RES MEDICA
Journal of the Royal Medical Society

James Parkinson and His Disease

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Abstract
James Parkinson was born in 1755 in Shoreditch, close to the City of London and like his father practised medicine there as an Apothecary and Surgeon. His earlier years in practice were disturbed by a rebellious spirit, roused by the poverty and injustices he saw around him. Inevitably he was drawn into politics and joined the provocative London Corresponding Society. He wrote a number of highly critical pamphlets under the pseudonym of "Old Hubert". His criticisms of government and administration were at times so bitter and fearless that eventually they led to his being subpoened and examined by the Privy Council. During the course of these examinations he had to answer to the Lord Chancellor, the Prime Minister, Mr. William Pitt and others in high office. Fortunately his explanations impressed his interrogators by their honesty and sincerity and he escaped imprisonment. By the time he was 40, with the increasing demands of a busy practice and a young family, he seemed to turn all his efforts to his own work and writings. His interests were broad. His first book was on "The Organic Remains of a Former World". Later he wrote on medical education, the preservation of health, and a brilliant criticism "Observations on Doctor Hugh Smith's Philosophy of Physics". Nevertheless it was not for another 22 years that he wrote his classic essay on "The Shaking Palsy" which was published in 1817 (Critchley 1955).

ISSN: 2051-7580 (Online) ISSN: 0482-3206 (Print)
Res Medica is published by the Royal Medical Society, 5/5 Bristo Square, Edinburgh, EH8 9AL

Res Medica, April 1967, 5(4): 8-12
doi: 10.2218/resmedica.v5i4.494

JAMES PARKINSON AND HIS DISEASE

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James Parkinson was born in 1755 in Shoreditch, close to the City of London and like his father practised medicine there as an Apothecary and Surgeon. His earlier years in practice were disturbed by a rebellious spirit, roused by the poverty and injustices he saw around him. Inevitably he was drawn into politics and joined the provocative London Corresponding Society. He wrote a number of highly critical pamphlets under the pseudonym of "Old Hubert". His criticisms of government and administration were at times so bitter and fearless that eventually they led to his being subpoened and examined by the Privy Council. During the course of these examinations he had to answer to the Lord Chancellor, the Prime Minister, Mr. William Pitt and others in high office. Fortunately his explanations impressed his interrogators by their honesty and sincerity and he escaped imprisonment. By the time he was 40, with the increasing demands of a busy practice and a young family, he seemed to turn all his efforts to his own work and writings. His interests were broad. His first book was on "The Organic Remains of a Former World". Later he wrote on medical education, the preservation of health, and a brilliant criticism "Observations on Doctor Hugh Smith's Philosophy of Physics". Nevertheless it was not for another 22 years that he wrote his classic essay on "The Shaking Palsy" which was published in 1817 (Critchley 1955).

It is not surprising that this energetic compassionate man with a keen sense of observation and flair for detailed recording, should turn his attention to that hitherto neglected group of patients suffering from the disease later to be called by his followers "Parkinsonism".

On Pages 15 and 16 of his monograph, (Parkinson 1817) he describes how the tremor of an aged patient disappeared following the onset of a "stroke" — a capsular hemiplegia. In about a fortnight the limbs had regained most of their movement. He says — "During the time of their having remained in this state, neither the arm nor the leg of the paralytic side was in the least affected with the tremulous agitation; but as their paralysed state was removed, the shaking returned."

The first surgical attempts to treat Parkinsonian tremor were in the early 1930's by destructive lesions at various levels of the cortical spinal pathways — the motor cortex, the internal capsule, the cerebral peduncle and later the posterior lateral quadrant of the upper cervical spinal cord. However, had this original observation of James Parkinson been carefully considered, a more successful surgical approach to this problem might have been achieved earlier. He clearly stated "As their paralysed state was removed, the shaking returned". These first operations often led to considerable disability from paralysis and neither the results nor their physiological basis encouraged pursuit of the problem in this way.

Nevertheless it was his experience with these procedures that led Russell Meyers (1942) to put forward his hypothesis that tremor and rigidity might be relieved by interruption of

