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Deep Brain Stimulation in Generalized Dystonia

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Eleven patients with diagnosed generalized dystonia (GD) were treated with deep brain stimulation (DBS). The clinical status of the patients was evaluated and recorded pre- and post-operatively. The target globus pallidus or subthalamic nucleus was identified with direct and indirect methods and confirmed electrophysiologically in the operating room. All eleven patients reported subjective improvement following the surgery what was confirmed using scales tailored for the group. The improvement lasted from 10 months to 40 months. DBS can be effectively and safely utilized to alleviate symptoms of generalized dystonia in selected patients.

K e y w o r d s: dystonia, deep brain stimulation, globus pallidus

1. Introduction

Dystonia is a movement disorder characterized by repetitive, patterned, or sustained muscle contractions causing twisting movements or abnormal postures. The clinical phenotype of dystonia may include several other motor abnormalities such as myoclonus, tremor, bradykinesia, and increased or decreased muscle tone. Depending on clinical symptoms, dystonia is classified as: focal, segmental or generalized, and dystonic movements are divided into mobile or fixed. Regarding aetiology, dystonia is considered to be primary (idiopathic) or secondary (symptomatic). Medically refractory generalized dystonia (GD) of primary or secondary origin is a very difficult therapeutic and socioeconomic problem [1–7]. Depending on their dystonic movements, some GD patients respond very well to surgical treatment, of which the most effective method is basal ganglia deep brain stimulation (DBS).

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2. Materials and Methods

We enrolled 11 eligible patients with a history of GD in a study group. Seven female and four male patients aged 22±8 years were qualified for the surgery. Three of the patients had a diagnosis of secondary GD, while three others had a diagnosis of primary GD. Pantothenate Kinase-Associated Neurodegeneration (PKAN) mutation was identified in four patients; DYT-1 mutation was identified in one case. All of the patients were qualified for surgery according to a neurologist specialized in movement disorders and a functional neurosurgeon. Eight patients underwent bilateral implantation of electrodes for DBS in globus pallidus pars interna (GPi) and three patients underwent bilateral subthalamic nucleus (STN) DBS implantation. The clinical status of the patients was evaluated with the Global Dystonia Scale, Fahn-Marsden Movement Scale and Unified Dystonia Rating Scale. The whole group of patients underwent brain MRI, neurological and neuropsychological evaluation prior to surgery. All of the pre- and post-operative evaluations were video recorded to allow a subsequent double-blinded evaluation [8–13].

3. Surgical Procedure

In all cases a Leksell stereotactic frame was used for MRI guided identification of GPi and STN in the surgical procedure. The target and entry point were identified and analysed with a neuronavigation system. Patients received a pre-operative antibiotic intravenously prior to transfer to the operating room. The frame was attached to the patient's head under local or tailored general anaesthesia that would not alter intrasurgical electrophysiological signals being monitored. A straight, 4 cm long skin incision was marked over the coronal suture, centered 3 cm from the midline. The operative field was shaved, prepared, draped and infiltrated with local anaesthetic. A 14 mm burr-hole was made in the skull and the dura mater was opened. The stereotactic arc was attached to the head ring, then microelectrodes were introduced and micro recording and macro stimulation commenced. During the microrecording, borders of GPe and GPi or STN were identified. Intra-operative macrostimulation helped to identify motor responses while sedation was swallowed. Once the position of the electrodes was confirmed electrophysiologically, a control X-ray was taken, and the probe was replaced by the definitive DBS electrode (3387–28, Medtronic, Minneapolis, MN). When the lateral control X-ray confirmed the location of the electrode to be identical to the probe, the electrode was anchored with a locking device (Stimlock, Medtronic, Minneapolis, MN) at the burr-hole and the scalp was closed. The stereotactic frame was removed and the second stage of the procedure was performed. An internal pulse generator (Soletra, Medtronic, Minneapolis, MN) was connected to the DBS electrode by an extension (7482–51 or 7482–95, Medtronic, Minneapolis, MN) and internalized in the chest or abdomen [14, 15, 16].

