Relief of intention tremor by thalamic surgery¹

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In 1960, it was first reported by one of us (Cooper, 1960a) that intention tremor could be relieved by a surgical lesion placed in the ventrolateral nucleus of the thalamus. Since then, a number of reports have appeared in the literature (Cooper, 1960b; Broager and Fog, 1962; Cooper, 1962b; Kravynbühl and Yasargil, 1962; Cooper, 1965; Laitinen, 1965; Fox and Kurtzke, 1966), corroborating the therapeutic value of thalamic surgery for intention tremor.

It is the purpose of this report to summarize our results and sequelae of cryothalamectomy, carried out on 73 consecutive cases of intention tremor of diverse aetiology. These operations were performed during the period of 10 August 1966 until 26 July 1968.

MATERIAL AND METHODS

The seventy-three patients were examined pre-operatively by the investigative team on the neurosurgical service at St. Barnabas Hospital. In the clinical analysis of the symptoms, intention tremor was rated on a five-point scale, ranging from 0 for absence of the tremor to +4 for maximum rating. Pre- and post-operative motion pictures were obtained in each case. In addition, a special objective method (Dierssen, Lorenc, and Spitaleri, 1961) of evaluation of individual motion picture frames before and after surgery, provided a measurable index of intention tremor (Fig. 1).

Language and speech assessments were made one to three days before surgery, within two weeks after surgery, and in some cases during follow-up re-evaluation of varying periods.

Pre-operative psychological data on each patient were derived from clinical interviews conducted by an experienced psychologist. On the basis of these initial interviews each patient was rated on a three-point scale as a good, fair, or poor candidate for surgery. Usually, patients with 'poor' pre-operative psychological ratings did not, and do not, undergo surgery. However, since the decision regarding advisability of surgery must take into account medical condition, neurological factors, and other variables, in addition to psychological findings, some patients with a 'poor' psychological rating may

sometimes undergo surgery because of extenuating circumstances. For example, a limited goal might be an attempt to decrease dependence on nursing care through surgical alleviation of the tremor affecting the arm and hand needed for feeding.

Investigative procedures were performed, when indicated, to determine the aetiology of the intention tremor, and included radiographs of the skull, CSF analysis, EEG, EMG, brain scanning, angiography, pneumoencephalography, and occasionally cortical biopsy.

PRE-OPERATIVE STATUS Variables pertinent to pre-operative status are shown in Table 1.

The causes of intention tremor in the present series were as follows: familial (26 cases); multiple sclerosis (25 cases); cerebellar degeneration of unknown origin (seven cases); post-traumatic (five cases); posterior fossa tumour (one case); Leber's disease (one case); and associated with torticollis in two cases and Parkinsonism in six cases. Thirty-nine patients were males and 34 were females. There was male preponderance in the familial group in contrast with the multiple sclerosis cases. The age incidence varied from 15 to 79 years with a mean of 42.3 years. All the patients, except one, were right handed. The average duration of the tremor was 17.9 years with a range of two to 50 years. The tremor was unilateral in three cases and bilateral in the remaining. The upper extremities were affected more than the lower; and the right side slightly more than the left. In 13 patients, there was neck tremor in addition to limb tremor. In all cases, the tremor was severe enough (3+ or more) to interfere with the patient's activities.

As expected, the patients with multiple sclerosis demonstrated other neurological deficits such as nystagmus (eight cases), optic atrophy, cranial nerve palsy, dysarthria, spasticity, sensory abnormalities, and sphincteric disturbances. Also, patients with cerebellar degeneration of unknown aetiology, showed other cerebellar signs such as nystagmus (three cases), ataxia (two cases), and dysmetria (two cases).

On the basis of pre-operative psychological evaluation, 41 patients were rated as good, 24 were labelled as fair, and eight were considered poor candidates for surgery.

Medical problems significant from a surgical standpoint included pre-existing hypertension (five cases), cardiac conditions (three cases), diabetes mellitus (three cases), urinary problems (six cases), and epilepsy (two cases).

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FIG. 1. Tracing from cinematographic record (technique of Dierssen) to demonstrate spatial and temporal elements of intention tremor. A = before surgery; B = after surgery.