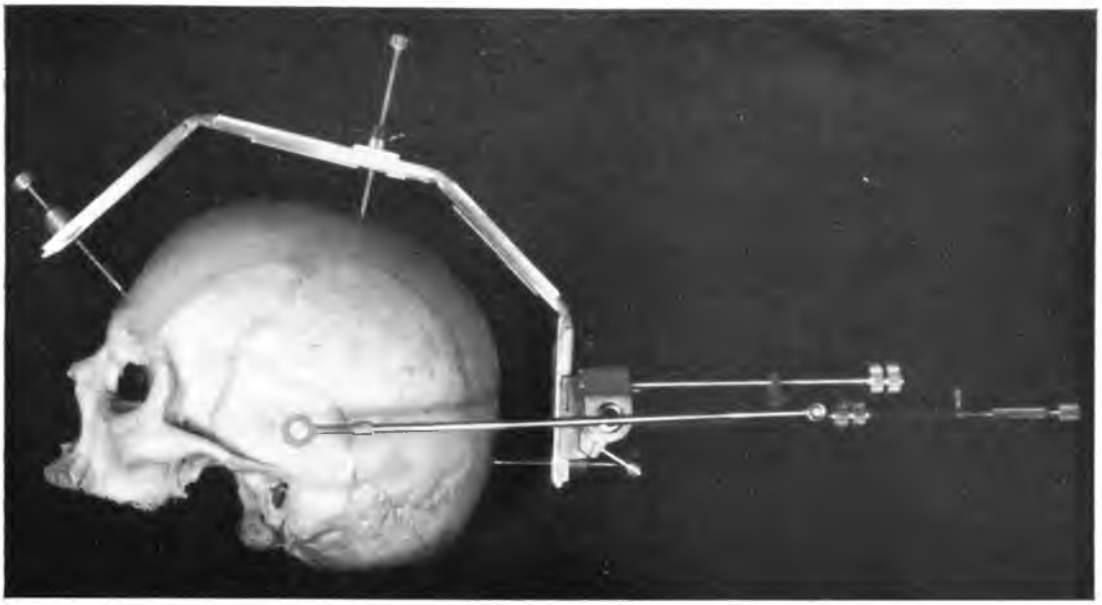

Figure 1

the pallido-fugal fibres and without any involvement of the cortico-spinal tract. This marked the great step forward but unfortunately his operation, designed to interrupt these fibres through the lateral wall of the third ventricle, was ill-conceived. The results although encouraging in some respects, were disappointing because of injury to diencephalic structures adjacent to the third ventricle with stupor and a high mortality and the operation fell into disrepute. Because of this and preoccupation with the medical problems of the Second World War, nothing more was done. Later Fenelon (1949) in Paris took up Russell Meyer's original observation and devised a new operative approach using a sub-frontal route. He followed the optic tract backwards beneath the frontal lobe to the point where the tract begins to merge with brain. Using this landmark and by directing his electrode upwards and slightly laterally for 1 cm., he was able to create an electro-coagulation lesion of the pallido-fugal fibres — the ansa lenticularis and adjacent globus pallidus. The results of this procedure were encouraging. Tremor and rigidity were often reduced and occasionally abolished, yet without any untoward side effects. In particular there was no evidence of stupor, paralysis, sensory deficit or akinesis. This work was soon taken up by Guiot who published a series of successful results in 1953 and it was Guiot who demonstrated this exciting new operation to me in Paris in 1954 (Guiot 1953).

Early in 1955 our first patient was treated. A miner of 50 with post encephalitic Parkinsonism, he had been unable to work for 10 years because of severe tremor and rigidity of left limbs. At least half of each week was spent in bed because of an exacerbation of akinesis, sweating and tremor. Over the years he had lost 2 stones in weight and had become gravely disabled. Following operation which of necessity had to be performed under local anaesthesia to observe the effect and effectiveness of the lesion, he rapidly improved. He lost his tremor and rigidity completely and there was no paresis. His sense of well-being and weight were quickly restored, his kyphosis lessened and he returned to surface work at the pit in two months. He has remained well since although some mild rigidity in the left limbs has returned in the last few years. However for twelve years he has been without tremor and a

