SURGICAL TREATMENT OF PARKINSONISM: INDICATIONS AND RESULTS*

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PARKINSONISM, also known as the parkinsonian syndrome and paralysis agitans, is a disease process which has long held the interest of physicians and research workers. There are several reasons which account for this interest. In the first place, the clinical picture is bizarre, presenting involuntary movements associated with rigidity which ultimately restricts all voluntary movement. Secondly, the plight of victims of this disease is truly pathetic. People of normal appearance are gradually transformed into caricatures of their former selves. The abnormal movements make them conspicuous so that they avoid outside contacts. Their helplessness becomes progressively greater and ultimately they are dependent upon others for assistance in every detail of daily living. Finally, although the disease process has long been studied in an effort to understand its basic mechanisms and provide relief for its victims, full understanding has not been reached. The etiology and pathology of Parkinsonism are for the most part known. However, the pathophysiology of symptoms of the disease is not fully known, and the problems of therapy have been baffling.

The disease is most frequently the manifestation of brain lesions resulting from encephalitis or arteriosclerotic disease. Less commonly it results from syphilitic vascular disease, multiple sclerosis, trauma, alcohol or manganese poisoning. Rarely, a slow-growing, deep intracerebral neoplasm may produce a clinical picture similar to that of paralysis agitans. The lesions are most commonly found in the globus pallidus and the substantia nigra of the midbrain; the thalamus, hypothalamus, putamen and cerebral cortex may also be affected. The chronic encephalitic group is said to show selective bilateral involvement of the globus pallidus and the substantia nigra. The arteriosclerotic group shows widespread pathologic changes, the cerebral cortex being involved as well as the globus

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pallidus and the substantia nigra. Microscopic study has consistently revealed atrophic changes in the ganglion cells of the globus pallidus and the substantia nigra. Deposition of lipochrome pigment in the cytoplasm, and swelling and disintegration of the cells have been noted.

Tremor is the most prominent symptom of the disease. It is rhythmic and alternating, at a rate of four to seven per second, and is seen most often in the upper extremities, usually in the distal portion. Tremor occurs most frequently in the flexors, extensors, pronators and supinators of the hand and in the flexors, extensors, adductors and abductors of the fingers. In the lower extremities the symptom is manifested as quivering of the knees and to-and-fro shaking of the feet. Tremor may be limited to one side of the body or to one extremity. It is present at rest but may be momentarily lost at the initiation of voluntary movement. In advanced cases tremor is present constantly.

Rigidity may be present in the musculature of the extremities, spine, head, neck or face. It may be associated with tremor or may exist independently. In those cases where rigidity exists without tremor, that symptom alone may be very disabling; in some cases effective voluntary movement is almost impossible. Another manifestation of rigidity is the "masklike" facies. Facial expression is slight and the normal movements of facial muscles associated with emotion are not seen. There may be marked slowness in movement. Initiation of movement is often difficult; once the movement has been started, it may progress smoothly. This symptom is usually associated with muscular rigidity.

Electromyographic studies have been reported by Hoefer and Putnam[1] in cases of paralysis agitans. It was noted that Parkinsonian rigidity is characterized by a continuous, slight innervation of the rigid muscles even when the limb is placed in its most relaxed position; rigidity thus results from simultaneous innervation of agonist and antagonist muscles at an average rate of 5.5 per second. The rate is surprisingly constant over a long period of time.

The course of the disease is in most cases progressive. Tremor and rigidity increase in severity producing acute discomfort and pain. This is associated with progressive incapacity; ultimately the patient can do very little for himself, requiring constant care.

When the disease has reached a moderately advanced stage, the patient must usually give up his work and find financial support in his family or community. The victim also becomes increasingly dependent

on his family for physical assistance and companionship. Visitors are often not encouraged to come, because of the embarrassment that is felt in their presence. Relations within the family become strained because of the irritability of the patient, and the inconvenience and deprivation imposed on the family by this chronic illness. Ultimately, the patient may reach a state of physical and financial helplessness, social isolation and great emotional disturbance.

Medical Therapy

Many drugs have been tested and used in the treatment of Parkinsonism. For many years the atropine series of drugs including hyoscine hydrobromide, stramonium, atropine and Bulgarian belladonna were the basis of medical treatment. Within the last few years, however, there has been an increasing interest in new medications.

In 1941 Bennett[2] suggested that the relaxant action of curare might be of value in the treatment of tremor and rigidity. D-tubocurarine suspended in peanut oil and wax was tested by Bird and Meyers[3] and reported in 1949 to be without value. Tolserol, a related drug, has likewise been used without benefit. The use of parpanit has been reported by European observers; the results have not been good. Diparcol, a synthetic muscle relaxant, has been evaluated by Duff,[4] who found some improvement in a series of eight cases, although one death which may have been related was reported. Other investigators have reported a mortality of 5 per cent in cases treated with diparcol. Lysivane, a member of the same series of drugs as diparcol, has been tested in sixteen cases by Palmer and Gallagher,[5] who reported improvement in some of their cases; there were no deaths in this series.

Artane, a synthetic chemical with anti-spasmodic effect, has been used by Doshay and Constable.[6] The drug was found to provide symptomatic relief comparable to or greater than that afforded by the belladonna alkaloids with fewer toxic reactions. Rigidity and tremor appear to be improved in the majority of patients, with greater relief of rigidity.

Anti-histaminics, including benadryl, pyribenzamine, histadyl and thephorin, have also been tested. Denker and Effron[7] reported on the use of benadryl in 46 patients with improvement in 76 per cent of the cases. Benadryl and hyoscine hydrobromide were found to be more effective in combination than either drug alone. Pyribenzamine and histadyl were comparatively ineffective in the great majority of cases.

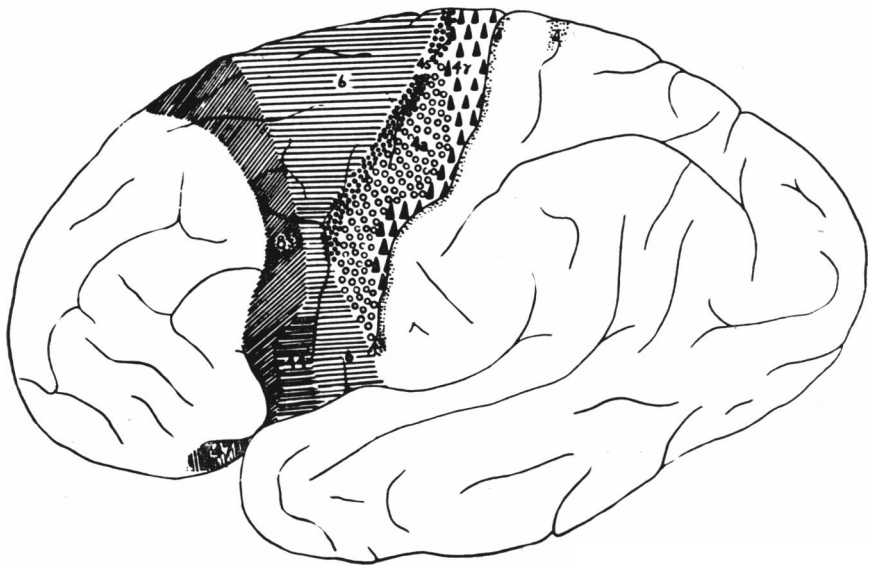

Figure 1—The human precentral motor cortex (areas 4γ, 4a, 4s, 6 and 44) and some adjacent areas. (From Bucy, P. C. Surgical relief of tremor at rest, Ann. Surg., 1945, 122:933.)