TABLE 1
CAUSES OF INTENTION TREMOR

Aetiology of I.T.	Cases (no.)	Sex		Age (mean) (yr)	Duration of I.T. (mean) (yr)	Positive family history	Side of I.T.			Psychological candidacy		
		M	F				Bilat.	Unil.	Neck	Good	Fair	Poor
Familial cerebellar degeneration	26	18	8	54.4	31.7	26	22	4	5	18	7	1
Multiple sclerosis	25	6	19	32	8.2	2	25	—	5	12	9	4
Idiopathic I.T.	7	4	3	43.4	19.4	—	5	2	1	3	3	1
Severe head injury	5	5	—	34	4.2	1	4	1	1	3	2	—
Post. fossa tumour	1	—	1	15	7	—	1	—	—	—	—	1
Leber's disease	1	1	—	15	6	—	—	1	—	1	—	—
I.T. and torticollis	2	1	1	42	12	—	2	—	—	1	1	—
I.T. and Parkinsonism	6	4	2	62.1	9.3	—	6	—	1	3	2	1
Total	73	39	34	42.3	17.9	29	65	8	13	41	24	8

OPERATIVE DATA The surgical procedure of cryothalamectomy (Cooper, 1962a), was used in all the cases. Sixty-four patients had unilateral surgery (49 on the left side of the brain and 15 on the right), and nine had bilateral surgery. The time interval between the first and second side surgery was at least six months. In all instances, the surgical target was the posterior aspect of the ventrolateral nucleus of the thalamus (VL) extending slightly posteriorly to include the adjacent anterior portion of ventroposterolateral (VPL) and/or ventroposteromedial (VPM) nuclei. The two cases of intention tremor associated with torticollis, required additional lesions in centromedianum (CM).

The ventricular landmarks used in determining the target area are shown in Fig. 2. After identification of the target on the ventriculogram, a lesion was created by the cryogenic technique. The mean temperature used was -90°C for two minutes with a range between -70° and -130°C . If one lesion was insufficient, a second or even a third lesion was tailored to produce the desired clinical results; so that if the first lesion was deemed slightly too

posterior, as evidenced by early development of paraesthesia, the second one was placed anterior to it, thus overlapping the optimum locus. More than one lesion was found necessary in 22 cases.

RESULTS

Each of the patients in this series was followed closely from the time of operation until the time of this report.

At the time of discharge from the hospital, 54 patients showed excellent relief of intention tremor on the side for which they underwent surgery; 12 had good relief, and four had mild improvement. The remaining three cases did not show any benefit from surgery (Table 2).

It is worth mentioning that 12 patients showed significant improvement in intention tremor of the extremities ipsilateral to the side of operation, in

FIG. 2. Ventricular landmarks used in determining the target area (T).

TABLE 2

RESULTS OF SURGERY

Aetiology of I.T.	Cases (no.)	Relief			No improve- ment
		Excellent	Good	Mild	
Familial cerebellar degeneration	26	22	3	1	—
Multiple sclerosis	25	13	7	2	3
Idiopathic I.T.	7	6	—	1	—
Head injury	5	4	1	—	—
Post. fossa tumour	1	—	1	—	—
Leber's disease	1	1	—	—	—
I.T. and torticollis	2	2	—	—	—
I.T. Parkinsonism	6	6	—	—	—
Total	73	54	12	4	3

addition to virtually complete relief of intention tremor on the side contralateral to surgery. Also, nine patients out of 13 who had neck tremor demonstrated marked improvement despite the fact that only unilateral operation had been performed. Another patient showed complete relief of the neck tremor after bilateral surgery. Nystagmus, which was a symptom present in 14 patients, showed notable diminution in four after unilateral surgery and in one after bilateral surgery. Symptoms like ataxia, dysmetria, and dysarthria were not influenced by surgery.

Recurrence of the tremor was noted in 10 patients: two had the recurrence while still in the hospital (second and sixth post-operative day), the rest developed recurrence at intervals that varied between two and six months. Seven patients had reinsertion with excellent results in six and good relief in one. The other three patients were left alone because of the mildness of the tremor.

