Deep brain stimulation for secondary dystonia

Hyo Sang Lee

Department of Medicine

The Graduate School, Yonsei University

Deep brain stimulation for secondary dystonia

Directed by Professor Jin Woo Chang

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Hyo Sang Lee

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This certifies that the Master's Thesis (Doctoral Dissertation) of Hyo Sang Lee is approved.

Thesis Supervisor: Jin Woo Chang

[Young Ho Sohn: Thesis Committee Member#1)

[Jae Young Choi: Thesis Committee Member#2)

The Graduate School
Yonsei University

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<TABLE OF CONTENTS>

LIST OF TABLES

ABSTRACT

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Hyo Sang Lee

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Jin Woo Chang)

Objective: Deep brain stimulation (DBS) of the GPi has been shown to be partially effective for some forms of dystonia. The purpose of this study was to analyze the effect of DBS on the patients with secondary dystonia.

Methods: 16 patients (12 males and 4 females) underwent DBS for secondary dystonia. DBS electrodes were placed under local anesthesia. The Burke-Fahn-Marsden Dystonia Scale (BFMDRS), both movement and disability score were assessed before and after the surgery.

Results: GPi DBS performed on 16 patients. The etiology of dystonia was cerebral palsy (*n*=11), drug induced (*n*=1), post-traumatic (*n*=3), post-encephalitic dystonia (*n*=1). The mean BFMDRS movement and disability scores improved by 34.9 ± 28.3 % (p=0.015) and 20.5 ± 18.9 % (p=0.011) at 24 months after surgery than it was at baseline in cerebral palsy group and 79.5 ± 20.0 % , 57.8 ± 36.7 % in post-trauma and post-encephalitic group. No patient had a permanent major complication or peri-operative complications.

Conclusion: Patients with secondary dystonia who have focal or discrete lesions could be a good indication for DBS. Because of limited number and heterogeneity of patients, more studies with greater number of patients are necessary to establish the role of DBS in the treatment of secondary dystonia.

Key words: dystonia, deep brain stimulation, globus pallidus

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I. Introduction

Dystonia is a clinical syndrome characterized by sustained muscle contractions, frequently causing repetitive twisting movements or abnormal postures.[1] The basic approach describes primary and secondary dystonia due to environmental causes, brain injury and other genetic or not diseases. Dystonia is classified as primary or idiopathic dystonia when it occurs without other neurologic signs and without brain abnormalities evidenced with magnetic resonance imaging.[2] Dystonia is classified as secondary when it occurs in association with a lesion in the CNS, which can be caused by stroke, cerebral palsy, encephalitis, other environmental insults, or neurodegenerative disease.

Initial treatment of dystonia includes oral medications such as Dopaminergic drugs, anticholinergic medications, baclofen, benzodiazepines, but these medications have limitations because of its adverse effect.

Deep brain stimulation (DBS) of the GPi has been shown to be partially effective for some forms of dystonia. But the improvement in secondary dystonia is less pronounced. In this study, we report 16 patients with secondary dystonia treated with DBS. The purpose of this study was to analyze the effect of DBS on the patients with secondary dystonia.

II. Materials and methods

16 patients (12 males and 4 females) underwent DBS for secondary dystonia. The clinical characteristics of the patients are summarized in Table 1. Their age ranged from 18 to 40 years (median 30.06 years). The etiology of dystonia was

cerebral palsy (*n*=11), drug induced (*n*=1), post-traumatic (*n*=3), post-encephalitic dystonia (*n*=1).

Table 1. Clinical characteristics of patients with secondary dystonia

Patient	Age	Sex	Etiology	Dystonia Type	Electrode placement	Follow up (months)
1	18	M	Cerebral palsy	Generalized	Bilateral	2
2	21	M	Cerebral palsy	Generalized	Bilateral	27
3	26	M	Trauma	Focal	Left	16
4	26	M	Cerebral palsy	Generalized	Left	41
5	27	F	Cerebral palsy	Generalized	Bilateral	24
6	27	M	Cerebral palsy	Generalized	Bilateral	27
7	28	F	Cerebral palsy	Generalized	Bilateral	18
8	31	M	Drug induced	Focal	Bilateral	27
9	31	M	Cerebral palsy	Generalized	Bilateral	12
10	32	M	Trauma	Focal	Left	26
11	33	F	Cerebral palsy	Generalized	Bilateral	20
12	33	M	Post encephalitic	Focal	Left	100
13	34	F	Cerebral palsy	Generalized	Bilateral	24
14	36	M	Cerebral palsy	Generalized	Left	20
15	38	M	Cerebral palsy	Generalized	Bilateral	88
16	40	M	Trauma	Focal	Left	46

All evaluations were performed before and after surgery (at 1, 6, 12, 24 months) using the Burke-Fahn-Marsden Dystonia Scale (BFMDRS), both movement and disability score.

The surgical procedures were operated by the same person. Under local anesthesia, quadripolar DBS electrodes (model 3389, Medtronic, Inc.) were implanted in the GPi following stereotactic localization with MR imaging guidance. Microelectrode recordings were obtained in all patients. The postoperative cerebral MRI confirmed the correct positioning of the electrodes. Ten patients underwent

bilateral GPi DBS, one unilateral GPi DBS with a contralateral lesion and five unilateral GPi DBS.