The new drugs, such as artane and benadryl, probably are an improvement over the atropine series of drugs in the treatment of the symptoms of Parkinsonism. However, at best there is only an amelioration of symptoms; the course of the disease is not checked. In most cases of moderate and severe involvement, drug therapy to date is only of slight benefit.

Surgical Procedures

The surgical procedures in use at present may be divided into three groups on the basis of anatomic level of approach: 1) Cerebral cortex, 2) Basal ganglia, 3) Spinal cord.

Studies of the details of cortical structure have revealed that the human brain contains several hundred areas, differently constructed; these may be grouped into a few regions corresponding to the lobes. Brodmann's numerical designation of the principal fields has been adopted for descriptive purposes. In a consideration of cortical procedures for relief of symptoms of Parkinsonism, interest centers on the motor area, area 4, which lies in the precentral convolution, and the

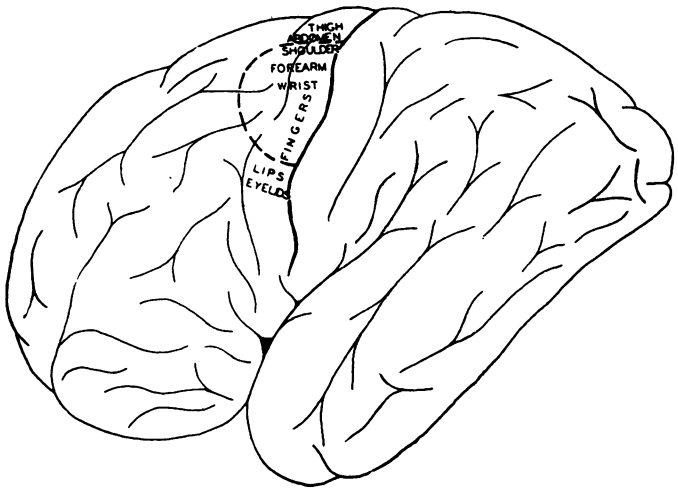

Figure 2—Schematic drawing in case of excision of areas 4 and 6 by Bucy and Case, showing motor representation of various parts of the right side of the body in the precentral gyrus as determined by electrical stimulation. The area of cortex excised is outlined by a broken line and includes all the representation of the upper extremity. (From Bucy, P. C. and Case, T. J. Tremor: physiologic mechanism and abolition by surgical means, Arch. Neurol. & Psychiat., 1939, 41:721.)

premotor area, area 6, which lies in the anterior part of the precentral convolution and the posterior part of the superior and middle frontal convolutions.

In a consideration of spinal cord procedures, interest centers on the pyramidal and extrapyramidal pathways into which all motor tracts may be divided. The pyramidal group includes the lateral and ventral pyramidal tracts. The extrapyramidal group includes the rubrospinal, vestibulospinal, tectospinal, reticulospinal, mesencephalospinal and olivospinal tracts; of these, the rubrospinal and vestibulospinal are probably the most imporant.

The cortical procedures are in part based on the observation of Parkinson[8] in 1817 that in one of his cases generalized tremor at rest was abolished on the right side during the time that the side was paralyzed as the result of a cerebral vascular accident. Parkinson stated: "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 tremulous agitation; but as their paralyzed state was removed, the shaking was returned."

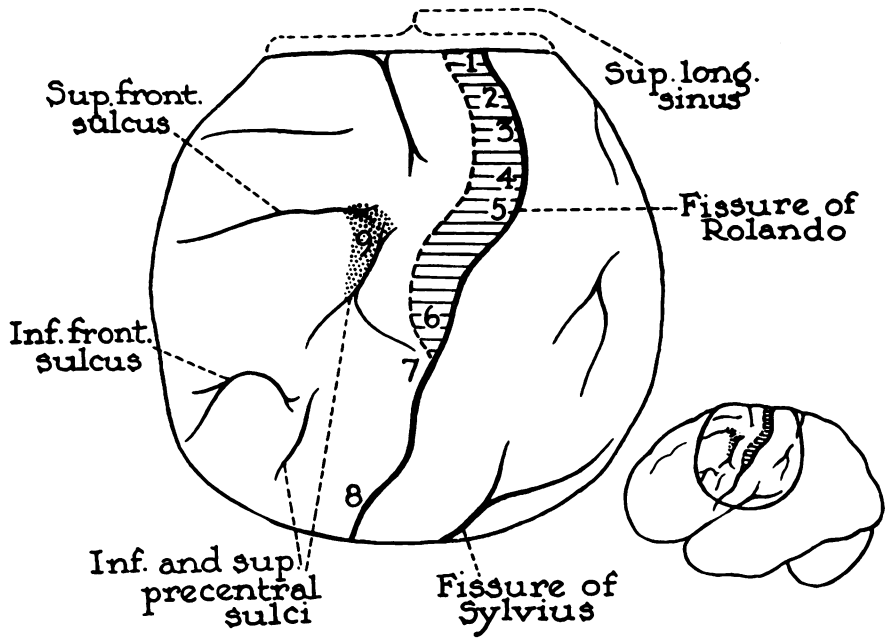

Figure 3—Artist's sketch of the cerebral cortex exposed at operation by Bucy in case of excision of area 4γ. The inset indicates the general relation of the exposed cerebral cortex. The numbers designate areas of various response to electrical stimulation The area for flexion of right hip is indicated by 1; for contraction of right quadriceps femoris muscle by 2; for contraction of right pectoralis major muscle by 3; for flexion of fingers of the right hand by 4; for flexion of the right elbow and wrist by 5; for movement of the neck and shoulder by 6; for movement of the right corner of the mouth and contraction of the right platysma myoides muscle by 7; for movement of the lower lip by 8; the suppressor area, 4s, is designated by 9. The area which was extirpated has been indicated by cross-hatching. (From Bucy, P. C. Surgical relief of tremor at rest, Ann. Surg., 1945, 122:933.)

