SURGICAL RELIEF OF TREMOR AT REST

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THAT TREMOR AT REST arises from the activity of the precentral cortex (regardless of the location of the lesions responsible for the disease) has gradually become increasingly clear. In 1817, Parkinson[11] noted in his Case 6 that the tremor at rest, which had been generalized, was abolished from the right side during the two weeks that side was paralyzed as the result of an apoplectic seizure. Patrick and Levy,[12] in 1922, and Balser,[1] in 1942, made similar observations. However, in such cases the damage from the cerebrovascular disease has been too extensive to permit one to determine accurately the cortical area and the pathway primarily concerned with the production of tremor (Balser[1]). In addition, in 1937, I had abolished both tremor at rest and intention tremor from the right upper extremity by extirpating the "arm" area from areas 4 and 6 of the left precentral gyrus and the neighboring frontal convolutions.[7] This observation definitely established the fact that these tremors, though probably released by destructive lesions in the subcortical nuclei, are produced by nervous impulses arising from the precentral motor cortex (areas 4 and 6). However, it left doubt as to whether these impulses responsible for the involuntary movements of tremor are mediated *via* the pyramidal fibers from area 4 or the extrapyramidal fibers from areas 4 and 6. Putnam[13] helped to clarify this question. In 1938, he demonstrated that tremor at rest is abolished by section of the lateral pyramidal tract in the cervical spinal cord. He subsequently confirmed this observation in several additional cases.

Fibers in the pyramidal tract arise from various places other than the precentral motor cortex (Tower[14]). Whether these nonprecentral origins are confined to the cerebral cortex (particularly the parietal region), as Mettler[10] believes, is not as yet a matter of general agreement. However, the clinical observations cited above demonstrate that only those pyramidal fibers arising from the precentral region are concerned with the production of tremor and in the precentral region pyramidal fibers arise only from area 4 (Tower[14]), which in man is confined to the precentral gyrus (von Bonin[2]). Architecturally, area 4 in man is divisible into three parts: area 4γ, area 4a and area 4s (von Bonin[2]), all of which probably contribute to the pyramidal tract. However, the large pyramidal fibers (over 9μ), which form only two to three per cent of all of the pyramidal fibers, probably arise from the Betz cells which are to be found only in area 4γ. Area 4γ, in turn, forms the posterior part of the precentral gyrus (Fig. 1). The possibility existed that only the Betz cells and these large fibers are concerned with the production of tremor. If this

were true then cortical extirpations could be restricted to the posterior part of the precentral gyrus (area 4γ), and areas 4a, 4s and 6 could be preserved. It seemed likely that such a limited extirpation would produce less paralysis and leave a more useful extremity than was obtained following the larger extirpation of areas 4 and 6. The following case presented an excellent opportunity to test this possibility.

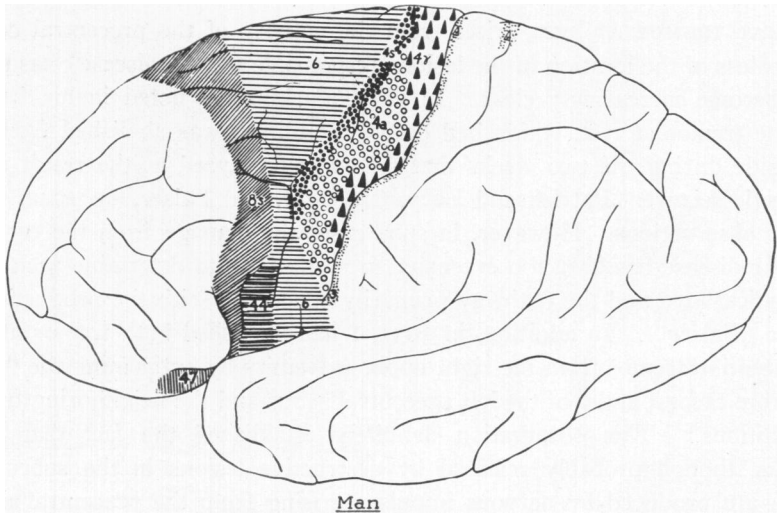

FIG. 1.—The human precentral motor cortex (areas 4γ, 4a, 4s, 6 and 44) and some adjacent areas.

