Hughes, 1961a). The lateral and third ventricles were outlined with air and Myodil, and certain landmarks were identified and measured, allowance being made for x-ray distortion and magnification. The reference points used were: the anterior and posterior commissures and the minimal distance between them, the thalamic height, *i.e.*, the distance between the intercommissural line and the highest point of the floor of the lateral ventricle, and the width of the body of the lateral ventricle. A series of outline diagrams of the various thalamic nuclei were prepared from standard atlases and a series of 30 brains sectioned after hardening. The nuclear outlines were constructed from percentage measurements of the distances given above and the outline chosen for the series of measurements which approximated most closely to those of the patient (Hughes, 1961a).

The primary location of the intracerebral electrode was then selected from the nuclear outline, usually in the centre of the nucleus. Two separate lesions were made in each case, in the ventro-oralis anterior and ventro-oralis posterior (Hassler, 1959). In half the cases the first lesion was made in the anterior nucleus and in the other half in the posterior nucleus.

After insertion of the electrode two sets of observations were made. First, records of electrical activity were taken from bipolar and unipolar electrodes, together with standard placement of scalp E.E.G. electrodes. In some cases, micro-electrode recording was made during the insertion of the electrode. Secondly, the effect of stimulation was tested using a square wave pulse, at three values, 8, 20, and 40 c/s., and pulse width 1 msec. Only effects produced by stimulation at a D.C. level of less than 5 volts were considered to be the result of local stimulation. In some cases the effect of a lesion was further tested by local cooling to +5°C. with a cooling probe (Clarke, 1963). From these various results a decision was then made as to making the lesion. If, for instance, stimulation had indicated close proximity to the internal capsule then the electrode would be moved 2-3 mm. medially, if proximity to sensory input nuclei it would be moved anteriorly, and so forth. Lesions were made with an R.F. lesion generator, electrode size 5 mm. × 1.2 mm., and the estimated size of lesions was 6 × 3 mm.

After each lesion an estimate was made of its effect on tone, tremor, and power, and further scalp and depth E.E.G. records were taken. The electrode might then be moved or the lesion extended following these tests. For instance, if rigidity had been abolished in the arm but not in the leg the electrode would be moved a little laterally and inferiorly. The second lesion was then made on the same principles. The appearance of theta and delta activity in the E.E.G. was considered an absolute contra-indication to further lesions.

It will be seen, therefore, that the site and extent of lesions varied slightly from patient to patient, in terms of brain coordinates. It was felt, however, that adjusting the

electrode on this basis probably achieved a closer anatomical or physiological uniformity of lesions than reliance on brain coordinates alone. The theoretical arguments concerning the location of these lesions is dealt with more fully below.

Post-operative assessments were made and E.E.G. traces repeated before the patient left hospital, usually after seven to 10 days. Follow-up assessments and E.E.G. records were made at three months and thereafter at yearly intervals.

CLINICAL MATERIAL

TREMOR AT REST It appears to be a universal finding that the tremor at rest of Parkinsonism is never aggravated by lesions in the thalamus, globus pallidus, internal capsule and structures included in this area. If degenerative disease in this area is the cause of tremor at rest this is a surprising finding but one which must be confirmed by experience of thousands of cases throughout the world. Three theoretical explanations suggest themselves. First, that such lesions inevitably destroy fibre systems that inhibit tremor as well as those that initiate it. It may well be that inhibitory/excitatory systems consist of fibre tracts lying side by side and only intrinsic degenerative processes are capable of destroying the one without the other. Secondly, that more than one lesion is required to produce this type of tremor and the second is remote from the sites usually damaged by surgery. Such an explanation seems unlikely, for in this group of patients tremor is already present and a second lesion, if such be needed, is presumably, already present. Thirdly, that lesions producing tremor are in some quite different area of the brain. This may be a possible explanation, for most pathologists who have studied Parkinson patients claim that the initial lesions, and the most advanced, are in the substantia nigra. Against such an explanation is the claim by Meyers, Fry, Fry, Eggleton, and Schultz (1960) that nigral lesions are very effective in controlling tremor.

That there may be some synergy between the two sides of the brain in the control of such motor functions seems amply confirmed by the common experience that whilst tremor is usually well-controlled on the contralateral side after such lesions, that on the ipsilateral side sometimes gets worse or appears if previously absent.