The following cases demonstrate the effect of thalamic surgery upon intention tremor of diverse aetiology:

CASE 1

Mr. J. A., a 30-year old man, had noted tremor of both upper extremities since early childhood. The tremor had remained rather static since that time, but was quite bothersome to the patient. There was a definite family history of intention tremor occurring in the grandmother, father, and a brother. Neurological examination revealed mild nystagmus and 3+ intention tremor in both upper limbs. Left cryothalamectomy was performed on 2 March 1967 and one lesion was made in VL nucleus with freezing down to -100°C for two minutes, with complete relief of the tremor on the right side. The post-operative course was smooth and the patient was discharged nine days after surgery. Follow-up evaluation, a year later, revealed that the patient was still maintaining good results of surgery.

CASE 2

Mrs. B. R., a 35-year old housewife, gave a history consistent with multiple sclerosis, of 11 years' duration. Her chief complaint was blurred vision, inability to walk, and intention tremor. The patient was admitted to St. Barnabas Hospital on 15 January 1968, and examination at that time revealed bilateral decrease of visual acuity to 20/200 pallor of the optic disc more marked on the right than the left, horizontal nystagmus, moderate to marked paresis of both lower limbs, more on the left. Deep tendon reflexes were hyperactive on both upper extremities and right lower extremity and hypoactive on the left lower extremity. Other neurological findings were bilateral Babinski reflexes, hypoaesthesia over the left lower limb and 4+ intention tremor on the right upper limb and 3+ in the left upper limb, with no tremor noted in the lower extremities. The patient was unable to stand or walk. General physical examination was found to be within normal limits. Psychologically, the patient was rated as a fair candidate.

On 16 January 1968 a left cryothalamectomy was performed and one lesion was placed in VL nucleus with freezing down to -70°C for two minutes with complete relief of the intention tremor. Post-operatively, the patient did quite well, although her speech seemed slightly slurred compared with her pre-operative level. She was able to drink from a glass without spilling it and was able to use the right hand with considerable improvement. The patient continued to do well with no particular alteration in her general multiple sclerotic condition and she was discharged from the hospital eight days after surgery. Six months later, she came back for a check-up and examination at that time revealed no tremor on either right side.

CASE 3

J.O., a 15-year old Puerto Rican boy, was referred for neurosurgical treatment from the Neurology Clinic of the Albert Einstein College of Medicine. This boy was born after an uncomplicated pregnancy and delivery. However, because his weight at birth had been only 4 lb 6 oz. (1.9 kg), he had been kept in an incubator for the first few weeks of his life. He developed normally, however, until the age of 9 when he was observed to have some incoordination in using the right hand.

During the next several years, the patient developed increasingly severe tremor of the right upper extremity which at first was prominent only during voluntary motion, but later became apparent even at rest. By the age of 12 both resting tremor and intention tremor were so severe as to render the right upper extremity essentially useless. He also gradually developed a dystonic posturing of the right hand, with flexion of the wrist and adduction of the thumb and small finger of the hand into the palm.

In 1963, the patient developed rapidly decreasing visual acuity, and a diagnosis of Leber's disease was made. He was treated with steroids, but without any perceptible benefit and he became totally blind by the age of 13.

In January 1967, at the time of admission to our service, the general neurological examination revealed

an alert and intelligent boy, with slight light perception in both eyes, but without useful vision. The pupils reacted to light bilaterally, the left pupil being irregular and somewhat larger than the right. Positive findings of a neurological nature were limited to the right upper extremity. There was some degree of postural tremor of the right hand and arm, which became markedly exaggerated during any attempt at motion. The finger-to-nose test was barely possible because of the violence of the involuntary motions which caused the boy to hit himself in the face. The patient requested operation because of the necessity of using the right arm and hand during the reading of braille.

It is interesting to note that radiographic examination of the skull revealed bilateral intracranial calcification, involving the lateral region of the thalamus with some invasion of the internal capsule.

Left cryothalamectomy was performed on 7 January 1967 (Fig. 3). A double overlapping lesion was created involving the posterior half of the ventrolateral nucleus of the thalamus, and invading the ventroposterolateral nucleus to a slight extent. This latter was identified by the

temporary production of paraesthesias at the finger tips, during creation of the lesion. Post-operative course was smooth and the patient was discharged nine days after surgery free of intention tremor and dystonic deformity of the right hand. Re-evaluation 20 months later showed no evidence of recurrence.

