

Pallidal Deep Brain Stimulation in the Treatment of Huntington's Chorea

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Abstract

Despite the success of deep brain stimulation (DBS) in various movement disorders, its use in Huntington's Disease (HD) has been limited. So far, promising results of pallidal DBS have been reported in 7 patients with HD. We performed bilateral pallidal DBS in a 59 year old woman with HD since 12 years and severe motor symptoms. At the evaluation after 12 months the effect was deemed satisfactory mainly concerning the patient's choreatic symptoms. However, the improvement according to the unified Huntington's disease rating scale was modest, with a score reduction from 92 to 81.

Keywords: DBS; Huntington's chorea; Pallidum

Introduction

Huntington's disease (HD) is an autosomal dominant progressive disorder characterized by cognitive decline and motor symptoms. The movement disorder is characterized by choreatic movements, dystonic symptoms and rigidity. Especially the choreatic symptoms can pose a major problem to patients and care-givers. The effect of pharmacological therapy on these symptoms is often limited. Perhaps because of the severity of the symptoms in combination with the lack of therapeutical alternatives, HD was the first movement disorder to be treated with a stereotactic functional procedure in the late forties [1,2]. The results of stereotactic lesions seem, however, to have been rather modest [3-7]. Deep brain stimulation (DBS) has proven its efficacy in other movement disorders such as dystonia and Parkinson's disease, but the interest for applying this technique to HD has been limited [8]. To date, the authors are aware of only 7 cases reported in the literature [9-14]. Based on these reports, and the similarity between the symptoms in HD and the choreo-dystonic symptoms seen in PD and dystonia, we decided to perform bilateral pallidal DBS in a patient with HD.

Case Presentation

The patient was a 59 year old woman who was diagnosed with HD 12 years prior to surgery. The disease was genetically confirmed (42 CAG repetitions) and was inherited from the mother. The patient was confined to a wheel-chair due to gait and balance impairment and suffered from severe choreatic movements in the extremities, as well as in the trunk, head, neck and face. Several anti-choreic medications such as Tetrabenazine, Risperidone and Haloperidol were tried but not tolerated. She had further a moderate dysarthria and dysphagia and suffered from weight loss, and percutaneous endoscopic gastrostomy (PEG) had been considered one year prior to the DBS procedure. She displayed mild psychiatric symptoms such as anxiety and irritability,

but no apparent cognitive decline. An MRI of the brain showed moderate cortical atrophy.

Due to the severity of the choreatic movements it was decided to perform a bilateral pallidal DBS. The target was visually identified on proton density stereotactic MRI in the posteroventral Globus pallidus internus (Gpi), and two DBS electrodes were implanted (Model 3389, Medtronic, Minneapolis, MN, USA) using the Leksell frame. The procedure was performed under general anaesthesia. Microelectrode recording was not used. The correct placement of the electrodes was verified on an intra-operative stereotactic computed tomography (CT) fused with the stereotactic MRI (Figure 1). The contacts used for chronic stimulation (contact #1) were well placed within the posteroventral part of the Gpi (Left side: 21.5 mm lateral of the intercommissural line (ICL), 2.2 mm anterior of the mid-commissural point (MCP) and 2.2 mm below the ICL. Left side: 20.9 mm lateral, 2.2 mm anterior and 1.3 mm below the ICL).

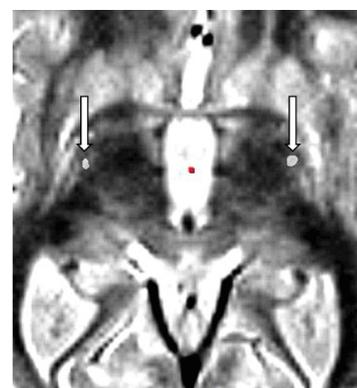


Figure 1: Preoperative MRI fused with postoperative CT demonstrating the electrodes in the target (arrows).

After surgery, the patient's choreo-dystonic symptoms displayed an almost immediate response to stimulation: During stimulation screening and titration, stimulation of the deepest contacts (contact zero) on each side resulted in weakness/cramps in the upper extremities at 3.0 V, possibly due to spread of current to the motor fibres in the internal capsule, whereas stimulation of the two highest contacts on each side had a more limited effect on the symptoms. Parameters chosen for chronic stimulation were monopolar stimulation with the second deepest contacts on each side (contact #1), 1.5/2.5 V, 60 µS, 130 Hz. Attempts to stimulate at higher amplitudes resulted in further improvement so the choreatic symptoms were almost abolished, but at the expense of provoking bradykinesia. On chronic stimulation with the above-mentioned parameters, the patient's walking ability further improved, as well as her speech and sleep. Three months after the procedure the patient complained from increasing dysphagia, and she later received a PEG. No other complications were noted. A video displaying the patient before surgery and at the 3 months follow up is available online.