This observation was confirmed by Patrick and Levy[9] in 1927, who reported a case of bilateral parkinsonian tremor in which, fourteen months after the onset of tremor, a right hemiplegia developed. With the onset of paralysis the tremor disappeared on the right side but gradually returned as the patient recovered the use of his right arm. Fulton, Liddell and Rioch[10] demonstrated that removal of the cerebellum in the cat resulted in a tremor of the extremities that appeared only on voluntary movement, i. e., an intention tremor. They observed that tremor in the contralateral extremities was abolished by removal of one cerebral hemisphere. Aring and Fulton[11] have shown in work on monkeys and baboons that intention tremor resulting from a cerebellar lesion is tem-

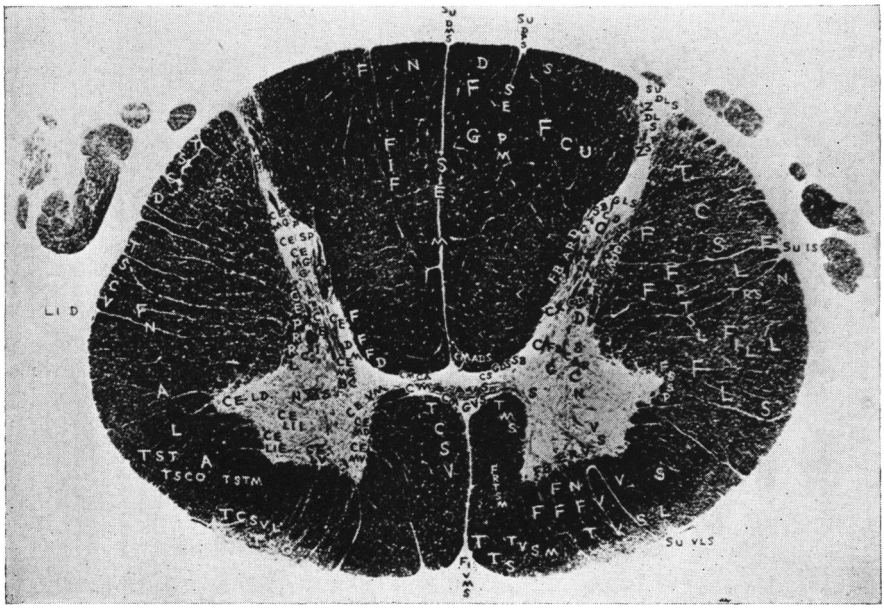

Figure 4—Cross-section of the spinal cord at the level of the fifth cervical segment. FCU, fasciculus cuneatus; FG, fasciculus gracilis; FRTSL, lateral reticulospinal tract; FRTSM, medial reticulospinal tract; TCSL, lateral corticospinal tract; TCSV, ventral corticospinal tract; TCSVL, ventrolateral corticospinal tract; TMS, mesencephalospinal tract; TRS, rubrospinal tract; TSCD, dorsal spinocerebellar tract; TSCO, spinocollicular tract; TSCV, ventral spinocerebellar tract; TSO, spino-olivary tract; TST, lateral spinothalamic tract; TSTM, medial spinothalamic tract; TTS, tectospinal tract; TVSL, lateral vestibulospinal tract; TVSM, medial vestibulospinal tract. (From Riley, H. A. An atlas of the basal ganglia, brain stem and spinal cord, Baltimore, Williams and Wilkins, 1943.)

porarily abolished and subsequently diminished by extirpation of area 4, is accentuated by extirpation of area 6, and permanently disappears after removal of areas 4 and 6.

These data were applied clinically by Bucy and Case[12] in 1939 in the case of a man, thirty-three years old, who had sustained a severe cerebral injury which was followed by a right hemiparesis and a coarse tremor, which was marked in the right upper extremity and slight in the right lower. Tremor was present at rest and in association with voluntary muscular activity. Hyoscine hydrobromide, phenobarbital and bulbocapnine had failed to influence the tremor. A left osteoplastic flap was reflected, centered on the precentral gyrus. Anesthesia was lightened and the cortex stimulated with a faradic current, using a unipolar electrode. The region of representation of the right shoulder, forearm,

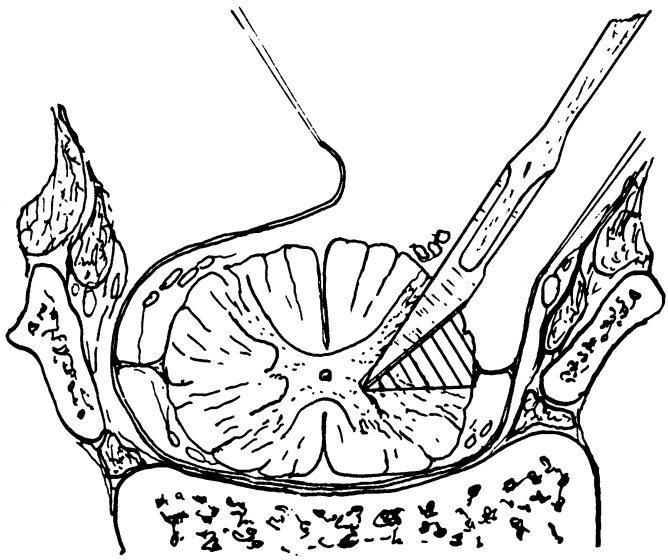

Figure 5—Diagram of the technique of section of the lateral pyramidal tract in the spinal cord, as performed by Putnam. (From Putnam, T. J. Operative treatment of the dyskinesias, A. Research Nerv. & Mental Dis., Proc., 1942, 21:666.)

wrist and fingers in areas 4 and 6 of the precentral gyrus was outlined. This segment was extirpated. It included the anterior wall of the Rolandic fissure down to its very bottom, and extended forward to include the posterior part of the neighboring frontal convolutions. The entire thickness of the cortex and some of the immediately subjacent white matter was removed, producing a defect 2.3 by 3.5 cm. on the surface; its greatest depth, 1.5 cm., was at the Rolandic fissure. The "face" area was spared. Following operation it was noted that there was a complete right hemiplegia. The paralysis of the face and lower extremity soon disappeared almost entirely. In the upper extremity there was moderate return of function, but movements were slow and awkward; discrete fine movements of the hand and fingers did not return. Of great interest was the fact that tremor both at rest and on voluntary movement completely disappeared and was still absent fifteen months after operation.