CASE 4

C.A., a 15-year old girl, was referred to us by Dr. Frank Palazzo from St. Louis, Missouri, because of an abnormal movement disorder on the right side of her body.

The history goes back to September 1961 when the child was admitted to Cardinal Glennon Memorial Hospital in a semi-comatose state. Examination at that time revealed bilateral papilloedema, dysconjugate eye movements, right hemiparesis, and marked incoordination of the left side. She had numerous café-au-lait spots. A pneumoventriculography was done and showed symmetrical dilatation of the ventricular system secondary to a fourth ventricle tumour. The child was operated upon on 12 September 1961 and the tumour was removed except for a small portion extending upwards and laterally into the basal ganglia area. Histologically the tumour was found to be grade III astrocytoma.

The child gradually recovered and was able to walk with help. However, there were severe ataxia and abnormal movements on the right side of her body.

The patient was admitted to St. Barnabas Hospital on 29 January 1968. Neurological examination revealed diminished vision in both eyes, bilateral optic atrophy, the right eye tended to deviate laterally at rest, horizontal nystagmus, and minimal weakness in the right upper extremity. Reflexes were almost impossible to elicit on the right side because of the continuous movement. There was severe abnormal involuntary movement on the right side, especially in the upper extremity, so that she had to sit on it to keep it quiet. The slightest attempt to move the limb resulted in this abnormal movement. There was very little movement if she could really be put at rest. In other words, it was really an intention tremor with a flinging ballistic component. The child walked only with help, using a stiff gait. Language and speech evaluation revealed both dysphasia and dysarthria, so that it was difficult to understand her. Psychological testing was very limited.

The skull radiograph simply showed the operative decompression and the metal clips still in place. Electromyography was unsatisfactory but it seemed, from the brief recording made, that there were simultaneous bursts of muscular activity from the flexor and extensor muscles of the right upper extremity. A brain scan showed increased uptake just above and behind the sella turcica. Pneumoencephalogram revealed a dilated ventricular system; the fourth ventricle was also dilated while the aqueduct was bowed upward and backward to some extent. A right brachial angiogram showed no significant abnormality added to the above.

Left cryothalamectomy was carried out on 6 February 1968 with some difficulty because of the enlarged ventricles (Fig. 4). A VL lesion was made by freezing

FIG. 3. Anteroposterior and lateral ventriculogram of case 3, showing the position of the cryogenic probe. Notice the calcification at the left basal ganglia area.

FIG. 4. Anteroposterior and lateral ventriculogram of case 4 with the cryogenic probe already in the target area. Notice the dilated ventricles.

down to -130°C for two minutes. There was marked improvement on the operating table but the tremor was not abolished completely. No additional neurological deficit developed and the patient withstood the procedure well. Her convalescence was superb. During that time the abnormal movements on the right side tended to improve still further. She was now able to use her right arm and hand and she no longer had to sit on her hand. Follow-up evaluation four months later showed that the patient was still maintaining good results from surgery.

CASE 5

I. H., a 29-year old man, suffered from intractable intention tremor of the right extremities after a severe head injury on 15 April 1963 that had rendered him comatose for several weeks. Bilateral carotid angiograms were performed at that time and were negative. The case was diagnosed as brain contusion and laceration.

The patient was admitted to St. Barnabas Hospital on 5 March 1967 and examination at that time revealed left

temporal field defect, mild weakness and spasticity on the right side, and right hemihypoalgesia, residual from the previous injury. There was mild head tremor and intention tremor limited to the right side of the body, with upper limb more affected than the lower. The patient could not dress himself, feed himself, or perform the activities of daily living because of the severe nature of this involuntary movement. The patient had a family history of intention tremor in the mother and one grandmother. Psychological examination revealed a good candidate for surgery.

A left cryothalamectomy was carried out on 7 March 1967 and one lesion was made by freezing down to -80°C for two minutes with good relief of the tremor on the opposite side. The patient's convalescence was marred by the occurrence of three convulsive seizures on the right side of the body, all on the day of surgery and occurring despite the use of primidone (Mysoline) and phenytoin (Dilantin) before surgery. Large doses of these drugs and sodium phenobarbital were necessary to control the convulsions. Thereafter, the patient did well and began to receive physiotherapy and rehabilitation and was discharged on the 10th post-operative day. Follow-up evaluation a year later showed that the patient was still maintaining good relief of tremor on the right side.