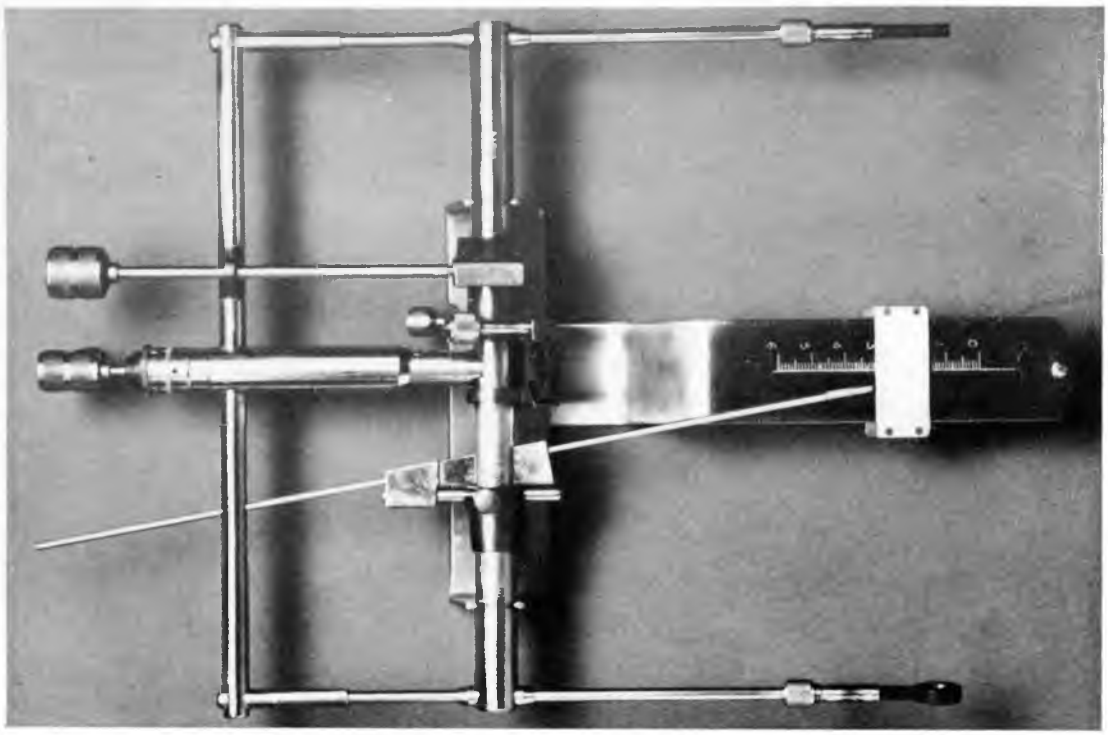

Figure II

steadily deteriorating condition has been greatly slowed or halted.

A further patient was treated in the same way shortly afterwards and a similar result obtained which has been maintained after twelve years.

In the meantime we were becoming increasingly interested in the development of the first stereotaxic human instrument devised and used by Spiegel and Wycis of Philadelphia in 1947 for the treatment of psychiatric disorder (Spiegel et al. 1947). This was designed very much on the pattern of that devised and used by Horsely and Clarke with such precision for animal work in 1908 (Horsley and Clarke 1908). The open operation of Fenelon, although very successful, was difficult and hazardous. If a discrete lesion could be sited accurately at a predetermined target through a burr hole by means of a suitable guiding apparatus fixed to the head, then much would have been achieved. This was the great contribution of Spiegel and Wycis for the field of stereotaxic surgery is now one of the major branches of surgical neurology not only in Parkinsonism and the dyskinesias, but also in epilepsy, intractable pain and some of the psychiatric disorders.

Guiot was soon to follow with a much simpler yet very precise apparatus, a modified version of which has been used in my own department for many years (Figs. I and II). I remember the early discussions we had in Paris with great pleasure and how ultimately we decided that the posterior stereotaxic approach using an occipital burr hole, even though it meant a longer track, would probably be the best. As subsequent events have shown it was a fortuitous decision not only because the best results were obtained in this way, but also because it led to a greater understanding of the basic problems of Parkinsonism and the effectiveness of the different lesions used.

These early procedures were sometimes inaccurate and we came to realise the stereotaxic method was fallible. The problem was not that of imprecise instrumentation or lesion making but of the anatomical variation of one brain to another and even of one hemisphere to another. We had to rely upon radiologically determined landmarks such as the septum pellucidum and

the third ventricle (the mid sagittal plane) and the anterior and posterior commissures shown by means of a radio opaque dye or air. These landmarks gave only a reasonable bearing for our target and we began increasingly to look for physiological methods such as electric stimulation and reversible lesions to help us. By fractionating the electro-coagulation lesion using low heat initially it was possible to show the damping down of tremor or the relief of rigidity and of equal importance, side-effects such as speech, motor or sensory disturbances, before the permanent lesion was created; this method has proved to be more reliable in our hands than stimulation. Gradually as a result of the marking of all lesions at operation by detaching the tiny stainless steel tip of the electrode, taking a skull Xray afterwards, then charting them on stereotaxic atlases, the sites of the most effective lesions for the relief of tremor and rigidity were soon determined. This was further helped by making as small a lesion as would be compatible with maintained improvement. We also began to map out for the first time the various tract systems such as the corticospinal fibres, the parieto-sensory projection within the posterior limb of the internal capsule and the tract systems concerned with speech. The results of this work using scattergram techniques have been published elsewhere (Gillingham 1962).

