

Deep brain stimulation as an effective treatment option for post–midbrain infarction-related tremor as it presents with Benedikt syndrome

Case report

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Benedikt syndrome is a rare but debilitating constellation of symptoms that manifests from infarction of the red nucleus, cerebral peduncle, oculomotor fascicles, and lower oculomotor nucleus. Clinically, it presents as ipsilateral cranial nerve III palsy, contralateral hemiataxia with intention tremor, contralateral hemiparesis, and hyperactive tendon reflexes. Commonly, the tremor upon purposeful movement proves to be the most debilitating manifestation of the infarction with significant impact on the patient's ability to perform activities of daily living and, therefore, quality of life. The authors report the successful management of this debilitating post–midbrain infarction tremor with the insertion of a deep brain stimulator with targets in the contralateral lenticular fasciculus. (DOI: 10.3171/JNS/2008/109/10/0635)

KEY WORDS • Benedikt syndrome • deep brain stimulation • lenticular fasciculus • midbrain infarction • post-stroke tremor

SINCE its introduction as a therapeutic modality for Parkinson disease, DBS has revolutionized the management of a diverse array of movement disorders. Despite this diversity of utility, poststroke movement disorders in particular have long gone untreated and are often considered the most debilitating postinfarction sequelae. We report the successful treatment of an intention tremor associated with Benedikt syndrome via DBS of the lenticular fasciculus. Clinically, Benedikt syndrome presents as ipsilateral cranial nerve III palsy, contralateral hemiataxia with intention tremor, contralateral hemiparesis, and hyperactive tendon reflexes.^{6,11} This account represents the first reported successful patient outcome of DBS of the lenticular fasciculus as an effective treatment modality of postinfarction tremor as it presents with Benedikt syndrome.

Abbreviations used in this paper: AC = anterior commissure; DBS = deep brain stimulation; PC = posterior commissure; Vim = ventral intermediate; WHIGET = Washington Heights–Inwood Genetic Study of Essential Tremor.

Case Report

History and Physical Examination. This 55-year-old man with a history of coronary artery disease, hypertension, hyperlipidemia, coronary artery bypass grafting, and surgical repair of an aortic dissection with prosthetic aortic valve replacement experienced acute onset of vertical diplopia, left eyelid ptosis, and mild right-sided weakness. The patient was noted to have been noncompliant with his prophylactic Coumadin (Bristol-Myers Squibb) anticoagulation regimen at the time of symptom onset. Seven months later he presented with physical examination findings consistent with Benedikt syndrome. The patient was found to have a sluggish pupillary response to light on the left with mild left ptosis. Motor examination showed a coarse, high-amplitude, low-frequency action and postural tremor of the right upper extremity with a mild resting component. The right leg exhibited a similar but less severe tremor. There was also right pronator drift and impaired dexterity of rapid fine movements of the right hand. Deep tendon reflexes were found to be hyperactive on the right with flexor plantar responses bilater-

ally. No pathological reflexes were observed. Sensation, cerebellar function, and gait were unremarkable.

Imaging. Magnetic resonance imaging of the brain was performed. Sagittal T1-weighted images; axial diffusion, T2-weighted, gradient echo, FLAIR, and T1-weighted images; and coronal T2-weighted images were obtained. Following Gd infusion, axial and coronal T1-weighted images were obtained as well. Diffusion coefficient mapping was also performed. Findings included small focal areas of increased T2 signal in the medial left thalamus, right cerebral peduncle, and bilateral cerebellar hemispheres (Fig. 1). Infarction of the left cranial nerve III fascicles, red nucleus, and cerebral peduncle was evident on MR images. Normal flow voids were present in the visualized arterial structures, and no abnormal enhancement was noted following Gd infusion.

