Acta neurol. belg., 2003, **103**, 125-128

Review articles

Fifty years of brain surgery for dystonia : revisiting the Irving S. Cooper's legacy, and looking forward

Laurent VERCUEIL
Neurological department, Grenoble University Hospital, Grenoble cedex 9, France

Abstract

As dystonia may represent a severe disease with possible fatal outcome or physical or social incapacity, and considering the limited efficacy of drug treatments (excepted doparesponsive dystonia), efforts have been made since the 1950s to propose alternative treatment. In this paper, an overview of the works done by neurosurgeons over fifty years to treat severe dystonia is presented. In this area of therapeutical research, the pioneering contribution of Irving Cooper is presented and discussed, and the way his publications were evaluated emphasized. Undoubtedly, Cooper observed striking improvement after performing basal ganglia lesions in patients with generalized dystonia, even in the long term. It should be noted that he early made almost the same statements as today's preliminary observations regarding the clinical criteria for the selection of good responders to brain functional surgery. However, the message was lost, given the amount of critics Cooper received, and, probably, the way he required to present them. This point emphasize the need we are today to carry out carefully designed, controlled, double-blind studies in this area.

Key words : Dystonia ; deep brain stimulation ; pallidotomy ; Irving Cooper ; thalamotomy ; globus pallidus internus.

Introduction

Dystonia is a potentially severe disorder of the motor system for which there are limited therapeutic resources. As dystonia, in its generalized form, imposes involuntary sustained muscle contractions, leaving the imprint of torsion movements or abnormal posture, it may become a cause of severe motor disability and even in some cases (with the so-called "dystonic storms") life-threatening. Because drug treatments are almost ineffective (with the exception of levodopa in dopa-responsive dystonia, which deserves systematic trial), surgical solutions have been advanced for young adults and children as early as the 1950s, with sometimes spectacular results. This brief review attempts to update the contribution of surgical procedures used in the past and the recent renewal of interest in this approach. Selective denervation surgery, which has been proposed for cervical dystonia refractory to treatment with botulinum toxin, will not be included in this paper, which deals exclusively with brain surgery.

The contribution of Irving S. Cooper

Irving Cooper is one of the inventors of functional surgery. In October 1951, when he accidentally tied off the choroid artery of a Parkinson's disease patient, he discovered that producing a pallidal ischemic lesion stopped tremor without causing a motor deficit. Extending this technique to other Parkinson's disease patients, he came to prefer a direct lesion, which avoided the risk related to variable vascularization depending on the anterior choroid artery territory, which sometimes included the internal capsula. Later, Cooper moved his lesion site from the pallidum (pallidotomy) to the thalamus (thalamotomy), and operated on nearly 10,000 Parkinson's disease patients until levodopa treatment was discovered.

Before the time of levodopa therapy, Parkinson's disease often evolved toward a severe generalized dystonic syndrome. In the patients he operated on for tremor, Cooper rapidly observed that the dystonic symptoms disappeared in relation to clinical efficacy, which led him to operate on patients suffering from primary dystonia as soon as the early 1950s. The results he obtained, in particular in dystonia musculorum deformans (or Ziehen-Oppenheim disease, today known as early limb onset primary generalized dystonia and mainly, although not exclusively, related to DYT1 mutation), were often remarkable. From a rapidly growing series, he published detailed accounts in one early article (1), in his book *Involuntary Movement Disorders* (2), and reported his experience with 226 patients in a tremendous article published in 1976 (3).

Unquestionably, Cooper obtained nearly complete cures, as shown in the photographs of his many publications, even in the long term. It is nowadays fair to observe that Cooper was never in favor among his peers. In his book *The Vital Probe*,

he tells how he rapidly found himself on the wrong side of Paul Bucy, the head of postwar American neurosurgery, and Houston Merritt, the powerful head of the American Academy of Neurology (4). The lively discussions following the presentation of his 1976 paper (3), or more recently, the retrospective view contribute by Lang in a review article (5) on the diagnosis of his patients (some of which, after careful examination of the published photographs, may have been suffering from psychogenic dystonia according to Lang), reveal the atmosphere surrounding his research. As with much of what Cooper did (cerebellar and thalamic stimulation in epilepsy, thalamic stimulation in dystonia, etc.), a rigorous, independent evaluation (without being inquisitorial, as was often the case brought against Cooper's works) was lacking, leaving the medical community with the impression of a wasted effort. Most definitely, the accumulated experience of Irving Cooper, who died prematurely in 1985, would have helped orient today's surgery in the selection of patients and target sites.

The decline of thalamotomy

Cooper's results, although controversial, aroused a definite interest and several surgical teams fell in behind him. As Cooper had abandoned the initial target of the internal globus pallidus (the area covered by the anterior choroid artery) for the thalamus, firmly established as a target in Parkinson's disease and in certain tremors, thalamotomies became the rule.