In 1940 Putnam[13] reported his experiences with cortical excision for the relief of unilateral tremor. The first case was that of a policeman, aged twenty-nine, who had been thrown from a motorcycle striking his

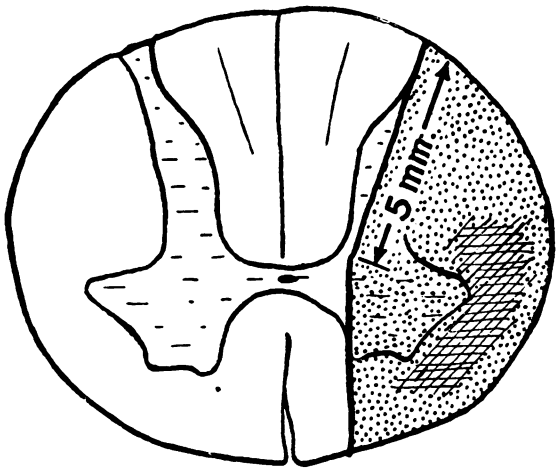

Figure 6—Sketch illustrating complete section of the lateral column of the spinal cord, as performed by Oliver. (From Oliver, L. C. Surgery in Parkinson's disease: complete section of the lateral column of the spinal cord for tremor, Lancet, 1950, 1:847.)

head against the ground. Three weeks later his left hand and arm began to tremble to a degree which forced him to give up active duty and become a police photographer. Examination disclosed an alternating tremor at rest in the left forearm and hand which was diminished by voluntary movement. The tremor was sufficiently troublesome so that the patient was willing to undergo surgical treatment. A right frontoparietal flap was turned adjacent to the superior longitudinal sinus. Face, hand and arm areas were identified by means of a current from an induction coil just strong enough to produce contraction of the temporal muscle. The area corresponding to the arm was found at the vertex; the leg region could not be reached, presumably lying on the medial surface of the hemisphere against the falx cerebri. Firm pressure was exerted with a spatula on the precentral convolution. After three seconds the patient stated that his arm felt weak, and simultaneously the tremor stopped; 2 cc. of procaine hydrochloride was injected into the region and the tremor remained arrested. After waiting ten minutes the strip of cortex was resected by means of the cutting current. It measured 2.5 cm. in length, 1 cm. in width and 1.8 cm. in depth, including a small amount of white matter. After operation there was noted a flaccid monoplegia, affecting the left arm, without sensory changes, which

gradually improved over the next month. Four months after operation there was little weakness but marked awkwardness of the hand and arm. Tremor was almost completely abolished. Microscopic study of the block of tissue removed indicated that it had been taken from area 6 and a small adjacent part of area 4.

The second case reported by Putnam was that of a 45 year old woman who had suffered an acute febrile illness of short duration which was followed by the appearance of tremor of the left upper and lower extremities. An operative exposure similar to that used in the first case was made. A block of cortex corresponding to the arm area measuring 2 cm. in length, .4 cm. in width and .6 cm. in depth was excised. Immediately after operation there was a flaccid monoplegia and complete absence of tremor. Seven months after operation moderately severe weakness of the left hand existed. Tremor at rest was abolished and there was only slight tremor on movement. Examination of the block of excised tissue indicated that it came entirely from area 6.

Klemme[14] has had a wide experience with cortical excision in the treatment of paralysis agitans and athetosis. However, he has never reported the details of the operative procedure other than that it involves "premotor cortical excision." In a letter to Putnam[13] he indicated that the extirpation was in the frontal region anterior to the electrically excitable cortex, suggesting excision of area 6. He bases his operation on the contention that there is a balanced functional relation between the premotor cortex and the basal ganglia, transmitted by a premotor corticospinal "bundle" to the ventral horn cells of the cord. He believes that in Parkinsonism this balance is destroyed by involvement of the basal ganglia, and that it is restored by excision of the premotor area.

Reid, [15] in 1948, reported on a series of 15 cases in which area 6 alone, and area 6 plus a small part of area 8, were removed. In this work an osteoplastic flap was turned down under local anesthesia to expose areas 4, 4s, 6 and 8. Area 4 was mapped out by bipolar stimulation, using a special thyratron spike-wave stimulator, at frequencies of 60 and 80 cycles per second with an output of 6 to 8 volts. Electrographic tracings were made directly from the cerebral cortex to locate the anterior suppressor strip, area 4s. Stimulation is carried out in front of the previously localized motor points in order to identify area 4s. If stimulation of a particular point abolishes the tremor and spontaneous electrical activity in the cortex for about 90 seconds, that point is regarded as being within

the suppressor strip, area 4s. This region is considered the posterior limit of the segment to be removed. All areas containing points identified as belonging to areas 4 and 4s are carefully preserved. The whole precentral convolution is thus left intact. The tissue immediately anterior to the precentral convolution is removed by careful subpial resection. Although it is possible that a small part of area 6 may be left behind by this method, it has been adopted to avoid as far as possible interference with the blood supply to areas 4 and 4s, thereby minimizing the chance of postoperative loss of motor power, or of impairment of suppressor effects of area 4s. It is believed that the continued activity of area 4s is an essential part of the postoperative result. The remaining three borders of the area removed are mapped out by anatomical inspection. The lower limit of removal corresponds to the level of the face area in area 4, except on the side of the motor speech area, in which the resection is not extended below the level of the arm area. The medial boundary of resection is the midline. The anterior boundary is gauged on morphological grounds, being as far as one can judge the junction between areas 6 and 8. It is not known what the result of removing all of area 8 would be, but in several of the late cases the anterior limit of resection was extended more and more forward into area 8 with more encouraging results.

In 1945 Bucy[16] reported on a further development of his work in the surgical treatment of tremor. After considerable research into the anatomy and physiology of the precentral cortex, he came to the conclusion that the impulses transmitting tremor travel specifically in the posterior part of the precentral gyrus, in area 4γ; the Betz cells, from which the large fibers of the pyramidal tract arise, are located in this strip. If this were true, cortical extirpation could be restricted to the posterior part of the precentral gyrus; areas 4a, 4s and 6 could be preserved. It seemed likely that such a limited excision would result in less paralysis than that which follows the larger removal of areas 4 and 6. The case of a young man, aged 23, who had suffered since the age of 8 from tremor at rest and mild spastic hemiparesis affecting the right extremities appeared suitable for trial. An osteoplastic flap was reflected under local anesthesia in the left fronto-parietal region, centered on the Rolandic fissure. The exposed cortex was carefully stimulated with a 60 cycle sine wave current, using a bipolar electrode. Motor responses were obtained only from the posterior part of the precentral gyrus.

The posterior half of the precentral gyrus, in those regions from which movements of the right upper and lower extremities were produced, was then removed subpially down to the bottom of the Rolandic fissure. Nine months after operation examination revealed complete absence of tremor. There was however considerable additional paralysis of the right upper extremity and some increase in spasticity.

Meyers[17] has done considerable work in surgery of the basal ganglia for treatment of tremor. His procedures involved extirpation of the head of the caudate nucleus and interruption of certain extrapyramidal fibers in the region of the anterior limb of the internal capsule.