Case Report.—P. di F. was referred by Dr. Daniel H. Levinthal of Chicago, Illinois. He was born in Chicago of Italian parents. He was 23 years of age and single. He had been under observation both in the hospital and in the dispensary at the Illinois Neuropsychiatric Institute for some time. On July 29, 1943, he was admitted to the hospital for operation. This young man came complaining of marked weakness of the right arm and leg and of a tremor, involving these extremities, for 15 years, since he was eight years old. His father informed us that the patient had been a normal healthy child until about the age of 5.5 years, when he had a rather severe attack of "influenza," or "pneumonia." He was ill for approximately three or four weeks. The exact nature of this illness we were unable to learn. However, he seemed to recover from it completely and to remain well until two years later, when he was 7.5 years old. At that time his school teacher noticed that he was beginning to limp and that the right extremities were weak. A short time later a tremor appeared in these extremities. This was, and always has been, worse on excitement and has disappeared during sleep. It has always been most marked with the extremities at rest, and often disappeared during the execution of voluntary movements. The termor and weakness gradually increased in severity, and, whereas, originally the tremor was not constantly present, it was present during all of his waking hours for the five years prior to admission. For three years, that is, since the age of 20, his speech had been much more indistinct than formerly.

Nothing else in the patient's past medical history or in the family history seemed relevant to his present condition.

Physical Examination.—The temperature, pulse and respiratory rate were normal, the blood pressure was 120/76. He was a fairly well-developed and well-nourished white man, with an expressionless face and a marked tremor of the extremities on the right side of his body. He spoke haltingly, and it was at times with difficulty that he was

understood. He was said to be right-handed. He walked with a marked limp, favoring the right lower extremity. There was a scoliosis and a rotation of the trunk, such that the right hip was thrown posteriorly and the right shoulder thrown anteriorly, and he leaned toward the right side. The general physical examination was otherwise negative. The cranial nerves were intact except that the left pupil was slightly smaller than the right and slightly irregular. Both reacted normally to light and on accommodation. There were no oculogyric crises. There was a slight transient nystagmus, particularly on looking to the right. At times fasciculation of the masseter muscles on the left side was seen. There was a definite right lower facial weakness, both on volitional and emotional movement. Auditory acuity was reduced slightly bilaterally. The right shoulder was held elevated and thrust forward. There was, however, no weakness of the sternocleidomastoid muscle or of the trapezius. The tongue protruded in the midline. Because of the violent tremor involving the right extremities, it was difficult to appraise the tendon reflexes. It was finally concluded, however, that they were definitely increased throughout the entire right side of the body, although they were normally active on the left side. The abdominal reflexes were active bilaterally, as were the cremasterics. Hoffmann's sign was not present. The jaw jerk seemed to be increased. There was a suggestive Babinski sign on the right side only. No clonus was elicited. There was weakness at the wrist on the right side but the grasp was quite strong. There was also weakness of the movements of the thumb and the fingers on the right side. Otherwise strength in the right upper extremity was good, although useful activity was practically prevented by the rigidity and the tremor. There was some weakness of the right lower extremity. He walked with a typical spastic hemiplegic gait, tending to drag the foot and circumduct it. The lower extremity was also internally rotated, so as to throw the greater trochanter forward. Actual weakness of the lower extremity, when individual groups of muscles were tested, was, however, slight. There was definite reduction in the volume of the muscles throughout the entire right side. This was perhaps most noticeable in the interossei of the hand. There was definite cogwheel rigidity throughout the right side. There was a pes equinus deformity of the right foot, with contracture of the gastrocnemius and soleus muscles on that side. There was definite diminution in size of the gluteus muscles on the right side. Finger-to-nose and heel-to-knee tests were reasonably well done except that on the right side the tremor interfered somewhat with these tests. Sensation in all forms was intact everywhere.

There was a marked tremor involving both the right upper and lower extremities. The oscillations were at approximately three to four per second. They involved the entire extremity but were most pronounced in the distal half. There was a tendency toward pill-rolling in the right hand, and a marked flexion tremor at the wrist. Both the tremor and the rigidity were more marked in the right upper than in the lower extremity. The tremor was predominantly a tremor at rest, although it was not completely absent during voluntary movement. He had a rather expressionless face; his speech was slow and drawling and hesitant. At times it seemed as though there were a slight motor aphasia in that he did not finally say the word that he started with. However, on detailed tests for aphasia, there were no definitely positive findings. He was slow in his responses, his intelligence was not above average, and he occasionally stuttered. A diagnosis of unilateral right parkinsonism resulting from a chronic encephalitis was made and was concurred in by all who saw and examined him.