For statistical analysis, SPSS software (version 17.0; 2008; SPSS, Inc., Chicago, IL, USA) was used. The statistical significance of the changes in rating scores at 1, 6, 12 and 24 months after surgery compared with the baseline was assessed using the Wilcoxon signed rank test (paired). A p-value less than 0.05 was considered statistically significant.

III. Results

GPi DBS was performed on 16 patients. The patients were regrouped by their etiology: cerebral palsy, miscellaneous and drug-induced. The age of patients with cerebral palsy ranged from 18 to 38 years (median 29.0). Mean follow up duration was 27.5 ± 22.3 months. The mean preoperative BFMDRS movement and disability scores were 61.5 ± 22.1 and 16.5 ± 7.1. The mean postoperative BFMDRS movement and disability scores were the following: 39.6 ± 20.4, 14.5 ± 7.3 at 1 month after surgery; 42.7 ± 22.3, 15.3 ± 8.4 at 6 months after surgery; 41.7 ± 27.5 13.8 ± 7.9 at 12 months after surgery; and 38.2 ± 23.5, 12.6 ± 6.9 at 24 months after surgery. The mean BFMDRS movement scores improved by 33.7 ± 31.2 % (p=0.008) at 1 month, 26.8 ± 30.0 % (p=0.028) at 6 months after surgery, 41.7 ± 27.5 % (p=0.059) at 6 months after surgery and 34.9 ± 28.3 % (p=0.015) at 24 months after surgery than it was at baseline. The mean BFMDRS disability scores also improved by 11.1 ± 10.4 % (p=0.008) at 1 month after surgery, 9.2 ± 22.7 % (p=0.168) at 6 months after surgery, 19.3 ± 19.0 % (p=0.010) at 12 months after surgery and 20.5 ± 18.9 % (p=0.011) at 24 months after surgery than it was at baseline. (Table 2.)

Table 2. Preoperative and postoperative BFMDRS movement and disability scores in cerebral palsy group

Visit month	Patients	BFMDRS-M		BFMDRS-D	
		Score	Improvement (%)	Score	Improvement (%)
Baseline	11	61.5 ± 22.1	-	16.5 ± 7.1	-
1 month	11	39.6 ± 20.4	33.7 ± 31.2	14.5 ± 7.3	11.1 ± 10.4
6 months	10	42.7 ± 22.3	26.8 ± 30.0	15.3 ± 8.4	9.2 ± 22.7
12 months	10	41.7 ± 27.5	41.7 ± 27.5	13.8 ± 7.9	19.3 ± 19.0
24 months	9	38.2 ± 23.5	34.9 ± 28.3	12.6 ± 6.9	20.5 ± 18.9

The miscellaneous group includes patients with post-traumatic dystonia (*n=3*) and post-encephalitic dystonia (*n=1*). Their mean age was 32.6 years (26 to 40). Mean follow up duration was 47.0 ± 37.7 months. The mean pre operative BFMDRS movement and disability scores were 13.5 ± 5.0 and 3.3 ± 1.3. The mean postoperative BFMDRS movement and disability scores were the following: 6.5 ± 3.4, 1.8 ± 1.5 at 1 month after surgery; 6.8 ± 4.6, 1.8 ± 1.5 at 6 months after surgery; 4.0 ± 2.9, 1.5 ± 1.3 at 12 months after surgery; and 3.7 ± 4.0, 1.7 ± 1.5 at 24 months after surgery. The mean BFMDRS movement scores improved by 54.5 ± 14.1 % at 1 month, 55.1 ± 22.0 % at 6 months after surgery, 73.2 ± 12.2 % at 12 months after surgery and 79.5 ± 20.0 % at 24 months after surgery than it was at baseline. The mean BFMDRS disability scores also improved by 47.5 ± 41.1 % at 1 month after surgery, 47.5 ± 41.1 % at 6 months after surgery, 55.8 ± 30.2 % at 12 months after surgery and 57.8 ± 36.7 % at 24 months after surgery than it was at baseline. The statistical analyses were not possible because the number of patients was small. (Table 3.)

Table 3. Preoperative and postoperative BFMDRS movement and disability scores

Etiology	BFMDRS-M			BFMDRS-D		
	Preoperative	Postoperative	Improvement (%)	Preoperative	Postoperative	Improvement (%)
Trauma	12	4	66.7	3	0	100
Trauma	14	3	78.6	5	3	40
Post encephalitic	20	8	60	3	2	33.3
Trauma	8	0	100	2	0	100

The Drug-induced dystonia group includes one patient. The pre operative BFMDRS movement and disability scores were 16 and 4. The post operative BFMDRS movement and disability scores were 8 and 4 at 1 month, 4 and 3 at 6 months, 4.5 and 4 at 12 months, and 2.5 and 1 at 24 months after surgery. The BFMDRS movement and disability score improved by 84.4 % and 96% at 24 months after surgery than it was at baseline.