Further Evaluation. The etiology of the infarction was considered to be thromboembolic. The patient was unresponsive to previously attempted pharmacotherapy and noted his tremor to be the most debilitating aspect of his poststroke symptoms. As determined by the WHIGET Tremor Rating Scale,¹³ he scored a 4/4 with regard to tremor severity preoperatively (Table 1). Given the failure of medical treatment options, the decision was made to proceed with DBS implantation of the left lenticular fasciculus for the right-sided tremor.

Operation. In the operating room, the patient's head was secured within a 4-pin head fixation CRW stereotactic frame (Integra Radionics, Inc.) followed by plane localization and orientation. Both the left Vim nucleus of the thalamus and the left lenticular fasciculus^{14,18,29} were selected as potential electrode targets using the coordinates as defined in the Talairach atlas.²⁶ The coordinates for the Vim nucleus in relation to the AC-PC plane are as follows: 0.2 × AC-PC distance anterior to the posterior commissure, 13–15 mm lateral to the AC-PC line and + 1.5 mm in the Z-plane.²⁵ We used the following coordinates for the lenticular fasciculus: 3–5 mm posterior to the AC-PC midpoint, 8–10 mm lateral to the AC-PC line, and -3 to 4 mm in the Z-plane (Fig. 2). Those coordinates were given by O. Howard Reichman, M.D., in 1979 (personal communication), and were confirmed in the Talairach atlas.

Once preparatory measurements were made, a left frontal curvilinear incision was made and the calvaria and dura mater were opened. The microelectrode (Medtronic, Inc.) was introduced subcortically, and test recordings were made at 2.1 A following the course of the zona incerta until tremor cessation was noted. Following localization of the point of maximal tremor relief, the electrode was anchored and the cranial incision was closed. The pulse generator (Medtronic Inc.) was then placed in the left infraclavicular region and the electrode was appropriately connected. The patient's wounds were dressed, and he was taken to the recovery room in stable condition (Fig. 3).

Postoperative Course. The patient was discharged home following an uneventful postoperative course. Two weeks later the patient was followed up in the neurosurgical clinic for a setting adjustment to his DBS unit. The

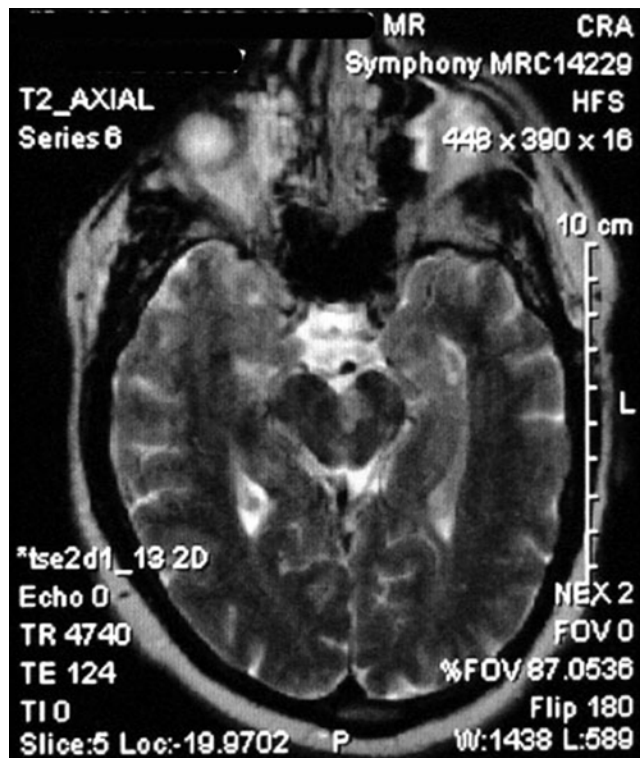


FIG.1. Preoperative MR image revealing a lesion in the medial aspect of the left thalamus extending inferiorly along the left cerebral peduncle into the left medial aspect of the midbrain.