INTENTION TREMOR Intention tremor is often present in Parkinson patients (*vide supra*) and in a few cases this may be aggravated following stereotactic lesions. Two such instances occurred in this series but both were quite transitory, lasting no more than a few days. Though my personal experience of lesions in the globus pallidus is small it would seem that such

happenings are commoner with thalamic lesions than those in the pallidum. It is commonly accepted that lesions of the red nucleus are associated with intention tremor and it may be that in these two cases post-lesion oedema had affected this nucleus temporarily. Against this hypothesis is the fact that lesions in the ventrolateral thalamus are highly efficacious in controlling intention tremor and in 18 cases so treated this type of tremor was not aggravated in a single case.

ATHETOSIS This was thought to have occurred in two cases. This qualification is made because the type of movement, although specified at the time as athetosis, was exactly similar to movements in another patient which became more severe and clearly ballismic.

No. 29 M.G., female, aged 49. A four-year history of tremor of right arm and leg. This was a wide amplitude 'flapping' tremor. Rigidity was moderate and akinesia slight. Total abilities rated at 74%. Post-operatively there was slight weakness of the arm and leg completely recovered in 24 hours. Athetosis was noted 12 hours after operation, was confined to the wrist and fingers, and completely disappeared in 48 hours. Follow-up at one and a half years showed no athetosis and an excellent overall result with total ability rated at 90%.

No. 36 Female, aged 39. A ten-year history of slurring of speech and seven-year history of tremor. Tremor was moderate and affected right limbs more than left. Rigidity was moderate, speech badly affected, and general akinesia severe. Ability rated at 84%. Left-sided operation resulted in abolition of tremor and rigidity and some improvement in speech. Athetosis was noted six hours after operation, was similar to the previous case, and involved the fingers and wrist and forearm. It was usually absent, came on when her attention was directed to the limb and she almost seemed to be able to bring it on at will. This had wholly disappeared within two weeks. Follow-up at three years showed continued absence of tremor and rigidity on the right side and no trace of athetosis. Her abilities had been in the 95% range but at the time of examination had fallen to 87% due to increasing tremor and rigidity on the left side.

In the first case check of lesion sites showed that these were rather more posterior than usual and in both cases the lesions had extended a little way below the anterior-posterior commissure line. It will be noted that both patients were rather younger than the average age of Parkinson patients.

CHOREA (BALLISMUS) The majority of patients in this series suffered from a post-operative involuntary movement which conformed to chorea or in its extreme forms ballismus. There were four in number.

No. 136 A.R., male, aged 45. A 24-year history of tremor on the left side. There was no history of encephalitis or stigmata to suggest this. There was severe tremor and rigidity on the left, slight on the right. Moderate akinesia and slight speech defect. Right-sided operation resulted in an excellent result and follow-up at one year showed improvement in ability from 63 to 86%. Mild ballismic movements were noted eight hours after operation and persisted occasionally for 10 days. These affected the left hand and forearm. There was no recurrence after 10 days.

No. 39 T.K., aged 39, male. Twenty-year history of tremor and stiffness of the right limbs with oculogyric crises. Classified as post-encephalitic. There was severe tremor and rigidity of the right limbs, slight rigidity of the left. Mild akinesia and no speech defect. Ability was rated at 74%. Left-sided operation was carried out and after the first lesion in ventro-oralis anterior short bursts of high-voltage slow activity were seen in the monitoring E.E.G. The significance of this was not realized and a second lesion was made in the posterior nucleus. About 30 minutes after the first lesion it was noticed that ballismic movements in the arm had appeared and followed each burst of slow activity in the E.E.G. These movements became worse for 48 hours and affected the arm severely and the leg slightly less. During the next two weeks they lessened to a mild degree but have persisted for a period of four years.

No. 120 W.E., male, aged 61. A history of encephalitis at the age of 24 followed by slowly progressive weakness, tremor, and stiffness of the left limbs. There was severe tremor on the left and slight rigidity, no abnormal signs on the right, mild akinesia and no speech or mental disturbance. His ability was rated at 58%. Right-sided operation was followed in 12 hours by the appearance of fairly severe ballismic movements in the arm and to a lesser degree in the leg. These got worse for three days and then improved, ceasing at two weeks. Follow-up at five months showed an excellent overall result with ability improved to 93%, no tremor or rigidity, and no recurrence of ballismic movements.

No. 21 E.F., female, aged 45. A five-year history of tremor and stiffness of the left arm, cramps in the legs, and slowing of speech. Right thalamotomy was carried out with no complications and an excellent result. Good results were maintained but owing to steady deterioration on the right side a left thalamotomy was carried out two years later. For 48 hours after operation there were rapid sweeping movements of the right arm, mainly adduction movement at the shoulder. These ceased after 48 hours and there has been no recurrence at nine months.