4. Stimulation Parameters

Deep brain stimulation was initiated on the first day after surgery. Initial parameters of the monopolar stimulation were set at a frequency of 90 to 185 Hz with a pulse width of 210 to 450 μs and a mean amplitude of 2.5 V. The parameters of the stimulation were readjusted over time according to the clinical effects determined at the follow up. If needed, the stimulation was changed to bipolar. Programming goals were to optimize clinical benefit, while minimizing adverse effects and current consumption. Overstimulation of GPi or stimulation of surrounding structures might result in: visual field disturbances, pseudodystonia, nausea, dizziness or decreased verbal fluency. Overstimulation of STN or stimulation of surrounding structures might result in: dyskinesia, pseudodystonia, dysarthria, eyelid opening apraxia, ocular deviation, ipsilateral mydriasis, ipsilateral perspiration, contralateral paresthesias, akinesia hemibalism, suicidal ideation, depression or manic behaviour. When any of those symptoms appeared, they were well controlled by reprogramming the parameters of stimulation [14–17].

5. Results

5.1. Benefits and Adverse Events

At the 12-month follow-up of the treated patients, improvement in dystonic movements, measured with the Global Dystonia, Fahn-Marsden and Unified Dystonia Scales, varied between 23% and 91% (Table 1).

Two hardware-related complications were encountered. One connector displaced from the occipital region to the subclavicular region in the patient with general dystonia and severe torticolis; the connector was replaced and reattached to the galea. Also one simultaneous bilateral malfunction of the intracerebral electrodes was identified. Radiologic evaluation did not reveal the location of the lesion and exchanging the connector did not solve the malfunction. Bilateral exchange of the intracerebral electrodes resulted in instant clinical improvement. Side effects related

Table 1. Efficacy of the DBS treatment depending on aetiology of generalised dystonia

Group	Global Dystonia Scale	Fahn-Marsden Scale	Unified Dystonia Scale
General	38%	42%	37%
SD	50%	57%	43%
PD	53%	60%	49%
PKAN	32%	23%	33%
DYT-1	87%	91%	89%

PKAN–Pantothenate Kinase-Associated Neurodegeneration

to the stimulation were always reversible and the stimulation could be readjusted to produce a good or excellent effect on dystonia with mild, side effects tolerable to the patients. There was no mortality in the group.

6. Discussion

For centuries GD was untreatable and often fatal. Introduction of stereotactic procedures in the first half of the 20th century gave physicians a tool to treat medically refractory GD, but ablative procedures used in those years carried a high risk of serious, irreversible complications. In 1960 Hassler at al. used low frequency current (4–8 Hz) to stimulate the globus pallidus, however, the stimulation induced torsion dystonia and athetosis. The same authors noted that high frequency stimulation of the same target suppressed dystonic movements. Mundinger at al. (1977) targetted VOA, ZI, Forel H1 and H2 to treat seven subjects with segmental dystonia. They used low (5–25 Hz) and high (125 Hz) frequency current with promising results. Cooper (1982) treated six subjects with generalized dystonia and two with torticolis by thalamic stimulation, also achieving good results.

A new era of the DBS treatment for generalized dystonia began in 1999 when Cubes et al. and Kumar et al. introduced GPi DBS to treat DYT-1 and non DYT-1 GD. Vilaret et al. (2001) and Brin et al. (2002) proved the superior efficacy of the bilateral over unilateral GPi DBS among patients with GD [1, 2, 13, 14].

A large number of publications in recent years have confirmed the high efficacy of DBS in GD treatment, which might be best shown by presenting the opinions of one author, five years apart: "….Despite the promising results of bilateral pallidal stimulation in selected cases of primary generalized dystonia, DBS still needs to be considered investigational for this indication …" and five years later —"….Deep brain stimulation (DBS) of the globus pallidus internus has been shown to be effective in both generalized and focal dystonia …" [13, 18].