During the 1980s and up to 1995, several articles reported disappointing results in the treatment of various forms of dystonia using thalamotomy (6-7). This led to the impression that beyond rare spectacular improvements (approximately one-quarter of patients), thalamotomy showed little efficacy and was potentially a source of severe side effects, particularly when it was bilateral, as was often necessary in the generalized forms of the disease. Moreover, these studies did not provide evidence for an etiological or clinical subgroup presenting a favorable prognosis, with generalized idiopathic dystonia sometimes made up of patients with the least improvement (6), in strong contrast to what is observed today. At the end of the 1980s, the impression was that thalamotomy led to a good result in only 25% of cases, and the rate of undesirable side effects was unacceptably high (7).

Emergence of chronic deep brain stimulation

The effects of deep brain stimulation had long been known. During the 1950s and 1960s, in order to identify the best definitive lesion placement site, surgeons and neurophysiologists carried out intraoperative electrical stimulations in the operating room, which allowed them to infer the effect a lesion would have at this anatomical site. Thus, the observation that tremors, for example, disappear following local application of high-frequency stimulation was a decisive argument in favor of placing the lesion in that area. In 1960, Hassler observed that high-frequency pallidal stimulation could remove dyskinesia, while low-frequency stimulation at the same site aggravated it (9). It was only in the 1970s that the idea emerged that stimulation could be applied chronically, beyond the operating room, but stimulation protocols were not yet established. Thus, in 1977, Mündinger stimulated patients presenting with cervical dystonia 1-2 hours a day, with favorably judged results (10). Andy (11) and then Cooper (12) reported larger series of patients with thalamic stimulations. The targeted nuclei were the motor relays of the basal ganglia. The stimulation parameters were not those used today. These pioneering articles did not specify the methodology governing stimulator adjustments, and in particular whether a rigorous study of the different parameters (intensity, pulse width, stimulation frequency) was conducted. The results, in the end not very favorable (in Cooper's series of dyskinetic subjects, the patients presenting with dystonia were less sensitive to the intervention), undoubtedly do not meet today's scientific assessment standards. Concurrently, other teams observed that stimulation of the sensory nucleus of the thalamus, using low frequencies producing paresthesia, could improve secondary dystonia in the same way as tactile stimulation (13, 14).

Return to the pallidum : lessons drawn from Parkinson's disease

Following the later stages of the development of dystonia surgery requires returning to the first target of stereotaxic surgical technique : Parkinson's disease. After the discovery of the therapeutic effect of levodopa, surgical treatment for Parkinson's disease was interrupted and taken up again only 10 years later, when the undesirable effects of levodopa therapy appeared. Dyskinesia induced by levodopa was a major target of therapy, rekindling an interest in surgical solutions. While in France deep brain stimulation developed rapidly, with the discovery of the remarkable effect of stimulating the subthalamic nucleus, the United States and Canada, in particular, returned to the old target of posteroventral pallidotomy (PVP).

It was quickly found that PVP was the source of a number of problems, notably poor neuropsychological tolerance of the bilateral intervention. Its efficacy in Parkinson's disease remained modest, but the remarkable effect on levodopa-induced dyskinesia made a less restricted use of the treatment possible, with finally, notable functional improvement. Extending the concept from dyskinesia to primary dystonia, these same teams

proposed PVP for children suffering from generalized dystonia, with rapidly encouraging results (15, 16). The idea only had to come back across the Atlantic for pallidal stimulation to be applied for this indication.

Pallidal target in the treatment of primary generalized dystonia

The observation of the remarkable efficacy of pallidum stimulation in a child presenting with primary generalized dystonia, the gravity of which required keeping the child in the ICU (17), led Coubes' team in Montpellier to recommend the intervention in severe forms of idiopathic dystonia, particularly in children (18-20). Many other teams in France (in Paris, Grenoble, and Lille), but also in Germany, Switzerland, and Great Britain have since reported on their experience (21-34). Even though the number of patients reported in the literature remains rather small, a certain number of notions were beginning to emerge : the mutation of the *DYT1* gene as the cause of the majority of dystonia cases with onset in one limb during childhood could be a factor of a good prognosis, although patients not presenting the mutation could also be considerably improved. The so-called mobile forms of dystonia, i.e., those during which spontaneous abnormal movements overcame fixed postures, were more rapidly improved. In general, authors agreed that the progression of improvement linked to stimulation required several weeks or months, even if certain symptoms were rapidly improved. However, it must be recognized that a study providing rigorous evaluation of these data is still lacking. A crucial point such as the position of the surgical target within the pallidum is still under debate (Which part of the globus pallidus interna ? Is the external part of the pallidum proscribed ?).