This group, although very small, seems to have certain characteristic features. The average age was low, 45 years, and the age of onset of disease much lower, being 25 years. Three were almost certainly post-encephalitic cases and the average length of history was long, 21.5 years, with a slow evolution of symptoms. In three the movements were mild

and short-lived, in only one did they persist in severe form over a period of several years. The site of lesions appeared to be similar to the majority of lesions made for Parkinsonism and in no case was the lesion estimated to have involved the sub-thalamic nucleus or, in fact, to have extended below the AC-PC line.

MYOCLONUS In two instances the abnormal movements following operation consisted of sudden jerks, usually flexion movements at elbow, shoulder, or hip. These were single movements occurring at irregular intervals. Usually absent at rest they were frequently initiated by drawing the patient's attention to them.

No. 206 V.M., female, aged 44. Onset of rigidity and weakness after parturition at age of 41. Extreme rigidity and akinesia was present. Left-sided operation with excellent results on tremor and rigidity. Twenty-four hours after operation sudden jerks of the right arm appeared, being flexion at the elbow. These were closely related to attention. They disappeared in 15 days and no return was noted in follow-up a year later. The general effect of operation on rigidity was excellent.

No. 233 S.C., male, aged 57. Onset of severe tremor six years ago aged 51. Extreme degree of tremor involving whole body. Right-sided operation including, in this instance, a lesion in the medial globus pallidus. Excellent control for tremor lasting a month only; operation repeated four months later with again an excellent result. He was so pleased with this that he persuaded me to do the other (left) side at the same admission. This was carried out two weeks later. Two types of involuntary movements developed within 24 hours of this second side. The first type was a myoclonic movement consisting of sudden jerks of flexion of elbow, adduction at shoulder, flexion at hip, or rotation of the head. These started in the left arm and hand and rapidly spread to involve the whole of the left side of the body and then the arm on the opposite side. These gradually subsided and ceased at 15 days, there being no return at follow-up three years later. There were good clinical results in so far as tremor was concerned. The second type consisted of screwing up of the eyelids with tight lid closure. In fact, he did not open the eyes for a week but even when tightly closed slow rhythmic movements of lid closure could be seen. These persisted for a further three weeks. The movement involved both eyes symmetrically, were irregular and occurred in short bursts lasting 15 to 20 seconds at a rate of less than one per second. The rate and symmetry remained the same throughout but as time went on the bursts became shorter and with longer intervals between.

OTHERS The only other type of involuntary movement following operation is that already described above, rhythmic blinking. Seen in severe form in S.C. described above it also occurred in lesser degree in one other patient.

No. 104 A.W., male, aged 53. After presumed encephalitis in 1922 he presented with a 23-year history of rigidity, immobility, and speech defect starting at the age of 33. There was no history of oculogyric crises or other tics. Operation on the left side was carried out in 1961 with good effect. The second side, right, was undertaken two and a half years later. This again produced excellent effects on rigidity and the slight tremor that had been present. Twelve hours after operation it was noticed that he continually blinked the eyes and this, as in the other case, occurred in short bursts lasting 15 to 20 seconds at a rate of less than one per second. He was unable to control this and it was closely related to attention being directed to this symptom. It gradually declined and stopped two weeks after operation without recurrence at follow-up three months later.

DELAYED ONSET OF INVOLUNTARY MOVEMENTS So far I was not unduly concerned at this incidence of involuntary movement, it seemed to be a universal experience and the incidence in our series was no greater than in most and less than some. All but one had cleared completely in a few days to two weeks without recurrence at fairly long follow-up. The one case that had persisted had given evidence during operation of such movement and if we had realized its significance and had not made a further lesion this might have resulted in a similarly happy outcome. During the course of routine follow-up examinations of these patients, however, three patients came to light in whom ballismus had appeared on the side treated for Parkinsonism some time after operation.

No. 61 J.Hd., female, aged 36, was the first to be identified. Tremor and mild rigidity had appeared in the left limbs at the age of 25 and had gradually progressed. Operation was carried out on the right side with excellent results. Six months later she had a fall without serious injury and immediately afterwards developed coarse ballismic movements in the left wrist and hand. These might well have been described in the early stages as athetosis but over the ensuing months they gradually spread to the whole arm and then appeared in the foot and ankle and became frankly ballismic. Two and a half years later, with some trepidation, further lesions were made in the ventro-lateral thalamus extending the original lesions further forwards and backwards. This resulted in a very temporary improvement in her movements which lasted only a few weeks and since then they have gradually become more and more severe.