No patient had a permanent major complication or peri-operative complications. But four patients had transient reversible side effects such as hemi-facial weakness, mood change, dysarthria.

IV. Discussion

The pathophysiology of dystonia is not well understood, but it is known that abnormal firing activity in the GPi is associated with dystonic patients.[3] The positive results from pallidotomy and pallidal DBS for dystonic symptoms in patient with Parkinson's disease gave an idea of pallidal surgery or pallidal DBS for secondary dystonia.[2] Secondary dystonia is frequently associated with the lesions in the putamen or globus pallidus.[4] As for dystonic syndromes, the optimal anatomical target is still under discussion.[5-7] Bilateral pallidal DBS has been an effective therapy for primary generalized dystonia.[8-11] But the results of pallidal surgery of pallidal DBS for secondary dystonia were not satisfactory literally. Eltahawy et al.

reported 15 patients treated with lesioning or DBS of the GPi, among whom 6 patients who had secondary dystonia did not respond as well as patients with primary dystonia did.[12] Katsakiori et al. reported significant improvement of BFMDRS scores after bilateral GPi DBS for secondary dystonia.[13] Pretto et al. reported notable improvement in objective scores 11 patients who underwent DBS procedure for secondary dystonia.[14] Vidailhet et al. reported 13 patients with dystonia-choreoathetosis CP treated with bilateral pallidal DBS. Improvement of dystonia-choreoathetosis after stimulation of the posterolateroventral part of the GPi was noted.[8] Zhang et al. reported DBS could be an ideal treatment for patients with tardive and posttraumatic dystonia.[15]

In our study, the overall BFMDRS movement and disability scores improved after DBS was performed in secondary dystonia patients. As for patients with cerebral palsy, the effects of DBS were minimal and only slight improvement of activities of daily living was acquired. In one patient, the BFMDRS movement score declined after surgery. This is in consistence with other reports.[16] The resulf of drug-induced dystonia case showed that the BFMDRS movement and disability scores improved by 84.4%, 96%, and these findings are in agreement with past studies.[16] Patients with post-traumatic dystonia and postencephalitic dystonia responded less well to DBS in previously published reports.[15-20] But in our study, the post operative BFMDRS movement and disability scores of patients without cerebral palsy (post traumatic and post encephalitic cases in our study) improved by higher mean percentage than past studies.

In cases without cerebral palsy, the lesion tends to be discrete and does not involve many areas. The type of dystonia in cases without cerebral palsy was focal dystonia, but in all cases with cerebral palsy, the types of dystonia were generalized dystonia. These findings can explain the reason why the patients with cerebral palsy did not respond well to DBS.

V. Conclusions

Patients with secondary dystonia who have focal or discrete lesions could be a good indication for DBS. In case of patients with cerebral palsy, the effects of DBS were minimal and only slight improvement of activities of daily living was acquired. Because of limited number and heterogeneity of patients in this study, more studies with greater number of patients are necessary to establish the role of DBS in the treatment of secondary dystonia.

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ABSTRACT(IN KOREAN)

이차적 근육긴장이상에 대한 뇌 심부자극술

<지도교수 장진우>

연세대학교 대학원 의학과

이효상

담창구에 대한 뇌심부자극술은 특정 형태의 근육긴장이상증에 대해 부분적으로 효과가 있는 것으로 알려져 있다. 이 논문의 목적은 이차적 근육긴장이상 환자에게 뇌심부자극술을 시행 후 그 결과를 분석하기 위함이다. 16명의 이차적 근육긴장이상 환자 (12명의 남성, 4명의 여성)에게 뇌심부자극술이 시행되었다. 뇌심부자극 전극이 부분 마취 하에 삽입되었고, 수술 결과는 Burke-Fahn-Marsden Dystonia Rating Scale(BFMDRS) 로 측정되었다. 16명의 환자에게 담창구 뇌심부자극술이 시행되었다. 11명의 환자가 뇌성마비, 1명의 환자가 약물 유도성, 3명의 환자가 외상 후, 그리고 1명의 환자가 뇌막염 후의 근육긴장이상으로 확인되었다. 수술 24개월 후 BFMDRS movement 와 disability scores 는 수술 전과 비교하였을 때 뇌성마비 환자의 경우 34.9 ± 28.3 % (p=0.015) 와 20.5 ± 18.9 % (p=0.011), 외상 후와 뇌막염 후 환자의 경우 79.5 ± 20.0 %, 57.8 ± 36.7 % 로 개선되었으며, 수술 전후의 주요 합병증은 보고되지 않았다. 이차적 근육긴장 이상 환자 중 병변이 광범위하지 않고 명확한 환자들에게 뇌심부자극술은 좋은 적응증이 될 수 있다. 환자의 병인이 다양하며 수술 사례가 많지 않았기 때문에 이차적 근육긴장 이상 환자에 대한 뇌심부자극술의 적용의 효용성은 보다 많은 환자에 대한 연구를 통해 확인이 필요하다.

핵심되는 말: 근긴장이상, 뇌심부자극술, 담창구