Insofar as surgery of the spinal cord is concerned, numerous abortive efforts were made to relieve the symptoms of Parkinsonism. Pollock and Davis[18] cut several posterior roots in a case of rigidity and tremor affecting one upper extremity. Rigidity was diminished but not tremor. The column of Burdach was cut by Puusepp[19] with decrease in rigidity but not in tremor. The antero-lateral column was cut by Foerster and Gagel[20] without producing any change in symptoms. Putnam[21] performed antero-lateral cordotomy in five cases without success. Machansky[22] reported permanent recovery in three and satisfactory results in five of a series of seventeen patients subjected to cervical antero-lateral cordotomy. Oldberg[23] sectioned the antero-lateral column in two cases of unilateral tremor without effect.

It was not until 1940 that a substantial advance was made in spinal cord surgery for relief of tremor. Putnam[13] observed that section of the long descending extra-pyramidal tracts in the antero-lateral and anterior columns greatly decreased movements of an athetoid character but had no effect on alternating tremor. It therefore seemed reasonable to believe that, since impulses producing tremor must pass along some motor pathway, the lateral pyramidal tract was essential to the production of tremor. It had been observed by Rothmann[24] that section of the lateral pyramidal tract in monkeys produced little disability, so that there seemed reason to believe that it might be well tolerated in human beings. After some effort a case was found in which unilateral tremor was sufficiently incapacitating to justify the possible risks involved in cutting the pyramidal tract. The patient was a 32 year old woman who had had tremor of the right upper and lower extremities for sixteen years. Tremor was more severe in the upper than the lower extremities and interfered greatly with function. Under avertin anesthesia cervical

laminectomy was performed and the 4th cervical segment of the spinal cord was exposed. A #11 Bard-Parker blade was inserted into the lateral column adjacent to the point of exit of the posterior roots at an angle of 15 degrees to the vertical, to a depth of 4 mm. and then withdrawn. On the following day it was found that the left arm and leg were flaccid, and only the slightest movements of the fingers were possible. Strength rapidly returned so that on the 18th day the patient was able to walk and use her hand for drinking and writing. No tremor was observed at rest and only slight tremor was seen on movement. There was no increase in muscle tone. Four months after operation tremor at rest returned to about one-half its original intensity. A more radical operation was therefore decided upon. This time the point of the knife was swept out laterally to the horizontal meridian of the cord, thus transecting a triangular area just lateral to the posterior horn, measuring approximately 4 mm. along each side. One year after the second operation it was noted that the patient had about one-third the preoperative strength of the hand and arm. Gait was definitely hemiparetic, but the patient could walk better than after the first operation. No tremor at rest was seen, but slight tremor appeared on movement.

Oliver[25] in 1949 reported on a series of 48 cases in which a procedure slightly more radical than that described by Putnam was performed. The postero-lateral column was incised to a depth of 5 mm. as compared with 4 mm. in Putnam's original report. Oliver noted that the results were better in those patients who after operation had patches of analgesia on the opposite side resulting from involvement of the lateral spinothalamic tract.

In an attempt to improve the results, Oliver[26] increased the extent of incision in the cord to include the whole of the lateral column so that complete analgesia was produced on the opposite side to a level high up on the thorax, sometimes including the upper limb. Cervical laminectomy at the level of the second and third cervical vertebrae was performed. A #15 Bard-Parker blade was clamped with an artery forceps so that 5 mm. of the blade projected beyond the beak of the instrument. The blade was pushed into the cord at the site of attachment of a posterior rootlet at an angle of 45 degrees to a depth of 5 mm. The division of the lateral column was then completed with a blunt instrument which was inserted into the cord and brought forward to emerge at the line of attachment of the anterior nerve roots.

In 1946 the writer[27] became interested in the surgical treatment of the symptoms of Parkinsonism. It was naturally of the first importance to determine the neural pathways through which the impulses producing these disorders travel. It would then be possible to select the best surgical site to interrupt them.

On the basis of his experiences with excision of area 4γ and Putnam's results following section of the lateral pyramidal tract in the spinal cord, Bucy[16] had suggested that tremor is transmitted from the Betz cells of area 4γ through the large fibers of the pyramidal tract, and that destruction of the substantia nigra or the globus pallidus or of both is the commonest lesion which releases the pyramidal system to this form of abnormal hyperactivity.

Area 4 in man is divisible into three parts, 4γ, 4a and 4s, all of which probably contribute to the pyramidal tract. The human pyramid just rostral to the decussation contains roughly about a million nerve fibers, of which 61 per cent are myelinated and the rest unmyelinated. Of the myelinated fibers, 90 per cent are 1 to 4 microns, approximately 7 per cent are 5 to 9 microns and approximately 2 to 3 per cent are more than 9 microns in diameter. It is from the large Betz cells of area 4γ that the large pyramidal fibers greater than 9 microns arise. The remaining fibers that make up the pyramidal pathways are believed to arise from areas 4a, 4s, from an indefinite portion of the parietal lobe and possibly from area 6.

The pyramidal pathways in man consist of a large crossed lateral bundle, the lateral corticospinal tract, a small uncrossed lateral bundle, the ventrolateral corticospinal tract, and an extremely variable uncrossed anterior bundle, the ventral corticospinal tract. The degree of decussation is more variable in the human brain than in the brain of other primates. Flechsig in 1876 found in his series of human brains some with large lateral and negligible ventral pyramidal tracts and others with large ventral and small lateral tracts.

The lateral corticospinal pathway runs the length of the cord and the ventrolateral corticospinal pathway may. The ventral corticospinal tract is believed to terminate in the thoracic region, although at times it may be traced to the lower lumbar region. The lateral pathway ends in the anterior gray column of the same side, whereas the ventrolateral and ventral tracts cross to the gray column of the opposite side.