No. 30 J.H., female, aged 46. Onset of tremor and rigidity 36 years previously at the age of 10. Advanced rigidity and severe tremor and numerous tics, the most frequent of which was a high-pitched scream. Left thalamotomy was carried out with excellent control of tremor and rigidity on the right side. Two and a half years later there was no tremor on the right and no rigidity. Akinesia and tics were not changed. At this time, however,

slight ballismic movements were noticed in the right hand and they have slowly increased since then.

No. 89 F.G., male, aged 57. An eight-year history of increasing weakness and stiffness of the limbs, akinesia, and severe speech loss. Left thalamotomy was carried out and tremor was abolished and rigidity greatly improved on the right side. Two and a half years later slight ballismic movements appeared in the right hand and wrist. These were mild and might have been mistaken for fidgeting. Over a period of six months they have got slightly worse.

Two of these patients were post-encephalitic and the third had a longer history than usual in the group with very slow progression. It might be considered that these events were part of the natural evolution of the disease and unconnected with the operation. The fact that in each case it occurred on the operated side is difficult, however, to overcome.

That such an event does occur from the disease alone is shown by one case in the series.

No. 170 E.S., male, aged 55, presented with a 20-year history of increasing tremor and rigidity on the right side. The left arm had been removed for an accidental injury as a child but three years after the onset of tremor involuntary movements were noticed in the left arm stump and have continued since, getting slowly worse. It was difficult to assess the true nature of these movements for they were confined to the shoulder muscles and the short stump, but they appeared to be true ballismic movements. Left thalamotomy was carried out which abolished tremor and rigidity in the right limbs. The ballismus was unchanged.

THE LOCATION OF LESIONS As with all stereotactic surgery the exact position of the lesions made in these cases can only be predicted approximately. Inaccuracy derives from three sources: that inherent in the machine used, that resulting from relating coordinates of the machine to structures in the brain, and, lastly, variations in the relationship between these reference points and nuclear masses and tracts in an individual brain.

The machine used is capable of locating an electrode in space with an accuracy of 1 mm. at the electrode tip, all coordinate settings are double-checked and written down at the time of operation and further checked after operation to ensure that no arithmetical error has been made.

The relating of the frame coordinates to the brain is accomplished by means of a pair of radiographs taken at right angles in constant relationship to the frame and to the x-ray tube which are coupled together on a special table. Standard allowance is made by mathematical means for x-ray magnification. These figures seem to be beyond reproach, and

in a number of cases early in the series a droplet of Myodil was used as a marker and post-operative check radiographs showed that this was exactly where it had been presumed to be.

Some error may appear when the machine frame is not exactly parallel to the sagittal plane or at right angles to this. When the frame was obviously out of alignment it was re-applied or direct allowance made for the angle of inclination according to the method described by Mark, McPherson, and Sweet (1954). Mathematical calculations showed, however, that when the angle of inclination was quite small and the target points close to the reference points, as is the case in this method, then the possible deviation was so small as not to constitute any gross error.

Fortunately, no patient in this series has died as a result of operation and only five have died sub-

sequently of other causes, usually a terminal bronchopneumonia. Of these five, two necropsies have been obtained but neither of them has been less than a year after operation and the appearance of the acute lesion remains unknown. In these cases gliosis and contraction of tissues distorts adjacent structures so that the exact coordinate position of the lesion is difficult to determine. Brain blocks were sectioned serially in the coronal plane, at right angles to the AC-PC line and at known distances along it. In these specimens the lesions appeared to be in the correct coordinate position. One can presume, therefore, that error from the first two factors is slight and probably not more than 2 mm.

Geographical error, however, may be considerable and no satisfactory method of overcoming the variability of nuclear position has yet been devised.

FIG. 1. The estimated position of lesions in some patients developing hemiballismus after thalamotomy. In each illustration the lateral view of the lesion is on the left and the antero-posterior view on the right. The horizontal solid line, marked A.P. in the first illustration, represents the intercommissural plane and the vertical from it, marked 500, represents the mid-point of this plane. In each illustration the position of the subthalamic nucleus (cross-hatched) is indicated below the intercommissural line.