CASE 6

A 59-year old male suffering from Parkinsonism more than 10 years. The course was progressive in spite of medication. The patient was admitted to our service on 31 October 1966 and neurological examination revealed mild to moderate rigidity on both sides of the body, more on the right; 3+ tremor on the right extremities and 2+ on the left. The tremor was both resting and intentional. The latter component was severe enough to interfere with his daily activities. Reflexes were hyperactive on both sides, with bilateral flexor plantar reflexes. The patient had moderate autonomic dysfunction in the form of oiliness of the face, hyperhidrosis, and hypersalivation. Speech evaluation revealed mild dysarthria. Psychologically, the patient was considered a good candidate for surgery.

Left cryothalamectomy was performed on 2 November 1966 and one lesion in VL nucleus was made by freezing down to -90°C for two minutes with complete relief of both tremor and rigidity on the right side. The post-operative course was smooth and the patient was discharged eight days after surgery. Follow-up evaluation 18 months later, showed that the good results of surgery were still maintained.

UNTOWARD SEQUELAE

Table 3 presents the relevant immediate post-operative sequelae.

Transient confusion, disorientation, drowsiness, lethargy, and depression were observed in 10.9% of the cases. These side-effects were largely related to the pre-operative psychological state of the patient.

TABLE 3

IMMEDIATE POST-OPERATIVE SEQUELAE

<i>Sequela</i>	(%)
Confusion, disorientation, etc. (transient)	10.9
Balance problems	10.9
Dysphasia and dysarthria	9.5
Motor weakness	5.5
Abnormal movements	1.3
Swallowing problems	1.3
Other side effects (nausea, dizziness, persistent paraesthesia, convulsions)	1.2
Mortality	0

patients with poor to fair ratings showed a higher incidence compared with those rated as good candidates.

Post-operative balance problems occurred in 10.9% of the cases. The incidence of this complication is higher in the multiple sclerosis group compared with others. Females showed almost twice the amount of balance difficulty as males. These balance problems were of a transient nature, responding well to physical therapy and rehabilitation.

Language and speech deficits occurred post-operatively in 9.5%. Such deficits were related to many factors. Cases subjected to bilateral surgery showed more dysphasia and dysarthria than unilateral cases; and cases operated upon their left cerebral hemisphere, more than the right. Also, multiple sclerosis (MS) patients had a higher incidence of post-operative speech disturbances compared with other groups. In general, these deficits improved with speech therapy and time.

Transient weakness was observed in three patients (two in the MS group and one in the familial group). In another case, a pre-existent spastic hemiparesis due to MS was aggravated by surgery. Abnormal choreiform movements were noticed in one case (familial group) which disappeared by the time of discharge. Swallowing difficulties were observed in one case (MS group), after bilateral surgery. This complication improved in time and was noted to have a striking similarity to pseudobulbar palsy, demonstrating also associated speech deficits.

Other side effects included nausea, dizziness, persistent paraesthesia around the lips, and epilepsy. The incidence of these sequelae was 1% to 2%. There was no mortality in the present series.

DISCUSSION

While the pathophysiology of the resting tremor of Parkinsonism is debated and remains elusive, there is at least one well-defined site of injury for the production of intention tremor: the outflow pathways of the cerebellum via the superior cerebellar peduncle

(Walker and Botterell, 1937; Brown, 1944; Carpenter and Stevens, 1957; Carpenter, Glinsman, and Fabrega, 1958; Cooper, 1960b). In 1937, Walker and Botterell demonstrated that unilateral section of the superior cerebellar peduncle in monkeys caused severe ataxia, intention tremor, dysmetria, and decomposition of movement with little or no hypotonia in the ipsilateral limbs. Carpenter and Stevens (1957) obtained similar results with section of the brachium conjunctivum in monkeys. They noted that the upper limb was more often and more severely affected. They traced the degenerating fibres from the dentate and interposed nuclei of the cerebellum via the dentato-rubrothalamic pathway to the contralateral red nucleus, the VL nucleus (via the fasciculus thalamicus), the globus pallidus (via the ansa lenticularis), and the medial longitudinal fasciculus and nearby brain-stem nuclei. In another study (Carpenter *et al.*, 1958) the dentate and interposed nuclei of monkeys were destroyed leading to hypokinesia, ataxic gait, asynergia, and intention as well as resting tremor. Another lesion in the contralateral globus pallidus or fasciculus and ansa lenticularis reduced or abolished both types of tremor 20 days later.