Trottenberg et al. (2001, confirmed the superiority of GPi over a thalamic target in GD treatment. Although the efficacy of the thalamic DBS (Vim or Vop) has been evaluated as ranging between 25% and 80%, the efficacy of GPi DBS is higher and estimated at up to 90% in cases with the identified DYT-1 mutation and 79% for primary dystonia. Much poorer results (up to 35%) were achieved among patients with secondary dystonia. GPi DBS has been shown to have positive effects on quality of life and is well tolerated by GD patients [19–22].

The focus on the subthalamic nucleus as the optimal target for surgical treatment of Parkinson's disease has drowned interest in whether it might be an equally optimal target for GD treatment as well. Probably the role of the subthalamic nucleus in pathophysiology of dystonia is still underestimated, and this target may be very promising.

Bilateral subthalamic nucleus deep brain stimulation has been used to treat patients with cervical dystonia, severe idiopathic dystonia and tardive dystonia. The

impact of STN DBS on severity, neuropsychological status, and quality of life of GD patients has been under study for much of the decade [23–26].

The efficacy of the DBS treatment has been accepted in several types of dystonia, with impaired quality of life and lack of a conventional treatment being the main indications for surgical treatment in GD. The additional presence of pain related to dystonia is another indication for the DBS treatment among patients with segmental dystonia.

It is important to identify certain issues during patient selection, i.e., whether the target symptom for surgery (dystonia) is the predominant source of disability, the probability of improving the target symptom by surgery, and the patient's own expectation from surgery in relation to these goals [3,6,13]. Contraindications for the DBS treatment in GD include: patient's age (advanced age or prematurely aged), cognitive impairment and dementia, unrealistic expectations, coagulopathies, severe uncontrolled hypertension, cerebrovascular disease, severe coronary heart disease, terminal state, cardiac pacemaker, and psychiatric disorders that include a psychosomatic background of dystonia [6,13,14,17].

What should researchers evaluate in dystonic patients? In addition to "abnormal postures and involuntary movements," one can observe myoclonus, tremor, bradykinesia, and abnormal muscular tonus, ranging from a clear hypotonia to a strong hypertonia (either spastic-like or Parkinson-like rigidity). Mobile dystonia symptoms are the first to improve after the stimulation is initiated, for the most part within hours. Mobile dystonic movements are the best symptoms to evaluate the acute effects of the stimulation. Fixed dystonic posture, on the other hand, tends to improve progressively over a period of up to one year, or even longer, after surgery. In the long term, clinical evaluation has to address improvements to the quality of life [17, 26].

7. Conclusions

The DBS treatment of abnormal, involuntary movements in medically refractory dystonia is effective, especially among patients identified as having the DYT-1 mutation. Further observation on larger groups of patients is needed in order to identify which is the optimal surgical target, globus pallidus or subthalamic nucleus, for patients diagnosed with Pantothenate Kinase-Associated Neurodegeneration.

References

1. Cooper I.S.: 20-year follow-up of the neurosurgical treatment of dystonia musculorum deformans. Adv. Neurol. 1976, 14, 423–452.
2. Krack P., Vercueil L.: Review of the functional surgical treatment of dystonia. Eur. J. Neurol. 2001, 8, 389–400.