Laboratory Data.—Urinalysis was negative, the blood count was normal, the Wassermann and Kahn tests on the blood were negative. A lumbar puncture was made, the cerebrospinal fluid contained 9 mg. of protein per 100 cc. of fluid, the Wassermann test was negative, the colloidal gold curve was flat, and the fluid contained two cells per cubic millimeter. An electro-encephalogram was made, which showed some spike-like waves of slow frequency to either side of the midline in the frontal region.

The patient was given hyoscine hydrobromide and tincture of stramonium without benefit.

Operation.—On August 3, 1943, under ether anesthesia, an osteoplastic flap was reflected in the left parietal region, exposing the central sector of the cortex of the left cerebral hemisphere up to the midline, and with the fissure of Rolando in the middle of the operative field. The exposed cortex did not appear abnormal. Photographs were taken of it (Fig. 2) and a sketch of the cortex was made by Dr. Percival Bailey (Fig. 3). All of the exposed cortex was then 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 (Fig. 3). As noted in a previous publication

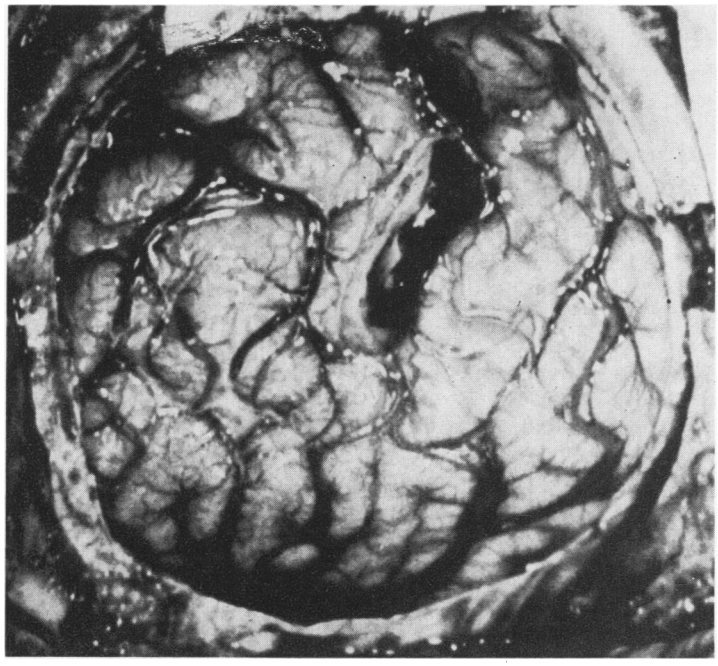

FIG. 2.—Photograph of the left central region after extirpation of the posterior half of the precentral gyrus and, thus, of area 4γ in the "arm" and "leg" fields.

with Dr. Garol,[9] stimulation of an area just anterior to the precentral gyrus and just ventral to the posterior end of the first frontal sulcus or superior frontal sulcus, caused a suppression of peripheral motor response. This area presumably corresponds to area 4s in the subhuman primates. As this response was previously described in detail,[9] it need not be further alluded to here. The threshold for motor responses from the posterior part of the precentral gyrus was 1.6 volts. Movements were elicited in the head region and in both the right upper and lower extremities, as indicated on the accompanying diagram (Fig. 3). When the current was increased to 2.5 volts, a typical motor after-discharge was produced. The posterior one-half of the precentral gyrus in those regions from which movement of the right upper and lower extremities had been produced, was then removed subpially down to the bottom of the central sulcus (Fig. 2). The great rolandic vein and the communicating vein, which crossed the region of the extirpation were left intact. The extirpation extended down the medial surface of the hemisphere to the first sulcus. The dura mater was then closed tightly, the osteoplastic flap replaced and held in place with silk sutures and the scalp wound closed as usual.