In 1960, Cooper postulated that intention tremor is due to pathological lesions anywhere between the ipsilateral dentate nucleus of the cerebellum and the contralateral red nucleus of the midbrain and that this results in impaired feedback of proprioceptive sensory information from the muscle spindles via the cerebellum to the cerebral cortex by way of the thalamus. A surgical lesion within the ventrolateral nucleus of the thalamus would block the faulty information from reaching higher centres. Others, however, have claimed that the good results of ventrolateral thalamotomy are not due to further interruption of already injured cerebello-thalamic fibres but rather to some limitation of the outflow from the globus pallidus (McCaul, 1961).

In a series of 73 consecutive cases of intention tremor, subjected to stereotaxic cryothalamectomy, the tremor was abolished or markedly lessened in 90.4% of the cases. Follow-up evaluation revealed a recurrence rate of 13.71%. The incidence of recurrence was directly related to the magnitude of pre-operative tremor. Nystagmus, a sign frequently associated with intention tremor, was occasionally relieved or diminished by thalamic surgery. Other cerebellar signs such as ataxia and dysmetria were not influenced by surgery. In 16.4% of the cases, there was apparent improvement in intention tremor of the extremities ipsilateral to the side of surgery. This finding of ipsilateral improvement has not been a significant feature in cases of Parkinsonism.

In six patients presented in this study, the in-

tention tremor was associated with Parkinsonism. The fact that a thalamic lesion can relieve both of these clinical syndromes stimulated us to seek additional common features in so-called resting and intention tremor (Cooper, 1966). Moreover, the fact that interruption of the rubrothalamic portion of the dentato-rubrothalamic pathway alleviates both 'resting' tremor and 'intention' tremor suggests that there may be an abnormal cerebellar mechanism in the tremor of Parkinsonism as well as in the tremor known to be due to cerebellar disease. In cases of pure cerebellar disease, the muscles of the body are hypotonic. As soon as the subject attempts to initiate movement—with consequent muscular contraction and shortening—the muscles become involved in a tremor which is indistinguishable electromyographically from that seen in Parkinsonism.

We have been beguiled by the fact that the tremor of Parkinsonism is usually referred to as a 'resting' tremor. However, this descriptive term is inaccurate. The basic abnormality in most cases of Parkinsonism is increased muscular tonus, usually recognized clinically as rigidity. The resting tremor of Parkinsonism actually involves chronically shortened or active muscles. These muscles are at complete rest only during sleep, at which time the tremor disappears.

Neither is the term 'intention tremor' an accurate one. Cerebellar tremor is a postural tremor, in that it appears as soon as the patient contracts a muscle, even though this contraction may be carried out

statically without the intention or attempt to perform motion. During performance of the finger-to-nose test, the tremor is usually most prominent as the finger approaches the nose, and muscular contraction takes place during the attempt to maintain the posture of the arm at this point. Consequently, both cerebellar tremor and that seen in Parkinsonism are postural tremors which occur as a muscle is contracted, whether motion is attempted or not. Electromyographically, these tremors are indistinguishable, both are at 5/sec (Fig. 5).

SUMMARY AND CONCLUSION

Seventy-three patients with severe incapacitating intention tremor, of varying aetiology, were subjected to stereotaxic cryothalamectomy. A lesion placed in the region of the ventrolateral nucleus of the thalamus successfully relieved or markedly lessened the tremor in about 90% of the cases.

The close relationship between the so-called 'resting' tremor of Parkinsonism and intention tremor was discussed in detail, with the conclusion that both types of tremor are postural in nature.

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FIG. 5. Five per second tremor, identical with that of Parkinsonism, provoked in patient by classic finger-to-nose test.

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