It seemed possible that the difference in the results following Bucy's

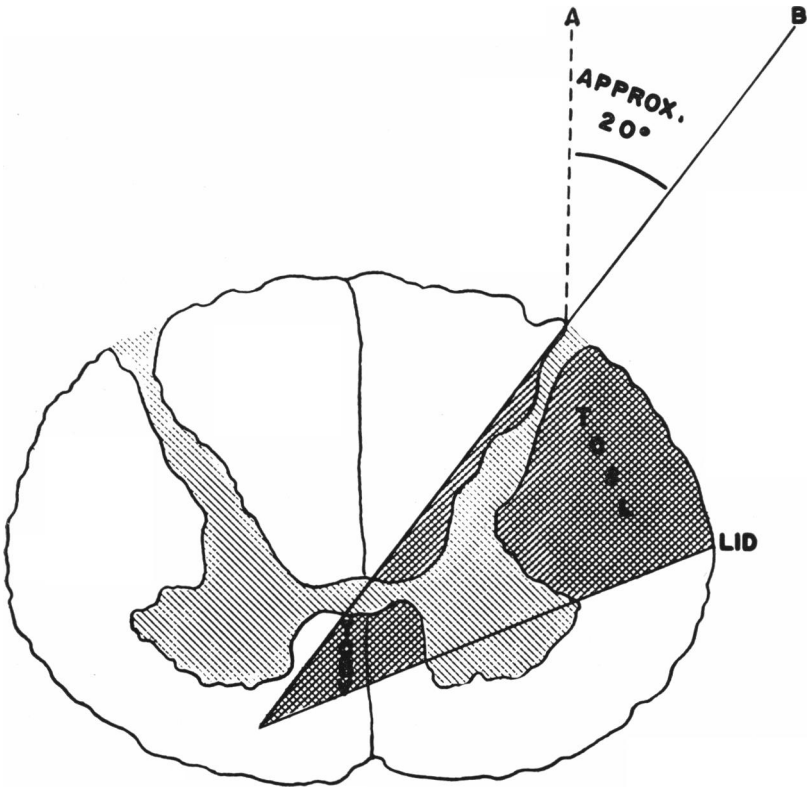

Figure 7—Diagram illustrating technique of combined lateral and ventral pyramidotomy. TCSL, lateral corticospinal tract; TCSV, ventral corticospinal tract; LID, dentate ligament; B, line of incision, at angle of approximately 20 degrees with the vertical, A, depth of incision, 8 to 9 mm. (From Ebin, J. Combined lateral and ventral pyramidotomy in the treatment of paralysis agitans, Arch. Neurol. & Psychiat, 1949, 62:27.)

section of area 4γ, in which case there was complete cessation of tremor, and Putnam's section of the lateral pyramidal tract, in which case there was partial relief of tremor, might possibly be attributed to the fact that lateral pyramidotomy does not interrupt all the fibers arising from the large Betz cells of area 4γ. It seemed possible that more complete relief of tremor by the spinal cord approach might be achieved by section of the ventral corticospinal pathway in addition to section of the lateral corticospinal. In view of the fact that at the level of the upper cervical portion of the cord the lateral pyramidal tract has already made its crossing and the ventral corticospinal pathway has yet to do so, the

contemplated procedure entailed section of the lateral corticospinal tract on one side and the ventral corticospinal tract on the opposite side.

The lateral corticospinal tract, lying in the posterolateral column, is easily sectioned. Interruption of the ventral corticospinal tract of the opposite side is more difficult, in view of its position in the posteromedial portion of the anterior column, alongside the anterior sulcus. The ventral tract might be reached in one of two ways: 1) By direct incision of the anterior white column, a procedure which is difficult and which would necessarily destroy most of its other tracts; 2) By cross incision from the opposite side, as seen in Figure 7, with the advantage that it would thus be possible to section the lateral corticospinal tract of one side and the ventral corticospinal tract of the other through one incision with relatively little unnecessary interruption of pathways.

Examination of specimens of the upper cervical portion of the cord indicated that this section could be accomplished by insertion of a blade in the line of the posterior roots at an angle of approximately 20 degrees to the vertical. The required depth of incision was 8 to 9 mm., the tip of the blade then being withdrawn in the line of the dentate ligament on the side of insertion.

The procedure was first used in the case of a man, aged 29, who had had encephalitis at the age of 10 years. This was associated with weakness and awkwardness of the right hand, which was followed shortly by the appearance of tremor and rigidity in the right upper and lower extremities. With the passage of time, shortening of the right upper and lower extremities became apparent. Of interest in the physical examination was the shortening of the right extremities. Neurologic examination disclosed right hemiplegic gait and coarse, rapid, alternating tremor of the right extremities, more pronounced in the upper. Tremor of the upper extremity was so severe that the patient found it necessary to sit on the hand and forearm to control it. Strength in the right extremities was almost normal except for the hand and fingers which could not be used because of flexion contractures. Muscle tone in the right extremities was greatly increased. Paralysis of the left oculomotor nerve was noted.

The operation was performed under local anesthesia so that tremor, rigidity and voluntary movement could be used to determine the proper extent of incision. Tremor was not reduced by preoperative medication, being strong enough to shake the operating table. Laminectomy of the 2nd, 3rd and 4th cervical vertebrae was performend. The dura was

opened to the right of the midline. The cord level between the 4th and 5th cervical segments was selected for incision so that there might be no interference with the function of the phrenic nerve which receives its main innervation from the 4th cervical segment. The posterolateral column on the right side was incised to a depth of 4 mm., sufficient to interrupt the lateral pyramidal tract, without abolishing tremor, rigidity or voluntary movement. A cataract knife was then inserted into the cord in the line of the posterior roots at an angle of 20 degrees to the vertical to a depth of 8 mm., and then drawn out at the dentate ligament. There was immediate cessation of the violent tremor in the upper and lower extremities on the right side and complete, flaccid paralysis of these extremities.

Bladder control appeared on the third day. Motor power began to return on the sixth day. The patient was able to walk at the time of his discharge from the hospital, two and one-half weeks after operation. Motor power reached its maximum in approximately three months. After twenty months it was observed that tremor at rest was absent except under the influence of extreme emotion. Tremor on movement was present but was much less severe than that noted preoperatively. Muscle tone in the right upper and lower extremities was almost normal. Muscle strength in the right lower extremity was the same as that observed before operation; in the right upper extremity motor power had returned to 90 per cent of its preoperative level. The patient was then doing manual labor.

This experience was of interest as it demonstrated the following points:

(1) Section of the lateral pyramidal tract alone does not immediately eliminate tremor, rigidity and voluntary movement.

(2) Cordotomy for section of the lateral pyramidal and the opposite ventral pyramidal tracts results in immediate disappearance of tremor, rigidity and voluntary movement.

(3) The procedure in this case produced great relief of tremor and rigidity, without regression, over a considerable length of time.

It was hoped that these results could be approximated in similar cases. The procedure was subsequently performed in 25 additional cases.

Postoperative Course—Urinary retention appears immediately after operation. Tidal drainage is therefore instituted on the patient's return from the operating room. Normal bladder control, appeared, on the

average, on the fifth or sixth day. Bowel function is aided by cathartics and enemas. The usual care of the skin is provided.

Paralysis has lasted on the average from eight to ten days, after which time there is gradual return of function. Function may return first in either the upper or the lower extremity, proximally or distally. Physical therapy which is begun on the fifth day includes heat, massage, passive and active exercises, reëducational exercises and sine wave stimulation. The patient is out of bed in a chair on the fourteenth day and is then gradually encouraged to stand and walk. The average period of hospitalization has been four weeks. Physical therapy is continued for five months after operation, treatments being given four times weekly.