The percentage system described above would seem to reduce this error to a minimum and it is thought that the adjustment of electrode position from stimulation and recording data further reduces this error. Nevertheless, one cannot be certain in all probability that more than 70% of such lesions will be wholly within a nucleus of the size of the ventro-oralis anterior or posterior. Certain reference points, however, have greater validity. In considering ballismus one is naturally concerned with possible damage to the subthalamic nucleus and in *all* brains this lies wholly below the anterior-posterior commissure line. This is a plane that can be ascertained with accuracy from radiological data and if the lesion is certainly above this line then the subthalamic nucleus cannot have been damaged directly. In only two cases in this series did the lesion appear to extend below the line, in one even the subthalamic nucleus itself may have been damaged, but in both these cases the ballismus was slight and transient (Fig. 1).

It was considered, in the light of the above arguments, reasonable to think that 70% of the lesions made were in the ventro-oralis nucleus whilst the remainder may have involved adjacent structures, especially the medial portion of the internal capsule and lateral areas of the ventro-oralis internus. The meagre post-mortem material available would confirm this supposition.

DISCUSSION

SITES OF LESIONS CAUSING HEMI-CHOREA In a series of 200 cases of Parkinsonism lesions in the ventrolateral thalamus have resulted in involuntary movements in 12 cases, either immediate or delayed by a period of up to two and a half years. In seven, the movements were choreiform or ballismic, in two athetotic, in two myoclonic, and in two rhythmic blinking. It may seem unreal to class all these together and, indeed, the rhythmic blinking would seem to be quite different from the others and possibly a manifestation of post-encephalitic disease akin to oculogyric crises. Close examination, however, both of the evolution in individual patients and of extra-slow motion film, shows that the other three types of movement merge imperceptibly into each other. In particular, the very early stage of ballismus is indistinguishable from athetosis.

To the purist hemiballismus constitutes a disease entity in which the whole of one side of the body is affected, the onset is acute, and so forth. It must be realized now that such a concept is a special one and probably related to a particular vascular pathology.

The present series of cases and innumerable examples from the literature make quite clear the

following facts. First, that the continuity of movement is related to the type and extent of pathology and not intrinsic in the type of movement. In many cases here and in the literature the movements were not constantly present, tended to be absent when the patient was relaxed and occupied with other matters but became aggravated under stress or when his attention was directed towards them. Denny-Brown (1962) has considered in great detail the reflex character of involuntary movements and their relationship to attention and especially visual, tactile, and positional stimuli.

Secondly, there is a clear topographic relationship to pathology. The shoulder, hand, or foot may be involved alone, whilst, as the disease progresses, it does so in an orderly manner spreading from its initial site to involve the whole limb or side of the body. Many authors have described this topographic relationship in the subthalamic nucleus, the face being represented anteriorly and the hind limb posteriorly (Martin and Alcock, 1934; Whittier, 1947; Dierssen *et al.*, 1961).

Thirdly, that there are progressions and regressions in the disease, most of the surgical cases having recovered completely within a few days. It was probably post-lesion oedema in these cases which had impaired function rather than destruction of cells or fibres and it may be noted that in the only case in which ballismus persisted there was E.E.G. evidence of abnormal function within a few seconds of making a lesion and overt ballismus appeared before the end of the operation.

Fourthly, that one physical insult at least may antedate the appearance of ballismus by at least two and a half years. It hardly seems possible that progressive gliosis from this lesion could continue for so long a period and one must presume the interposition of one or more further lesions on the first surgical one, presumably due to the progression of the disease itself.

The major and over-riding concern of the surgeon is to ascertain the cause of such a complication and avoid it in future operations. If the cause could be ascertained it might well throw some light on the neurophysiological basis of involuntary movements.

Most authors have assumed, even in the early papers, that ballismus results from damage to the subthalamic nucleus or its tracts. There can be little doubt that in the animal such damage usually results in ballismus, and that in most of the human cases of vascular aetiology this nucleus is involved (Papez, Bennett, and Cash, 1942; Thurel and Grenier, 1947; Carpenter, 1955; Bedwell, 1960). An increasing body of evidence has accumulated, however, to show that ballismus can occur from lesions not affecting this nucleus or its tracts and, indeed, from

lesions in quite a remote part of the brain (Wilson, 1954; Martin, 1957; Schwarz and Barrows, 1960). The sites of lesions, though usually in the basal ganglia, are so widespread that it is difficult to accept this type of involuntary movement as resulting from damage to a single neural circuit.