Postoperative Course.—The operation was completed at 4:30 P.M. At 6:00 P.M., the patient was awake and able to coöperate in a limited examination. There was a com-

plete paralysis of the right upper extremity, and although there was marked weakness of the right lower extremity, he was able to flex the hip. There was definitely increased resistance to passive stretching of the flexors of the right upper extremity. All tendon reflexes on the right side were hyperactive; clonus could be elicited at the right ankle; Hoffmann's sign could be elicited in the right hand; Babinski's sign was present on the right side; the right abdominal reflexes were absent; but the cremasteric reflexes were all present; there was a right facial weakness; all sensation was intact, including

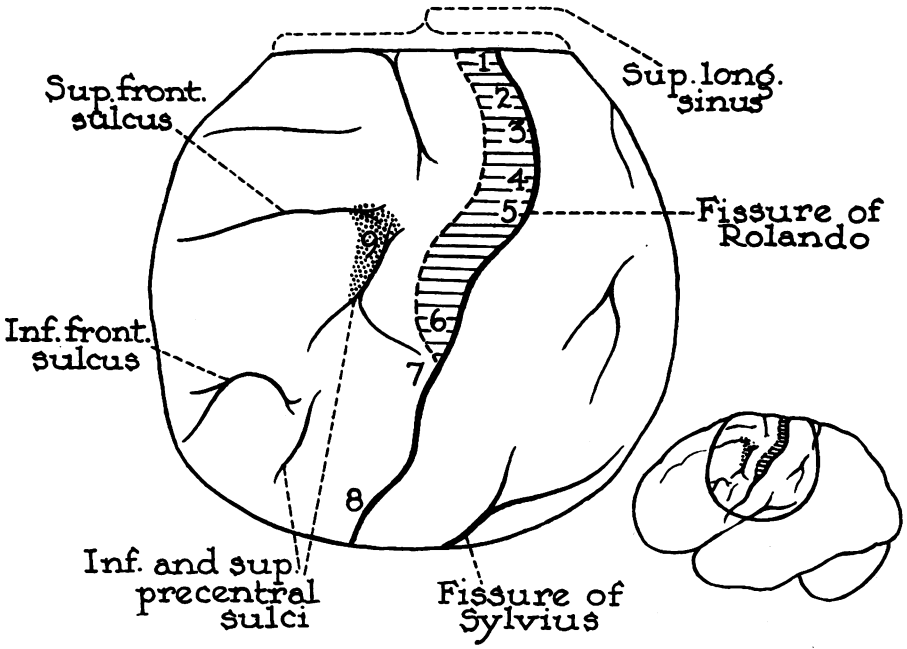

FIG. 3.—Artist's elaboration of a sketch of the cerebral cortex exposed at operation. The insert indicates the general relation of the exposed cerebral cortex. The numbers designate areas of various responses to electrical stimulation. The area for flexion of the right hip is indicated by 1; for contraction of the right quadriceps femoris muscle, by 2; for contraction of the right pectoralis major muscle, by 3; for flexion of the fingers of the right hand, by 4; for flexion of the right elbow and wrist, by 5; for movement of the neck and right 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 on the right side, by 8, and for the suppressor area—areas 4s, by 9. The area which was extirpated has been indicated by cross-hatching.

light touch, pain sensibility as determined by pinprick, the perception of differences in temperature, vibratory sense, position sense and the recognition of the shape of objects (stereognostic sense).

On the first postoperative day (8-4-43), at 9:00 A.M., his speech was the same as before operation. He was able to abduct the right arm at the shoulder for about 10° to 15°. This movement was performed only after a considerable latent period and with considerable difficulty. He was also able to flex the right elbow after a considerable latent period, and also weakly. He could flex the right hip quite well, probably as well as he could before operation. He was able to extend the right knee about 50 per cent as well as prior to operation. However, he was unable to flex the knee or to move the ankle, the toes, the wrist or the fingers. There was a moderately increased resistance to passive flexion of the elbow, but only after the elbow had been flexed to 90° and a similar resistance to passive extension of the right elbow, after it had been extended to approximately 135°. There was a definite reduction in the sense of position in the right fingers to approximately 50 per cent of absolute accuracy. However, he

was conscious of each passive movement of the finger, and he was able to identify each finger touch accurately. With his eyes closed he erred by as much as six to ten inches in trying to find his right hand with the left. There was no reduction in pain sensibility, as tested with pinprick on either side. All of the tremor which had been present preoperatively was completely abolished and remained so thereafter. There was marked perspiration, involving the entire right arm and right leg, while the left extremities were perfectly dry. Babinski's sign was present.