Complications—(1) In two cases the postoperative course was stormy. In the first patient, who presented bilateral tremor, quadriparesis appeared on the second postoperative day. This was associated with severe cystitis and pyelitis which cleared up with urologic care. Hospitalization was extended for almost two months. At the time of discharge, the patient was able to walk with help and had moderate use of the upper extremities; return of function was greater on the side opposite to operation. Tremor was absent bilaterally. This patient was able for a time to get about and superintend the workings of his farm. However he is now bedridden with recurring bouts of pyelitis.

In the second patient quadriparesis also appeared on the second postoperative day. Severe cystitis and pyelitis were also associated with this complication. The infection ultimately responded to drug therapy. The patient was hospitalized for two months at the end of which there was only slight return of function.

(2) There were several cases of mild bladder infection which responded readily to treatment with drugs.

(3) Pain in the back of the neck, shoulder or arm lasting from several days to several months was a frequent complaint. In two cases this symptom was severe; burning pain was noted in the arm and forearm. It was thought that pain might have been due to damage inadvertently done to posterior rootlets. In subsequent cases particular care was taken to avoid these structures. Nonetheless, the symptoms continued to appear. They may be the result of damage within the cord to nerve fibers of the posterior root, or to the cells of the gray column.

(4) In eight cases there was difficulty in holding the head erect. It tended to be drawn toward the unoperated side.

(5) Pain and temperature sensibility was lost on the opposite side, usually in the lower extremity. In some cases it cleared up after several months; in others the loss was permanent. This was of course the result of section of some of the fibers of the lateral spinothalamic tract.

(6) A psychiatric reaction characterized by negativism was observed in one case.

(7) There was one postoperative wound hemorrhage which was satisfactorily cared for.

Results

Bucy and Case[12] have reported on the results of excision of areas 4 and 6 in several cases. Tremor was said to be completely abolished in each case and the motor function of the involved extremities was only slightly reduced. Putnam[13] reported on two cases of cortical excision of area 6. In one case tremor was markedly reduced, but motor function was also impaired to a marked degree. In the second case tremor was only slightly reduced and usefulness of the extremity was much impaired. Bucy[16] reported on excision of area 4γ. There was complete absence of tremor, but considerable additional paralysis of the upper extremity and some increase in spasticity. The results of Klemme[14] are difficult to evaluate.

Reid[15] has described his experiences with 15 cases in which area 6, and in some cases part of area 8, were removed. The response of tremor to the operation was problematical and inconsistent. In some cases relief was almost complete; in the majority it was somewhat reduced, but it was not abolished in any. He felt that increased muscle tone was generally reduced and that fine movements were more readily performed.

In the series of cases reported by Meyers,[17] in which the head of the caudate nucleus was resected and certain extrapyramidal fibers in the region of the anterior limb of the internal capsule were sectioned, the results have been equivocal. Tremor was completely relieved in several cases but not in others. In the series of cases in which section of the lateral pyramidal tract had been performed by Putnam,[13] there was substantial decrease in tremor. Function of the upper extremity was improved in all. Walking was better in some.

Oliver[25] reported on 48 cases of lateral pyramidal tract section. There was a mortality rate of 6 per cent with 3 deaths. Tremor was completely abolished in 12 per cent, reduced to a negligible degree in

37 per cent, unchanged in 12 per cent, and worse in 12 per cent. Usefulness of the arm was improved in 43 per cent, was unchanged in 23 per cent and was worse in 27 per cent. Walking was improved in 25 per cent, was unchanged in 33 per cent and was worse in 35 per cent; 54 per cent considered the operation worthwhile.

Oliver[26] subsequently reported his results following section of the lateral column, anterolateral as well as posterolateral. The operation was performed on 18 patients. With one exception, all of these patients were pleased with the result and were free of tremor except sometimes during moments of excitement. There were no deaths in this series.

With the passage of time the results of new techniques are seen in better perspective. Bucy[28] has more recently indicated that the results of cortical excision have not been satisfactory to him. Meyers' work on the basal ganglia has been of great interest from an investigative point of view. It seems questionable whether the procedures are of therapeutic value in cases of paralysis agitans. In so far as spinal cord procedures are concerned, several years ago Putnam[29] wrote that he was no longer performing lateral pyramidal tract section. Oliver[30] has recently indicated that he regarded surgery of the spinal cord as a last resort, to be used only when the patient was insistent in demanding relief of severe tremor.

At this point the results of cordotomy for section of the lateral and ventral pyramidal tracts, performed in 26 cases, will be reported. The follow-up period ranges from 7 months to 4 years. The results follow:

(1) There were 2 deaths in the series, a man of 22 and a woman of 69. In each case death occurred three months after operation. The patients were from out of town and had returned home six weeks after operation. The cause of death is not known in either case.

(2) Tremor was a prominent symptom in 23 cases. It was greatly reduced in 19 cases (82 per cent) and moderately reduced in 4 cases (18 per cent). The usual result was absence of tremor at rest, and slight or moderate tremor on movement or stress. There was no case in which tremor was not relieved.

(3) Rigidity was a prominent symptom in 8 cases before operation. After operation it was reduced in 4 and unchanged in 4. In 4 others, who had not been troubled with the symptom, increased muscle tone resulted from the operation.

(4) Muscle strength was diminished in all cases on the side of

operation. However, as tremor was relieved, the total function of the extremity was in some cases increased. In the upper extremity 7 (27 per cent) showed improvement, 12 (46 per cent) were unchanged and 7 (27 per cent) were worse. In walking, 2 (8 per cent) were improved, 12 (46 per cent) were unchanged and 12 (46 per cent) were worse.

It was observed that the personality make-up of the patient was of great importance in determining the final outcome. Since it is obviously not possible to restore the patient to a completely normal condition and since damage must be done to nervous tissue if tremor is to be relieved, the patient must adjust to a situation which is less than ideal. Patients of irritable, gloomy temperament found fault with even good results. Those of more sanguine, optimistic nature were pleased with results that were objectively less satisfying.

The over-all results of combined lateral and ventral pyramidotomy in which improvement is considered in terms of relief of symptoms, retention of moderate function and absence of complications of surgery follow:

Deaths	2	7.6%	
Improved			
Greatly	3	11.5%	
Moderately	4	15.4%	
Slightly	3	11.5%	38.4%
Unchanged	7	26.9%	
Worse	7	26.9%	

Study of the results in this group of cases suggests that the proper indications for cordotomy for section of the lateral and ventral pyramidal tracts in the treatment of Parkinsonism are the following:

(1) Relief of tremor is the only symptomatic indication. The results in cases presenting rigidity as the main symptom have been variable.

(2) Tremor must be severe and troublesome, without adequate response to thorough medical treatment. All drugs and combinations of drugs should be tested first.

(3) Cases with unilateral involvement are to be preferred.