initial settings were as follows: case positive, electrode 1 negative, amplitude 2.6 V, pulse width 120 microseconds with a rate of 185 Hz. At these settings, the patient was noted to have remaining tremor in the right upper extremity, especially on exertion. The DBS unit was reprogrammed as follows: case positive, electrode 0 negative, amplitude 2.5 V, pulse width 120 msec with a rate of 185 Hz. The patient left the office with excellent tremor control to the point that he could open the office door, a task that he could not manage the previous week. One month later, the patient was found to be doing extremely well with almost complete resolution of his postural and intention tremors; however, mild to moderate spasticity of the upper extremity was notable and persistent. Activities of daily living were performed with little or no tremor, and the patient scored 1/4 on the WHIGET Tremor Rating Scale. At the 16-month postoperative follow-up

TABLE 1
The WHIGET Tremor Rating Scale*

0	no visible tremor
1	mild/intermittent tremor
2	obvious consistent tremor that oscillates btwn 2 extremes; writing & drawing moderately impaired, bothersome to most patients
3	large amplitude, jerky tremor; writing & drawing severely impaired
4	marked tremor; interferes w/ most activities, unable to maintain pen to paper contact w/ writing/drawing challenge

* From Louis et al., 2001.

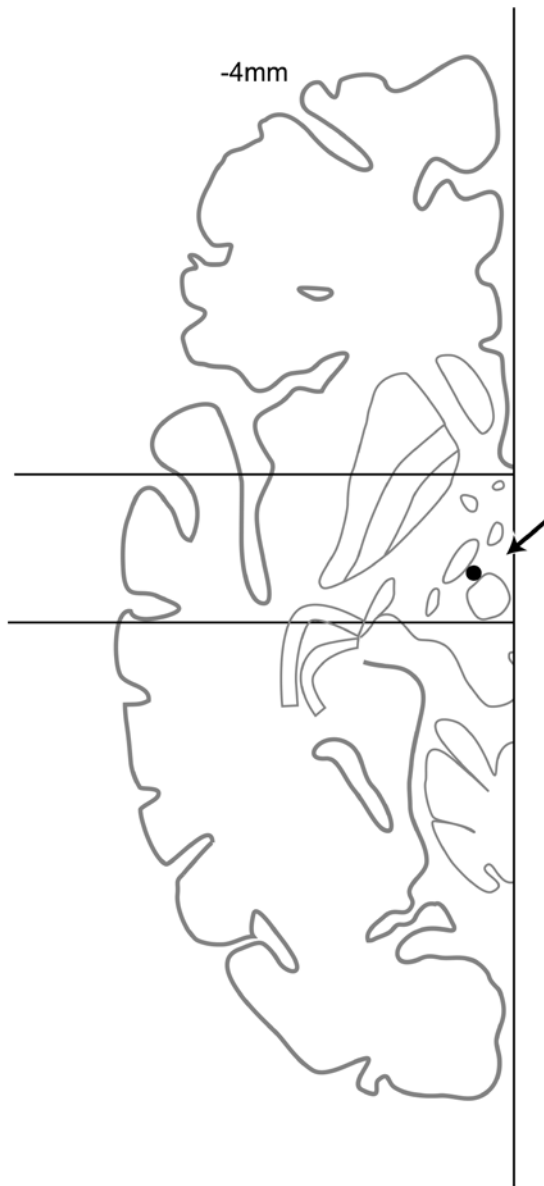


FIG. 2. Diagram of the brain 4 mm below the AC-PC line illustrating the approximate coordinates of the thalamic fasciculus (arrow).

examination, it was noted that the patient continued to demonstrate persistent tremor improvement with a stable degree of upper extremity spasticity; the unit had been preprogrammed to change at 8 months after surgery to case positive, electrode 3 negative, amplitude 3 V, pulse width 120 msec, rate 170 Hz.