The results obtained can be very extensive and spectacular and sustainable improvements have been reported. Generally, the improvement on dystonia scales for idiopathic generalized form can range from 50% to 95%. Data on the secondary forms of dystonia are much more scattered and it is not clear whether the pallidum is the ideal target for these patients (35). Finally, in the focal or segmentary forms, in particular cervical dystonia not improved by botulinum toxin, some teams have had good results (on average 50% improvement on the scales used), perhaps even better results for the associated pain phenomena.

Conclusion

Today is most certainly a time of promising development in dystonia treatment. It could even be said that we are now reaching that point with dystonia, as was the Parkinson's diseae DBS treatment in 1995-6, when subthalamic nucleus stimulation was increasingly showing excellent results around the world. However, certain aspects point to a need for patience. Contrary to Parkinson's disease, the physiopathology of dystonia remains excessively obscure and currently there is no functional model for the basal ganglia in this disease. Moreover, dystonia is not a specific disorder based on homogenous pathogenicity. Patients differ greatly in clinical semiology (fixed or mobile dystonia, associated neurological signs, topographies, etc.) and the variety of etiologies. What has been learned from surgical successes obtained in DYT1+ dystonia can not necessarily be applied directly to other forms of dystonia. There is today a strong need for carefully conducted, well-designed, controlled and double-blind studies.

REFERENCES

1 Cooper I. S. Dystonia Musculorum Deformans alleviated by chemopallidectomy and chemopallidothalamectomy. *Arch. Neurol.*, 1959, **81** : 5-19.

2 Cooper I. S. Involuntary Movement Disorders. Hoeber Medical Division, Harper & Row, New York, 1969.

3 Cooper I. S. 20-year follow-up study of the neurosurgical treatment of dystonia musculorum deformans. *Adv. Neurol.*, 1976, **14** : 423.

4 Cooper I. S. The vital probe. My life as a brain surgeon. WW Norton & Company, New York, London, 1981.

5 Lang A. E. Surgical treatment of dystonia. *Adv. Neurol.*, 1998, **78** : 185-98.

6 Andrew J., Fowler C. J., Harrison M. J. Stereotaxic thalamotomy in 55 cases of dystonia. *Brain*, 1983, **106** : 981-1000.

7 Tasker R. R., Doorly T., Yamashiro K. Thalamotomy in generalized dystonia. *Adv. Neurol.*, 1988, **50** : 615.

8 Cardoso F., Jankovic J., Grossman R. G., Hamilton W. J. Outcome after stereotactic thalamotomy for dystonia and hemiballismus. *Neurosurgery*, 1995, **36** (3) : 501-7.

9 Hassler R., Riechert T., Mundinger F., Umbach W., Ganglberger J. A. Physiological observations in stereotaxic operations in extrapyramidal motor disturbances. *Brain*, 1960, **83** : 337-356.

10 Mundinger F. Neue stereotaktisch-funktionelle Behandlungsmethode des torticollis spasmodicus mit Hirnstimulatoren. *Med. Klin.*, 1977, **72** : 1982-1986.

11 Andy O. J. Thalamic stimulation for control of Movement disorders. *Appl. Neurophysiol.*, 1983, **46** : 107-111.

12 Cooper I. S., Upton A. R. M., Amin I. Chronic cerebellar stimulation (CCS) and Deep brain stimulation (DBS) in Involuntary movement disorders. *Appl. Neurophysiol.*, 1982, **45** : 209-217.

13 Siegfried J. Effet de la stimulation du noyau sensitif du thalamus sur les dyskinésies et la spasticité. *Rev. Neurol.* (Paris), 1986, **142** : 380-383.

14 Sellal F., Hirsch E., Barth P., Blond S., Marescaux C. A case of symptomatic hemidystonia

improved by ventrolateral thalamic stimulation. *Mov. Disord.*, 1993, **8** : 515-518.

15 IACONO I. P., KUNIYOSHI S., LONSER R. R., MAEDA G., INAE A. M., ASHWAL S. Simultaneous bilateral pallidoansotomy for idiopathic dystonia musculorum deformans. *Pediatr. Neurol*., 1996, **14** : 145-148.

16 LOZANO A. M., KUMAR R., GROSS R. E. *et al.* Globus pallidus internus pallidotomy for generalized dystonia. *Mov. Disord.*, 1997, **12** : 865-870.

17 COUBES P., ECHENNE B., ROUBERTIE A., VAYSSIERE N. *et al.* Traitement de la dystonie généralisée à début précoce par stimulation chronique bilatérale des globus pallidus internes. A propos d'un cas. *Neurochirurgie*, 1999, **45** : 139-144.

18 COUBES P., ROUBERTIE A., VAYSSIERE N. *et al.* Early onset generalised dystonia : neurosurgical treatment by continuous bilateral stimulation of the internal globus pallidus in sixteen patients. *Mov. Disord.*, 2000, **15** ; suppl. 3 : 154.