(4) Cases with bilateral involvement, in which tremor is severe on only one side, may be considered.

(5) Personality of the patient should be optimistic, courageous and buoyant.

(6) Weight should be within average range. In obese patients too much weight must be borne by a weakened lower extremity. Walking has been more difficult in obese patients.

(7) Age should preferably be under 50.

(8) General physical condition should be good.

The results following combined lateral and ventral pyramidotomy have indicated that the chances of improvement are slightly better than 1 out of 3. In this group were a number of patients who do not meet what is now regarded as the proper indications for surgical therapy. If surgery is now limited to those who present these indications, the chances of improvement may be greater.

Pathophysiology

Prior to the investigations of the past fifteen years very little was known of the pathophysiologic mechanisms underlying the production and transmission of tremor and rigidity, the most prominent symptoms of Parkinsonism. The various surgical procedures performed for the relief of these symptoms have provided information which might be expected to shed light on their neural mechanisms and pathways.

In so far as rigidity is concerned, the mechanisms of production and the pathways of transmission are even at this time not definitely known. More is known about tremor.

The pathophysiology of tremor must be considered in two parts:

(1) How is it produced?

(2) Over which pathways is it transmitted?

In so far as the first part is concerned, there have been two prominent points of view. According to the "irritative" theory, tremor is the direct result of damage to nervous structures. According to the "release" theory, tremor is "released" by damage to an inhibiting neural mechanism. Bucy has supported the "release" theory. As noted earlier, he has suggested that tremor is transmitted from the Betz cells of area 4γ through the large fibers of the pyramidal tract. Bucy[31] has further suggested that the pyramidal system is released by interruption of an inhibiting mechanism which functions under normal circumstances. This circular inhibitory or suppressor mechanism is believed to originate in the precentral cortex, passing to the substantia nigra, to the globus pallidus, to the thalamus and back to the precentral cortex. Lesions of the substantia nigra, globus pallidus, or both, interrupt the suppressor mechan-

ism; the pyramidal system is released from control and tremor appears.

Study of the surgical experiences of the various workers in the field of surgical therapy of Parkinsonism reveals certain inconsistencies and contradictions. Bucy and Case removed areas 4 and 6 with permanent (4 year follow-up) abolition of tremor. Bucy has removed area 4γ with complete (9 month follow-up) relief of tremor. Reid has reported on excision of area 6 and part of area 8. In one case performed under local anesthesia, removal of a small portion of area 6 alone produced immediate cessation of tremor of the right hand, without impairment of voluntary movement. (Tremor gradually returned and after 18 months it had returned to the preoperative level.) Klemme, who has never published details of his technique, has excised cortical tissue anterior to the excitable motor cortex, which presumably included area 6 and perhaps area 8. Abolition of tremor has been reported in a high proportion of his cases; the writer has seen two of his patients who were almost entirely free of it. Thus, in the group of cortical procedures, excision of area 4γ has been reported to abolish tremor, as have excision of area 6, and excision of area 6 plus a small portion of area 8.

In the group of spinal cord procedures, Putnam had originally reported that section of the posterolateral column in the cervical region interrupting the lateral pyramidal tract caused great reduction in tremor. Oliver reported that in his hands more complete relief of tremor was provided by section of the anterolateral column and the lateral portion of the anterior column in addition to the posterolateral column. It is of interest that Putnam had observed earlier that extensive destruction of the anterolateral column and the lateral portion of the anterior column was of some value in the relief of athetosis, but was of no value in tremor. It was my experience that section of the lateral pyramidal tract did not provide satisfactory relief of tremor. Better results were obtained with the more extensive cordotomy interrupting among other tracts the lateral pyramidal and the opposite ventral.

Certain facts emerge from this group of experiences:

(1) It is not wise to attach too great significance to the results of surgical procedures on the human brain and spinal cord in attempting to work out precise details of pathophysiology. The procedures are gross; it is often not possible to be certain of topographical areas. This is particularly true of the cortex; in the living brain it is difficult to identify specific convolutions, and much more difficult to identify Brod-

mann architectonic areas. Furthermore, since deaths have fortunately been rare, it has not been possible to check on the precise location and extent of the incision or excision, which is always done in valid investigations in experimental animals.

(2) In so far as Bucy's theory regarding tremor is concerned, relief of tremor by excision of area 6, and by excision of areas 6 and 8, as well as by excision of area 4γ,—and the greater relief obtained in the spinal cord approach by extensive cordotomy than by lateral pyramidal tract section alone, suggest that the impulses transmitting tremor are not restricted to area 4γ and the pyramidal tract. It seems likely that these impulses actually pass or may potentially pass through all motor pathways, extrapyramidal as well as pyramidal.

The relief of tremor by cordotomy for interruption of the lateral and ventral pyramidal tracts is probably to be attributed to the fact that the incision interrupts all the pyramidal innervation to a side and also much of the extra-pyramidal, including the rubrospinal, lateral reticulospinal and mesencephalospinal tracts.

(3) As a corollary of (2), effective relief of tremor cannot be accomplished by surgery of the brain or spinal cord without at least moderate loss in motor power.

Future Therapy

At this point it might be of interest to consider what the future may hold in the treatment of Parkinsonism. As matters stand now, drug therapy can provide moderate relief for cases presenting slight involvement. Among the cases of moderate and severe involvement, which are only slightly benefited by even the new drugs, some will find relief in the surgical procedures that are known today. These will include cases of unilateral tremor, and occasional cases of bilateral tremor more severe on one side in people of well-integrated personality. However, many cases of moderate and severe involvement have at present no means of significant relief. From what direction may help for these cases come?

There are three possibilities:

(1) Prophylaxis—It is possible that advances in the understanding of virus and degenerative diseases may point out methods of preventing the development of the Parkinsonian syndrome. However, this does not appear likely in the near future.

(2) Drugs—This is an age of scientific marvels. It is possible that

new drugs will be developed which will control symptoms in even the most severe cases.

(3) Surgery—In so far as surgery of the nervous system for the relief of tremor and rigidity is concerned, it is almost certain that we have gone as far as we can go. Since it appears likely that the impulses mediating tremor may travel along all motor pathways, both pyramidal and extrapyramidal, it is improbable that a surgical procedure can be developed which will provide greater relief of tremor with less interference in function. Rigidity has not been consistently relieved by any of the surgical procedures used in Parkinsonism, even though the motor system has been thoroughly investigated.

In summary, the outlook for the treatment of cases of Parkinsonism with slight involvement is good; drugs are effective in this group. Certain selected patients with moderate and severe involvement in whom tremor is the main complaint may be benefited by surgery of the brain or spinal cord. However, for many patients in the last two groups there is at this time no effective treatment. Nonetheless, in view of the unprecedented activity in all fields of medicine and related science, the outlook is by no means without hope.

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