The patient was formally evaluated at baseline and 12 months after the procedure, on stimulation, using the unified Huntington's disease rating scale (UHDRS), the Hamilton depression rating scale (HDRS), the Global assessment of function (GAF), the short form 36 item health survey (SF-36), the Mini mental state examination (MMSE) and a neuropsychological test battery. Several of the cognitive tests that the patient was unable to perform before surgery due to the motor symptoms and the stress caused by them could be completed at the 12 months follow up (Table 1). There was a modest improvement in the UHDRS scores mainly concerning the choreic movements. The global assessment of function did not change, nor did the MMSE score.

Before surgery (12 months)	On stimulation	
Motor UHDRS	92/125	81/125
Chorea	26/28	19/28
Dystonia	10/20	14/20
GAF	50	50
Cognitive assessment		
Verbal fluency	20	17
Symbol digital modality	†	11
Stroop interference	†	†
Colour naming	†	40
Word reading	†	49
Interference	†	24
Behavioural assessment	11	4
HDRS	12	11
SF- 36	††	††
PCS	29.5	22.8
MCS	36.4	61.3

MMSE	26	26
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Table 1: Evaluation at baseline before surgery, and at 12 months follow up on stimulation. † Could not complete, †† Higher scores indicate higher levels of functioning, UHDRS = Unified Huntington's Disease Rating Scale; GAF=Global assessment of function scale; HDRS=Hamilton depression rating scale; SF-36=Short form questionnaire; PCS=Physical component score; MCS=Mental component score; MMSE=Mini mental state examination.

The effect of DBS on the patient's choreic symptoms was deemed to be satisfactory (see video), although the improvement according to UHDRS was very modest. Nevertheless, the improvement was such that the patient was able to complete formal cognitive evaluation tests that were impossible to perform before surgery. Furthermore, there was no deterioration of mental status after one year of continuous DBS. Verbal fluency showed modest improvement and the behavioural assessment improved substantially. However, while the Global assessment of function did not change, quality of life showed an improvement concerning mental health status.

Although reports on DBS for Huntington's disease are very rare, it is of interest to note that the first operation ever performed with the stereotactic technique was in fact a pallido-thalamotomy performed by Spiegel and Wycis in 1946 in a patient with HD [1,2]. A few years later chronic depth electrodes were implanted during surgery, and for scientific reasons, on HD patients by Sem Jacobsen et al. at Mayo Clinic [15]. The number of HD patients operated during the lesional era, before the introduction of DBS, was limited, and the results seem not to have been encouraging [3-7]. DBS has today largely replaced lesional procedures, and 7 patients with pallidal DBS for HD have recently been presented in 6 different reports [9-14]. Moro et al. [10] presented one patient in which UHDRS was improved with 31.4 % after 8 months. The effect was most pronounced regarding chorea, followed by dystonia, and with limited effect on bradykinesia. In fact, these authors chose low-frequency stimulation with 40 Hz since the effect on bradykinesia was better at lower frequency. Hebb et al. [13] reported a reduction of UHDRS scores from about 70 before surgery to about 60 on stimulation after 12 months (and a score of 97 in off-stimulation condition at one year). The authors did not use low frequency stimulation due to a poor effect on the chorea. It is of interest that the authors noticed a deterioration in laryngeal function resulting in dysphagia after 10 months, which was not improved when the stimulation was turned off. Fasano et al. [12] reported a 72 year old patient in whom high frequency stimulation was more efficient for chorea, but induced bradykinesia and gait disturbance, therefore low frequency DBS was chosen. When evaluated on stimulation after 12 months, dystonia was abolished, chorea reduced with 76.5% and rigidity with 57.1%, as compared to the pre-operative baseline. There was, however, no difference at 12 months on stimulation as compared to off stimulation, suggesting the presence of a microlesional effect. Further, from the fourth month and onwards, gait and apathy worsened progressively, and a there was clear deterioration of their patient's cognition. Biolsi et al. [9] reported the results at 4 years follow-up in a 60 year old patient. No complications were seen, with the exception of stimulation induced bradykinesia, which was successfully treated with L-dopa. At the evaluation after 4 years the chorea was improved with 56% on stimulation as compared to off stimulation, and motor function improved with 32%. Kang et al. [11] reported 2 patients evaluated after 2 years, where chorea improved with 50-60% compared to baseline. Both patients did demonstrate

further progression of the disease, including neuropsychological deterioration. One of the patients presented a deterioration of swallowing function, not improved by turning the stimulation off. Spielberger et al. [14] presented one 30 year old patient with UHDRS score of 79 before surgery, which was reduced to 67 at 18 months after surgery on stimulation, and later progressed to 82 after 4 years. An increased bradykinesia was seen over time, but low-frequency stimulation could not be applied, since this reduced the effect on the chorea.

Thus, the results of pallidal DBS in previous studies and in our patient are encouraging, especially concerning the choreatic component. However, deterioration of various symptoms, such as bradykinesia, gait, swallowing and cognition, has also been reported, even if it is unclear what might be attributed to surgery and what to progression of disease. Considering the progressive nature of HD it is essential in future studies to evaluate effects and side effects of pallidal DBS in a randomized manner compared with a non-surgical control group.

Conclusion

Pallidal DBS appeared to be a worthwhile treatment in the patient presented here especially as a treatment for choreatic movements. Randomized studies and a longer follow up are required before the role of DBS in HD can be decided.

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