On the second postoperative day, the right abdominal reflexes had returned, but they were not as active as those on the left side. The cremasteric reflexes, however, were equally active on the two sides. The marked perspiration continued on the right side of the body and involved the head, right arm and upper part of the trunk more than it did the lower part of the trunk and the right lower extremity. Position sense was grossly defective in the right fingers but quite accurate in the toes.

Movement in the right upper extremity was much less than it had been on the first postoperative day and was reduced to limited feeble twitch-like movements at the right shoulder. Movement in the right lower extremities were, likewise, reduced as compared with the first postoperative day. Resistance to passive movement in both the flexors and extensors, in both the upper and lower extremities, on the right side, was more marked. On August 7th, the fourth postoperative day, the excessive perspiration on the right side of the body still continued. The tremor was still completely abolished. He was able to identify individual fingers on the right side, but his sense of position in the right fingers and his ability to find the right hand with his left hand when his eyes were closed was grossly defective. Vibratory sense was only very slightly diminished on the right side. Sense of position was excellent in the toes and at the wrists. The reflexes were the same as they had been on the first and second postoperative days. Perception of pinprick was normal and the perception of alterations in temperature was acute over his entire body. The ability to recognize objects with his right hand, although not abolished, was definitely impaired. He could recognize numbers written on the palms of the hands, but on the right side it was necessary for these numbers to be three and one-half centimeters high, whereas numbers one and one-half centimeters high were properly recognized on the left side. He was able to detect gross differences in the weight of objects placed in his right hand. Movements at the right shoulder and elbow continued to increase in strength, but there was still no movement at the wrist or of the fingers. Likewise, movements of the hip and knee on the right side continued to increase, whereas there was still no movement at the ankle or of the toes. This condition continued gradually to improve. By the twentieth postoperative day, August 23, 1943, the tremor continued to be entirely abolished; he was able to walk almost as well as before the operation and he had become able to flex his fingers, but could not extend them. In the lower extremities individual movements at the hip and knee had continued to gain in strength, but he was unable to move the ankle or the toes. There was a slight increase in resistance to passive movement on the right side. All tendon reflexes on that side were markedly increased and Babinski's sign was still present. Clonus could be elicited at both the knee and ankle. Hoffmann's sign was present on the right side. Both the abdominal and cremasteric reflexes were active on both sides of the body. There was no disturbance of sensation including light touch, pinprick, alterations in temperature, vibration and position sense. On September 4, 1943, one month after the operation, the patient was discharged from the hospital. The tremor was still completely abolished, and has remained so up to the present time.

By September 30, 1943, almost two months after the operation, he was walking better than prior to the operation. He was able to shake hands using his right hand. Strength in the right extremities had improved greatly. He now could not only flex the right hand and fingers, but could extend the fingers and thumb as well. In October he obtained a job in a laundry handling bundles, but he found that he had to discontinue

it because of difficulty in maintaining his balance when attempting to carry bundles and walk up stairs. By January 4, 1944, five months after the operation, he was able to tie his shoes and his necktie, using both the right and the left hand, to grasp. His right hand had increased in strength.

On May 3, 1944, nine months after the operation, he was able to walk with his body upright, although with a definite hemiparetic gait. He did not swing his right arm as he walked. There was a definite moderately spastic hemiparesis on the right side, much the same as prior to the operation. All tendon reflexes were increased on that side. Hoffmann's sign was present on the right side, as was Babinski's sign. Ankle and patellar clonus were still readily elicited. The musculature on the right side was definitely atrophic as compared with the left, just as it had been prior to the operation. There was no disturbance of sensation anywhere. The violent tremor at rest which had been present prior to operation had never returned. His speech was still slow and rather monotonous as it had always been. When last seen, on December 13, 1944, over 16 months after the operation, the tremor was still absent. Useful voluntary movements of the right upper extremity were very limited. He walked better than before the operation, although in a similar fashion.

DISCUSSION.—These observations present several points of interest, particularly as concerns the effect of the extirpation of area 4γ upon tremor at rest, upon paralysis and spasticity, upon sensation and upon perspiration.

Tremor: Extirpation of the "arm" and "leg" portions of area 4γ (the posterior part of the precentral gyrus) abolishes tremor at rest in the contralateral upper and lower extremities. The tremor was abolished immediately after the operation and has not returned during the subsequent 16 months that the patient has been observed. This would indicate that tremor at rest arises from the activity of the Betz cells and is produced by nervous impulses mediated by the large (9 to 22μ fibers), which form two to three per cent of the pyramidal tract.