The first concern of the surgeon in considering this problem is the site of the lesion. Has he reasonable evidence of its site and is it involving the subthalamic nucleus? In this series, for the reasons explained above, the exact geographical site in the antero-posterior and lateral planes cannot be predicted with certainty, that is to say, with respect to particular nuclei, probably not more than 70% of lesions being wholly within the ventrolateral thalamus. One can predict with certainty, however, the relationship to the intercommissural plane and in 10 of the 12 it would be a justifiable assumption that the subthalamic nucleus was not damaged. In the one case in which this nucleus may have been damaged the movements were mild and transient. One would feel justified in saying, therefore, that direct damage to this nucleus was not the cause of abnormal movements in this series. Indirect damage, however, cannot be excluded and it is possible that damage to vessels may have occasioned lesions remote from the primary surgical one. A study of the disposition and direction of feeding vessels in this area, however, would make one think that a lesion lying superior to the subthalamic nucleus would be very unlikely to interfere with its blood supply. The many cases in the literature when the nucleus has been undamaged make it unnecessary, of course, to assume damage to this area to produce ballismus.

It seems clear from the literature, and probably from evidence in this series, that lesions outside the subthalamic nucleus can cause ballismus. The caudate, lenticular nucleus, portions of the internal capsule, zona incerta, Forel's fields, and the parietal cortex have all been invoked as a site of origin and in a number of cases the ventrolateral thalamic area (Martin, 1957; Dierssen *et al.*, 1961). Whilst in many cases occurring spontaneously multiple lesions have been present, or a single lesion has involved a number of structures, in the present cases and that of Dierssen *et al.* the lesions were confined to the ventrolateral thalamus. One must accept this site, therefore, as one capable of inducing ballismus. Two further matters have to be taken into consideration here. First, though the lesions in most cases involved a large area of the ventro-oral nucleus the movements in all but one case were mild and transient. This suggests that they result from lesion oedema involving adjacent structures, and subsequently subsiding, rather than involvement of this nucleus itself. In talking about the subthalamic

nucleus Hyland and Forman (1957) suggest that recovery in spontaneous cases is more likely when the lesion involves the afferent tracts than the nucleus itself. Whether this is true in these cases can only be speculation but it would be reasonable to assume that the onset and recovery in these cases was most likely to be due to the onset and resolution of traumatic oedema rather than the particular area affected. The only evidence against this hypothesis is the case of J.Hd. quoted above. Here deliberate surgical extension of the first lesion resulted in some improvement in movements; one might have expected it to make them worse if the surgical lesion can be incriminated in this case.

The second matter for consideration is the small number of cases in which this complication occurs. Though there may be some small variations in the coordinate position of lesions and rather more geographical variation with respect to nuclei, surgical lesions of this nature are, in comparison with the size of nuclei in the area, relatively large and one would not expect such variations from patient to patient to provide the explanation of this phenomenon. Some indication of the reason may be deduced from the three patients in whom ballismus appeared some time after the surgical lesion and on the same side as that treated. This may have been fortuitous and indeed, as in the case of E.S. quoted above, such abnormal movements do occur spontaneously in Parkinsonism. That in all the cases in which this has occurred it appeared on the same side as the surgical lesion would seem to make coincidence unlikely.

The probable explanation is that in such cases at least two lesions are necessary to produce ballismus. One of these is in the ventrolateral thalamus; where the other may be we do not know. Both these lesions can be produced by the disease itself, as in the case of I.S. In other cases the unknown lesion is already present and the second, the thalamic, is provided by the surgeon. In another group the thalamic lesion is provided by the surgeon and, at a later date, the progress of the disease provides the second lesion. The logical evidence here, of course, only infers that at least two lesions are necessary; in fact it may be many more than this.

Since this is a rare occurrence it may be worthwhile to look into the pattern of disease in these patients to see if it differs from the general spectrum of disease in Parkinsonism. Anyone who sees a large number of these patients over a short period of time realizes that there are many patterns of clinical disease. Tremor may occur almost as an isolated factor with little or no rigidity, akinesia, or speech defect. Akinesia may appear in similar manner, often proceeding to mental deterioration and minimal

rigidity and hardly any tremor. There are many other groupings which may be made on a clinical basis. It seems likely, therefore, that Parkinsonism comprises a number of different disease entities, possibly with differing aetiology.