Discussion

Deep brain stimulation represents the third generation of stereotactic neurosurgery. It has evolved over a natural progressive course following the success of thalamotomy first performed by Spiegel and Wycis for psychiatric and motor disorders in the 1940s.²³ Later, Spiegel et al.²⁴ advocated campotomy, a lesion of the pallidotha-



FIG. 3. Postoperative CT revealing successful implantation of a DBS unit (on the left side of the brain) that extends to the region of the subthalamic nuclei.

lamic fibers at field of Forel H, for parkinsonian tremor. Velasco and Velasco, Guiot, Ojemann and Ward, as well as Narabayashi and Ohye have since suggested their own variations on Spiegel's original campotomy location indicating a degree of homogeneity within the subthalamic white matter.²⁸ Following the development of a series of human stereotactic atlases based on the relationship between various cranial and ventricular landmarks, a reference grid evolved. This 3D grid allowed the mid-20th century neurosurgeon to measure a series of coordinates and thereby localize a subcortical target for coagulation.⁷

Surgeons who followed and developed further surgical experience based on Spiegel's early campotomy success found that the mere insertion of an inert electrode into the subthalamic area could provide a transient respite from both parkinsonian and essential tremor.^{2,27} Benabid's group furthered the therapeutic concept of DBS without subsequent lesioning with the observation that the high frequency discharges emitted by the stimulating electrode used to guide lesion placement for Vim thalamotomy themselves resulted in tremor abolishment.^{3,4,19} As a result of this realization, DBS became a viable treatment option for the tremor of Parkinson disease without the extensive side effect profile of bilateral thalamotomy.

Since its introduction in the late 1980s, DBS has become one of the primary treatment modalities for medically refractory movement disorders. Deep brain stimulation with targets in the contralateral Vim nucleus of the thalamus has been so widely accepted and utilized that it has all but replaced thalamotomy as the treatment of choice for Parkinson disease-associated tremor and essential tremor.^{1,9,10,16,20,21} This efficacy has been investi-

gated up to 6 years following implantation and found to provide durable tremor relief.^{16,20} Although there is still progress to be made understanding DBS's effect at the neuronal level, there is little doubt of its utility at the clinical level.

While the pathophysiology of tremor is still a widely researched topic, the classic cerebellar tremor appears to result from a disturbance of the cerebellar feed-forward control of voluntary movements.⁵ Holmes tremor and its successful treatment have aided in the delineation of particular regulatory cell populations involved in various tremor components. Holmes tremor is a combination of both cerebellar and parkinsonian-type tremors. Early use of DBS for its treatment found stimulation of the contralateral thalamic Vim nucleus to be very effective in treating the distal parkinsonian component of the tremor but left the proximal cerebellar component unimproved.^{8,15} The concept of multiple-target DBS evolved from these findings. Kitagawa et al.¹² reported that subsequent DBS of targets in the subthalamic white matter markedly improved the proximal tremor that had been refractory to prior Vim thalamotomy. Our report indicates that the lenticular fasciculus represents a target that may prove useful for the treatment of intention tremor, possibly due to its involvement in the modulation of the cerebellar feed-forward control of voluntary movements. This interplay between the basic and clinical sciences will further the specificity of DBS target selection and thereby facilitate the advancement of symptom resolution and side effect minimization.

Conclusions

As targets in the cerebrum become implicated in various disease pathologies, DBS continues to evolve. It has been touted as having potential efficacy for such conditions as Tourette syndrome, intractable obsessive-compulsive disorder, intractable pain, refractory depression, and refractory epilepsy, as well as tremors associated with multiple sclerosis and phenylketonuria.^{1,17,22} A further understanding of the cell populations and neuronal pathways responsible for these and other debilitating conditions will improve the utility of DBS in managing a variety of heretofore untreatable neurologic conditions. The side effect profile of DBS implantation is favorable and often reversible, further contributing to its broad therapeutic applicability. The successful management of our patient's debilitating intention tremor following midbrain infarction lends further support to DBS as an effective treatment modality for infarction-associated movement disorders.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Acknowledgments

The authors thank Ms. Dianne Martia for her editorial assistance.

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Manuscript submitted June 19, 2007.

Accepted December 3, 2007.

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