These conclusions relative to the mechanism responsible for the actual production of tremor at rest have no bearing upon the question of what structures must be destroyed for tremor at rest to appear. It is very likely, as I[5] have previously noted, that destruction of the substantia nigra or of the globus pallidus, or of both, is the most common lesion which releases the pyramidal system to this form of abnormal hyperactivity.

Paralysis: This young man was not the ideal patient upon which to determine the degree of paralysis resulting from the removal of area 4γ. He had some paralysis before the operation. Nevertheless, following the operation he had much more paralysis particularly in the upper extremity and particularly in the distal parts (hand, fingers and foot) than before the operation. In the hand this has prevented much utilization of the upper extremity, although the disability has been somewhat less than in those cases where areas 4 and 6 were removed (Bucy[4]). In the lower extremity the disability does not appear to be much, if any greater than before the operation.

Spasticity: Although the resistance to passive manipulation of the right extremities is not great it is definitely more than before the operation. Furthermore, the tendon reflexes are much more active than before the operation,

clonus is readily elicited and Hoffmann's sign has appeared in a forthright manner. This all strongly indicates that in man inhibition of the postural and myotatic reflexes is not limited in the precentral motor cortex to area 4s but is also represented to some degree in area 4γ. Admittedly, this case does not definitely establish that as a fact for there is no evidence as to possible operative or postoperative damage to area 4s.

Sensation: This case, along with previous similar observations (Bucy[6]), leaves little doubt that the precentral gyrus is not concerned with the conscious perception of sensory stimuli. Earlier, many individuals had observed that removal of the precentral gyrus results in impairment of some forms of sensibility on the opposite half of the body. In the vast majority of instances this sensory impairment is temporary. This case clearly establishes the fact that the sensory loss does not appear immediately after the destruction of the precentral tissue as would be the case if it resulted directly from that cortical extirpation. Rather the sensory deficiency appears gradually several hours after the extirpation as would be expected if it were due to the impairment of the circulation of the neighboring structures, notably the postcentral gyrus, from edema and venous thromboses secondary to the operation.

Perspiration: The observation that the right half of the body perspired very profusely for several days after the extirpation is peculiar, in my experience, to this case. This would seem to indicate that area 4γ is concerned with the control of perspiration, probably through the sympathetic system. In this instance the excessive perspiration could be interpreted as resulting from the removal of cortical inhibition from the sympathetic nervous system, releasing it to temporary hyperactivity. Similarly, several years ago, I[3] reported another case in which a presumed capsular hemiplegia was associated with unilateral vascular spasm, abolition of the pulse, inability to obtain the blood pressure, cyanosis and coldness of the paralyzed extremities. In this instance, too, a release of cortical inhibition over the sympathetic nervous system was postulated.

How the present observation correlates with that previously reported with Pribram,[8] in which a tumor beneath the lower end of the right precentral gyrus was associated with epileptiform convulsions of the left half of the face and associated attacks of localized sweating of the left side of the face and left upper extremity, is not as yet entirely clear. Both observations indicate that the precentral region exercises some control over the mechanism of sweating and that control is a localized one, as evidenced by the unilateral sweating in the present case and the limitation of the sweating to a small part of one side of the body in the case recorded with Pribram[8]

Aphasia: In previous cases where a more extensive extirpation of the left precentral region was made for the relief of involuntary movements a temporary motor aphasia developed.[4] In this case, with a much more limited extirpation, there was at no time any such disturbance of speech.

Suppression: Garol and I[9] have already reported the demonstration for

the first time of the suppressor activity of area 4s in the human brain, in this case.

SUMMARY

The case of a young man, 23 years of age, is reported. He suffered from a severe tremor at rest and a mild spastic hemiparesis involving the right extremities, from the age of eight years. The "arm" and "leg" portions of area 4γ, the posterior part of the precentral gyrus, were removed. This procedure completely abolished the tremor, produced considerable paralysis particularly of the hand and fingers, resulted in some increase in spasticity, caused no immediate disturbance in sensory perception, and was followed by excessive perspiration on the right half of the body for a few days. In this same case, at the time of the operation, the suppressor effect of area 4s was demonstrated for the first time in the human brain.

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