In the present series no clear clinical picture emerges: most were the usual combination of rigidity, tremor, moderate akinesia, speech defect, and so forth. The evolution of the disease in this group, however, was markedly different from the group as a whole. The average age at treatment was much lower than the group, being 47.5 years as against 54.6 ($P = > 0.01$). But the age of onset of disease was significantly lower than the group, being 32.1 as against 46.0 ($P = > 0.001$). The evolution of the disorder appeared to be slower than usual with an average length of history of nearly twice that of the whole group, 15.6 years as against 8.4, but this was not significant statistically ($P = > 0.05$). As a group, therefore, it would seem that this complication occurred in people whose disease started at a much younger age and ran a slower course. The suggestion may be that all these cases were of the post-encephalitic variety.

TREATMENT OF POST-OPERATIVE HEMI-CHOREA The considerable literature on hemiballismus combined with recent clinical experience in stereotactic surgery offers little help in planning avoidance of this complication or in treating it when established. The data given above would suggest that such a complication should be anticipated when treating patients in the post-encephalitic group, or who start Parkinsonism at an early age with slow evolution. Such patients should be treated with extreme care and most probably warned before operation that this is a possible complication. Placing the lesion should be most rigidly controlled and continuous E.E.G. monitoring from scalp and depth electrodes should be carried out during operation. It has been my practice to confine all lesions to the area above the anterior-posterior commissure line, thus ensuring that the subthalamic nucleus is not directly damaged. Certainly this manoeuvre has not prevented the complication occurring, though the incidence in this series is lower than in most. Furthermore, recent work has suggested that lesions in the subthalamic area are most probably those most suitable for the control of tremor (Andy *et al.*, 1963; Spiegel *et al.*, 1963). Nevertheless, the incidence of ballismus in the cases treated with subthalamic lesions (Andy *et al.*, 1963) was much higher than in other series with more conventional lesions (five cases in 58 patients, 8.6%). My own experience of such lesions has not been very impressive and such excellent results on tremor have been obtained from standard

ventrolateral thalamic lesions that it would seem reasonable to continue this safeguard.

The treatment of established ballismus provides an interesting and difficult problem. Most of the cases reported are of the 'spontaneous' variety; they are in elderly people, with a poor life expectancy and already with advanced cerebrovascular degeneration. It must also be taken into account that the prognosis in these cases, as far as involuntary movements is concerned, is not bad, probably as many as half remitting spontaneously (Hyland and Forman, 1957). In many reports the alleviation has been only partial and therefore the assessment of surgical results is extremely difficult.

Many records date from the time before stereotactic surgery was commonplace and involve open operations on the motor pathways. Operations on the cortex (Russell Meyers *et al.*, 1949; Alpers and Jaeger, 1950; Talairach, Paillass, and David, 1950) have been well-documented as have those on the cerebral peduncle (Walker, 1949; Bucy, Keplinger, and Siqueira, 1964). The report by Bucy *et al.* is a most carefully documented one in which a close study was made of the post-mortem pathology, the patient dying two and a half years after operation during which he had been quite free of involuntary movements. Some degree of motor loss seems inevitable from such operations but such is the nature of these gross and exhausting movements that even a severe degree of paralysis may be preferable, provided that no better treatment is available.

Operations on the ventral quadrant of the spinal cord have also been successful and in some relief of involuntary movements has been achieved without any motor deficit (Brown and Walsh, 1954; Strain and Perlmutter, 1957).

Stereotactic operations have also been well documented in recent years though there seems to be wide variation in the site of election for such lesions. Hassler (1959) did not achieve much success from lesions in the ventrolateral thalamus (ventro-oralis anterior) but suggested that lesions in the internal capsule rostral to the main pyramidal tract were effective in two of his cases. Andy (1962) recommended lesions in the 'diencephalic' area, largely below the inter-commissural plane. In one case movements were improved and in three others they stopped, though the survival periods were short in two of them (10 days and four and a half months). The sites of his lesions were varied, and from the illustrations the subthalamic nucleus itself may have been involved in two. In some cases lesions in the ventrolateral thalamus have been successful (Martin and McCaul, 1959). Though case reports are few, conversations and correspondence with other neurosurgeons suggest that such lesions are as successful

as any. What should be the treatment, therefore, when a lesion already made in this area has been the cause of ballismus? There can be little doubt that the situation is modified considerably by the pre-existing disease. Dierssen *et al.* (1961) in one case extended a lesion in the ventrolateral thalamic area a little deeper and this made the ballismus worse in the leg. In one case above (J.Hd.) the thalamic lesion was extended both anteriorly and posteriorly with only transient improvement. The very wealth of sites for successful operations indicates both the variability of the disease and the lack of a universally effective operation for this condition. The position was well summarized by Dierssen *et al.* as follows: 'Hemi-ballismus represents a physiological expression of a functional state of the nervous system produced by a combination of pre-existent pathological alterations with a releasing lesion. We cannot assume that either the underlying alterations or the releasing lesion is necessarily located identically in all cases. Consequently, we should not expect that the same acute lesion will yield identical clinical effects in all instances.'