3. Vercueil L., Krack P., Pollak P.: Results of Deep Brain Stimulation for Dystonia: A Critical Reappraisal. Mov. Disord. 2002, Vol. 17, Suppl. 3, S89–S93.
4. Ondo W.G., Desaloms J.M., Jankovic J., Grossman R.G.: Pallidotomy for generalized dystonia. Mov. Disord. 1998, 13, 693–698.
5. 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.
6. Tronnier V., Fogel W.: Pallidal stimulation for generalized dystonia. J. Neurosurg. 2000, 92, 453–456.
7. 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.
8. Burke R.E., Fahn S., Marsden C.D., Bressman S.B., Moskowitz C., Friedman J.: Validity and reliability of a rating scale for the primary torsion dystonias. Neurology 1985, 35, 73–77.
9. Comella C. for the Dystonia Study Group.: Rating scales for dystonia: A multicenter assessment of three dystonia rating scales: The unified dystonia rating scale (UDRS), the Burke-Fahn-Marsden (BFM) and the Global Dystonia Rating Sale (GDS). Neurology 2001, 56 (Suppl. 3), A387.
10. Pillon B.: Neuropsychological Assessment for Management of Patients with Deep Brain Stimulation. Mov. Disord. 2002, Vol. 17 (Suppl. 3), S116–S122.
11. Saint-Cyr J.A.: Trépanier L.L.: Neuropsychological assessment of patients for movement disorder surgery. Mov. Disord. 2000, 15, 771– 783.
12. Lang A.E., Houeto J.L., Krack P., Kubu C., Lyons K.E., Moro E., Ondo W., Pahwa R., Poewe W., Troster A., Uitti R., Voon V.: Deep Brain Stimulation: Preoperative Issues. Movement Disorders 2006, Vol. 21 (Suppl. 14), S171–S196.
13. Volkmann J., Benecke R.: Deep Brain Stimulation for Dystonia: Patient Selection and Evaluation. Mov. Disord. Vol. 17(Suppl. 3), 2002, S112–S115.
14. Coubes P., Robertie A., Vayssiere N., Hemm S., Tuffery S., Echenne B., Frerebeau P.: Early-onset generalized dystonia: Neurosurgical treatment by continuous bilateral stimulation of the internal globus pallidus in sixteen patients. Mov. Disord. 2000, 15 (Suppl. 3), S155.
15. Lozano A.M., Kumar R., Gross R.E., Giladi N., Hutchison W.D., Dostrovsky J.O., Lang A.E.: Globus pallidus internus pallidotomy for generalized dystonia. Mov. Disord. 1997, 12, 865–870.
16. Starr P.A.: Placement of deep brain stimulators into the subthalamic nucleus or globus pallidus internus: Technical approach. Stereotact. Funct. Neurosurg. 2002, 79, 118–145.
17. Deuschl G., Herzog J., Kleiner-Fisman G., Kubu C., Lozano A.M., Lyons K.E., Rodriguez-Oroz M.C., Tamma F., Troster A.I., Vitek J.L., Volkmann J., Voon V.: Deep Brain stimulation: Postoperative Issues. Mov. Disord. 2006, Vol. 21 (Suppl. 14), S219–S237.
18. Schrader C., Benecke R., Deuschl G., Hilker R., Kupsch A., Lange M., Sixel-Doring F., Timmermann L., Volkmann J., Fogel W.: Deep brain stimulation for dystonia. Consensus recommendation of the German Deep Brain Stimulation Association. Nervenarzt. 2009, 80(6), 656–661.
19. 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.
20. Vitek J.L., Chockkan V., Zhang J.Y., et al.: Neuronal activity in the basal ganglia in patients with generalized dystonia and hemiballismus. Ann. Neurol. 1999, 46, 22–35.
21. Anderson M.E., Postupna N., Ruffo M.: Effects of high-frequency stimulation in the internal globus pallidus on the activity of thalamic neurons in the awake monkey. J. Neurophysiol. 2003, 89, 1150–1160.
22. Bennazzous A., Hallett M.: Mechanism of action of deep brain stimulation. Neurology 2000, 55(Suppl. 6), S13–S16.
23. Chou K.L., Hurtig H.I., Jaggi J.L., Baltuch G.H.: Bilateral subthalamic nucleus deep brain stimulation in a patient with cervical dystonia and essential tremor. Mov. Disord. 2005, 20 (3), 377–380.

24. Kleiner-Fisman G., Liang G.S., Moberg P.J., Ruocco A.C., Hurtig H.I., Baltuch G.H., Jaggi J.L., Stern M.B.: Subthalamic nucleus deep brain stimulation for severe idiopathic dystonia: Impact on severity, neuropsychological status, and quality of life. J. Neurosurg. 2007, 107(1), 29–36.
25. Montgomery E.B. Jr., Baker K.B.: Mechanisms of deep brain stimulation and future technical developments. Neurol. Res. 2000, 22, 259–266.
26. Sun B., Chen S., Zhan S., Lee W., Krahl S.E.: Subthalamic nuleus stimulation for primary dystonia and tardive dystonia. Acta Neurochir. Suppl. 2007, 97(Pt 2), 207–214.