In 1955, when most of us were working on the globus pallidus and the pallido-fugal fibres, Hassler suggested that the most effective lesion for the relief of tremor should lie in the ventro-lateral nucleus of the thalamus (Hassler 1955). This was subsequently proved by Riechert, Cooper, ourselves and many others as successful operations on the thalamus were reported (Riechert 1955, Cooper 1959, Gillingham 1960). Nevertheless with follow up the lesion of the globus pallidus remained the most effective for the relief of rigidity. By elevating our posterior track to the globus pallidus, we found that a double ipsilateral lesion 15 mm from the mid-sagittal plane could be made quite successfully with only one insertion of the electrode. The posterior lesion for tremor was made first in the ventro-lateral nucleus posterior to the capsule, and the second for rigidity in the globus pallidus anterior to the capsule. This technique even after some 700 operations have been performed for Parkinsonism has remained the most effective.

There still seemed to be room for error and our restless search for further accuracy was eventually rewarded. For some years the neurophysiologists had relied on electrical recording rather than stimulation for locating the electrode tip and this was beautifully demonstrated to me by Professor David Whitteridge during explorations of the external geniculate ganglion of the cat. The borders of grey and white matter were clearly defined with a degree of accuracy which so far we had not known. The subsequent development of the technique and its value in stereotaxic surgery has been published elsewhere (Gaze et al. 1964) and followed very closely the work of Albe-Jessard (1962). Since then, depth micro-electrode recording has become almost standard practice as further information has accumulated from greater experience and the use of smaller electrodes (1 to 10μ tips). The borders of the thalamus and its sensory relay nucleus, of the internal capsule and the globus pallidus, are identified with confidence and target siting is no longer a problem.

Detailed study of electrical activity from the basal ganglia is continuing for there is much to learn about sensory mechanisms and the basic pathology of Parkinsonism. Of particular interest has been the recognition of spontaneous rhythmical activity arising in the thalamus synchronous with tremor yet not evoked by any sensory stimulus. It is not always found and as yet its relation to tremor has not been fully determined. The more sophisticated techniques of frequency analysis of the various patterns of cell activity may give some of the answers.

Perhaps of equal importance to the understanding of the basic pathology of Parkinsonism is the biochemical changes which occur. Recently Barbeau (1962) and others have shown a disturbance of dopamine metabolism and we have followed this work by a study of this substance in the cerebro-spinal fluid of the lateral and third ventricles in patients with Parkinsonism and in controls. The team responsible for this study, working in my department and that of Professor Perry, will be reporting about it shortly. Future research in the field of the Dyskinesias would seem to depend very much upon the pursuit of the abnormal electro-chemical changes which are present.

The surgeon, stumbling as he does, often in an empirical way, responds to each challenge thoughtfully and with the improvement of the patient as his primary concern. The rewards of such an exercise in understanding the problems of Parkinsonism have been considerable, and in particular perhaps in the outlining of a "pathway" which lies within the diencephalon,

interruption of which at any point relieves tremor and rigidity and to a greater or lesser extent some of the other associated symptoms as well, such as oculogyric crises and the compulsive thinking that sometimes go with them. This "pathway" which has been defined by a whole series of differently sited yet successful lesions by surgeons across the world, extends from the inferior aspect of the globus pallidus anteriorly, upwards and posteriorly through the globus pallidus, across the posterior limb of the internal capsule at and above the intercommissural plane into the ventro-lateral nucleus of the thalamus. There it turns downwards through the zona incerta just lateral to the red nucleus to the substantia nigra. Its distance from the mid-line and its width varies from point to point and there would seem to be "bottlenecks" within it. A lesion placed strategically within it brings immediate relief of symptoms and signs but if it is poorly placed the results are inadequate and side effects follow. Its connections with the cortex above and spinal cord below have not yet been defined but in the diencephalon we would seem to have shown "the pathway" to be the ansa and fasciculus lenticularis (Gillingham 1966).

Much of what I have said has been about research and the solution of our problems of accurate placement of effective lesions for the relief of this relentlessly progressive disease, but we must now look at the results and the indications and contraindications of operation.

Not all patients are benefitted by stereotaxic surgery. Those who are deteriorating rapidly with bilateral tremor and rigidity and who show widespread effects of their disease, notably intellectual impairment, gross reduction of voice volume and disturbances of micturition, cannot be improved and are often made worse. Fortunately the majority are not so severely affected and in these patients operation will always effect some increase in independence, and in a reasonably high proportion great improvement, particularly in those with strictly unilateral rigidity and tremor. Bilateral operations, if staged with at least a month between them, are being carried out increasingly as precision has increased. (Gillingham 1964).

Post-operative drugs are usually necessary although the dosage is often progressively reduced as the months and years pass. It is the accumulating evidence, with prolonged follow-up, now of twelve years in some patients, of the greatly slowed or halted disease process which is perhaps the most exciting observation of all and which now poses the important question "How has it happened?"

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