In recent years a view has circulated amongst stereotactic surgeons, though I have never seen it expressed in print, that ballismus is associated with partial lesions of the subthalamic nucleus, or its tracts. This probably derives from the work of Carpenter, Whittier, and Mettler (1950) who described the effects of subthalamic lesions in 48 rhesus monkeys. They noted that ballismus developed if more than 20% of the nucleus was destroyed but that thereafter lesion size had little effect on the severity of movements. In lesions that were 'too large' ballismus did not develop, nor did it if the number of adjacent structures involved by the lesions was more than six. The implication was that partial lesions of the nucleus were most successful in producing ballismus, whereas, if the whole nucleus, together with a number of adjacent structures were destroyed ballismus did not develop. In another report on this material (Mettler and Carpenter, 1949) they analysed lesions which had modified ballismus produced in this way. They indicated that lesions in the medial globus pallidus were most effective in stopping ballismus, though in some animals major portions of the adjacent internal capsule were involved as well and in one a ventrolateral thalamic lesion stopped the movements. The implication read into this work has been that total destruction of the nucleus together with adjacent structures might be the best form of treatment. No one, so far as I am aware, has yet put this idea into practice.

The available theoretical and practical evidence would suggest that destruction of the fibre pathway between the subthalamic nucleus and the medial

globus pallidus would be most likely to modify or abolish ballismic movements and it would seem reasonable to attempt this as a first step in the treatment of the post-operative cases. Capsular lesions rostral to the main pyramidal tract would also seem effective in the human and if the medial pallidal lesion proved ineffective, or only partially so, it would seem also reasonable to extend the lesion into the capsular area adjacent to the medial pallidus. If neither of these lesions were effective in stopping the movements it would probably indicate that some motor deficit must be accepted and a pedunculotomy on the lines suggested by Bucy should be undertaken.

SUMMARY

In most reported series of stereotactic operations for Parkinsonism involuntary movements resembling athetosis or chorea have been noted post-operatively in a small percentage (2%). In the majority of cases these are mild and transient. In rare cases they persist for months or years. In the present series of 200 cases the incidence of immediate movement was 3%.

The types of movement encountered are described and the nomenclature of involuntary movements in general is discussed. Aggravation of Parkinsonian tremor was not encountered. Two cases had intention tremor slightly aggravated by operation. Two developed athetosis and four hemi-chorea. Two patients developed myoclonus and two rhythmic blinking. It is suggested that athetosis is a definite entity and conforms to the description given by Denny-Brown (1962) as a regular alternation of posture. Where there is a continual flow of movement and there is alternation between many different postures in a random manner the term chorea should be used. Ballismus can be used to designate the wild flinging movements seen in these patients but is probably better used to define a special clinical syndrome of spontaneous sudden onset in elderly and atherosclerotic patients.

The method of operation is described and the technical procedures of locating lesions in individual patients. The location of lesions was determined primarily by anatomical coordinates based on percentages of measurable distances, anterior-posterior commissure separation, height of thalamus, and width of lateral ventricle. The final position of lesions was guided by information from E.E.G. scalp and depth recordings, stimulation, and local cooling.

The clinical material is discussed in detail and summaries given of the case histories of individual patients. Three cases are then discussed in which

chorea appeared on the side treated for Parkinsonism at some interval from the time of operation, six months in one and two and a half years in the others. It is indicated that chorea may occur spontaneously in Parkinsonism and one case is cited.

The probable anatomical location of the lesions in these patients is discussed with special reference to their relation to the subthalamic nucleus.

The nature and significance of this complication is discussed and the literature on the subject reviewed. It is stressed that such a complication usually follows lateral thalamic lesions and is rare with those of the globus pallidus. It is significantly related to Parkinsonism which is post-encephalitic or where the onset has been early in life and the progression slow. The incidence of delayed onset suggests that at least two lesions are necessary to produce hemichorea from a lateral thalamic lesion. One is provided by the surgical lesion and the other, which may post-date the surgical lesion, by the disease process of Parkinsonism. The anatomical location of lesions, therefore, is probably different from the cases of spontaneous hemi-ballismus.

Forms of treatment are reviewed and suggestions made as to the lines of treatment which may be adopted in the post-operative cases.

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