19 COUBES P., ROUBERTIE A., VAYSSIERE N., HEMM S., ECHENNE B., 2000, Treatment of DYT1-generalised dystonia by stimulation of the internal globus pallidus. *Lancet*, **355** : 2220-2221.

20 COUBES P., CIF L., AZAIS M., ROUBERTIE A., HEMM S., DIAKONOVA N., VAYSSIERE N., MONNIER C., HARDOUIN E., GANAU A., TUFFERY S., CLAUSTRE M., ECHENNE B. Traitement des syndromes dystoniques par stimulation électrique du globus pallidus interne. *Arch. Pédiatr.*, 2002, 9 (Suppl. 2) : 84-86.

21 KUMAR R., DAGHER A., HUTCHINSON W. D., LANG A. E., LOZANO A. M. Globus pallidus deep brain stimulation for generalized dystonia : clinical and PET investigation. *Neurology*, 1999, **53** : 871-874.

22 TRONNIER V., FOGEL W. Pallidal stimulation for generalized dystonia. *J. Neurosurg.*, 2000, **92** : 453-456.

23 VERCUEIL L., POLLAK P., FRAIX V., CAPUTO E., MORO E., BENAZZOUZ A., XIE J., KOUDSIE A., BENABID A. L. Deep brain stimulation in the treatment of severe dystonia. *J. Neurol.*, 2001, **248** : 695-700.

24 FOGEL W., KRAUSE M., TRONNIER V. Globus pallidus stimulation in generalised dystonia : clinical data. *Mov. Disord.*, 2000, **15** (suppl. 3) : 144.

25 LOHER T. J., HASDEMIR M. G., BURGUNDER J. M., KRAUSS J. K. Long-term follow-up study of chronic globus pallidus internus stimulation for posttraumatic hemidystonia. Case Report. *J. Neurosurg.*, 2000, **92** : 457-460.

26 THOMPSON T. P., KONDZIOLKA D., ALBRIGHT A. L. Thalamic stimulation for choreiform movement disorders in children. *J. Neurosurg.*, 2000, **92** : 718-721.

27 GILL S., CURRAN A., TRIPP J., MELARICKAS L., HURRAN C., STANLEY O. Hyperkinetic movement disorder in an 11-year-old child treated with bilateral pallidal stimulators. *Dev. Med. Child Neurol.*, 2001, **43** : 350-353.

28 TROTTENBERG T., PAUL G., MEISSNER W., MAIER-HAUFF K., TASCHNER C., KUPSCH A. Pallidal and thalamic neurostimulation in severe tardive dystonia. *J. Neurol. Neurosurg. Psychiatry*, 2001, **70** : 557-559.

29 KRAUSS J. K., POHLE T., WEBER S., OZDOBA C., BURGUNDER J. M. Bilateral stimulation of globus pallidus internus for treatment of cervical dystonia. *Lancet*, 1999, **354** : 837-838.

30 PARKIN S., AZIZ T., GREGORY R., BAIN P. Bilateral internal globus pallidus stimulation for the treatment of spasmodic torticollis. *Mov. Disord.*, 2001, **16** : 489-493.

31 ISLEKEL S., ZILELI M., CAKMUR R., ZILELI B. Pallidal stimulation : an effective method in the treatment of spasmodic torticollis. *Mov. Disord.*, 2000, **15** (Suppl. 3) : 162.

32 ANDALUZ N., TAHA J. M., DALVI A. Bilateral pallidal deep brain stimulation for cervical and truncal dystonia. *Neurology*, 2001, **57** : 557-558.

33 KULISEVSKY J., LLEO A., GIRONELL A., MOLET J., PASCUAL-SERRANO B., PARES P. Bilateral pallidal stimulation for cervical dystonia : dissociated pain and motor improvement. *Neurology*, 2000, **55** : 1754-1755.

34 MUTA D., GOTO S., NISHIKAWA S., HAMASAKI T., USHIO Y., INOUE N., MITA S. Bilateral pallidal stimulation for idiopathic segmental axial dystonia advanced from Meige syndrome refractory to bilateral thalamotomy. *Mov. Disord.*, 2001, **16** : 774-777.

35 GHIKA J., VILLEMURE J. G., MIKLOSSY J., TEMPERLI P., PRALONG E., CHRISTEN-ZAECH S., POLLO C., MAEDER P., BOGOUSSLAVSKY J., VINGERHOETS F. Postanoxic generalized dystonia improved by bilateral Voa thalamic deep brain stimulation. *Neurology*, 2002, **58** : 311-3.

L. VERCUEIL, M.D.,
Neurological department,
Grenoble University Hospital,
F-38043 Grenoble cedex 9, France).
E-mail : LVercueil@chu-grenoble.fr.