



Letter to the Editor

Multiple source current steering – A novel deep brain stimulation concept for customized programming in a Parkinson's disease patient[☆]



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Side effects

Deep brain stimulation (DBS)

This case report is in accordance with the Declaration of Helsinki. Deep brain stimulation was carried out with the adequate understanding and written consent of the patient involved and with the ethical approval of the authors' institutional review board.

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is a safe and effective treatment for Parkinson's disease (PD). However, small variations in stimulation current can cause excessive neural activation of neighboring anatomical structures or the non-motor portions of the STN which might induce unintended side effects. Therefore, in a number of patients, this leads to the dilemma of choosing suboptimal stimulation parameters to avoid side effects at the cost of suboptimal suppression of motor symptoms. In conventional, single-source DBS systems (voltage- and current-control systems), precision and stability of therapy delivery may be limited since each contact cannot be controlled independently. In contrast, simulation models of DBS indicate that current steering with multiple stimulation sources might be able to transfer current more precisely and more constant over time [1,2]. In principle this approach might be a helpful tool for the clinician to control side effects thereby improving the overall outcome of DBS.

Here, we report of our experience with a novel DBS-system capable of multiple source current steering and describe how this novel programming capability added to a more customized DBS-programming in a PD patient treated with bilateral STN-DBS. This case report is in accordance with the Declaration of Helsinki. Deep brain stimulation was carried out with the adequate understanding and written consent of the patient involved and with the ethical approval of the authors' institutional review board.

A 60 year old male diagnosed with PD for 13 years presented at our clinic. He suffered from severe parkinsonism, resting and postural tremor more dominant on the left side, and a history of depressive symptoms. Dopaminergic drugs induced severe sleep apnea and day-time sleepiness. The patient experienced off-time freezing of gait episodes and severe dyskinesia, limiting his daily activities and quality of life. The patient reported

having normal mobility for only 4–6 h per day. The UPDRS III score was 45 points (off medication) and 10 points in the on-medication state after administration of 200 mg of soluble L-Dopa (Madopar LT, Roche) which is a L-Dopa response of almost 80%. Medication reached a daily L-dopa dosage of 800 mg, in addition to 2.1 mg of pramipexole. Medications improved UPDRS III scores but also resulted in severe dyskinesia. The medical treatment was not found to be effective in controlling the patient's symptoms resulting in social life exclusion due to severe impairment.

In November 2010 bilateral DBS of the STN was performed with a DBS system capable of multiple source current steering (Boston Scientific DBS, 8-contact lead, Vercise™ Implantable Pulse generator, Boston Scientific Corporation, Natick, MA, USA). Intraoperatively, rigidity, tremor and hypokinesia responded well to test stimulation, microelectrode recordings detected specific STN activity at the target area and electrode localization was confirmed with intra- and postoperative stereotactic orthogonal X-ray and postoperative CT. The days after implantation we saw a marked stun-effect. A monopolar review one week after implantation identified contact #2 on both electrodes to be best for suppression of motor signs. Whereas the left electrode was programmed with a simple monopolar setting, the right electrode controlling the left - more affected - hemibody needed more fine tuning. In the following, the programming steps over the course of several months are outlined in detail: Monopolar stimulation of the right STN - through contact #2 with a pulse width of 60 μ s, frequency of 130 Hz and amplitude of 2 mA, led to motor improvement (Fig. 1A). However, further increasing the amplitude on contact #2 induced dyskinesia, and was insufficient to completely control the patient's tremor. We therefore adjusted the stimulation field into a 'teardrop-shape' by shifting the stimulation toward a more proximal contact (contact #3), and slowly increasing amplitude. This resulted in improvement in motor symptoms, without driving dyskinesia (Fig. 1B). The patient also continued to experience some apathy, and problems with mood and drive possibly also by reduction of dopaminergic medication postoperatively. Apathy could be reduced through monopolar stimulation of contact #1 with very low amplitude possibly through affection of the limbic portion of the STN [3] (Fig. 1C). In another follow-up visit, the patient suffered from slight aggravation of resting tremor and also dyskinesia which prompted us to additionally activate contact #4 which led to tremor improvement possibly via affection of the zona incerta [4] and dyskinesia possibly through stimulation of pallidofugal fiber tracts [5]. In order

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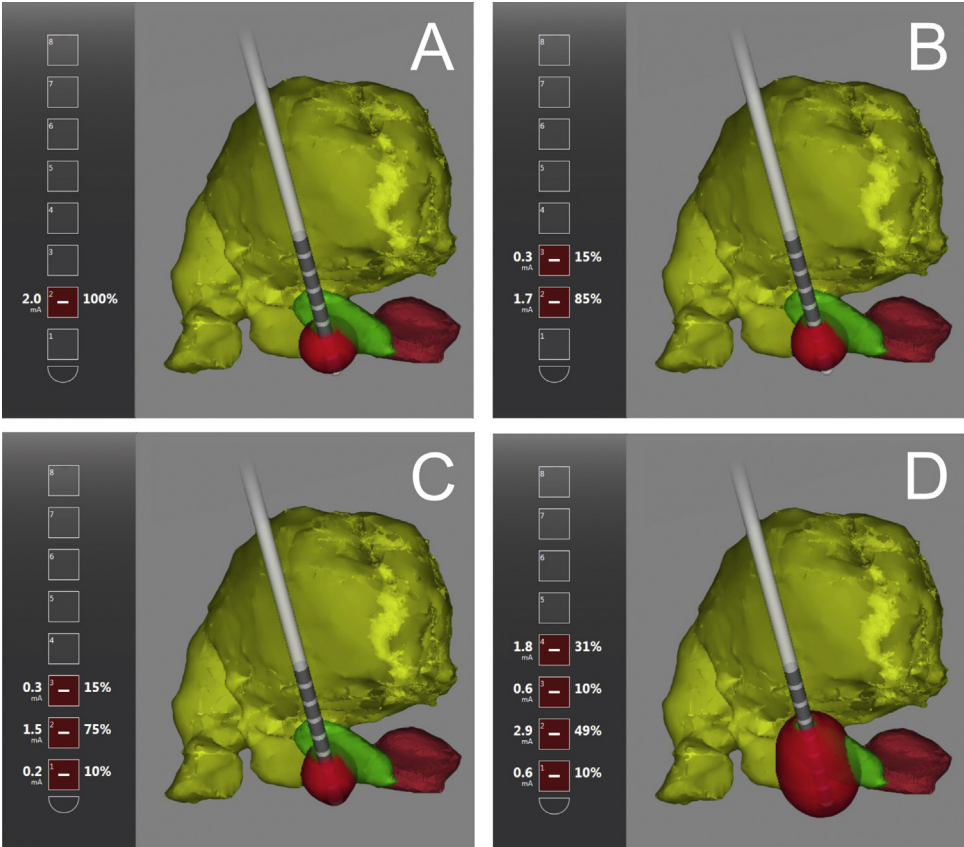


Fig. 1. Right-sided electrode location is shown in anatomical relation to the thalamus (yellow), STN (green) and red nucleus (red). A: 100% stimulation on contact #2 with 2.0 mA, 60 μ s, 130 Hz which resulted in motor improvement but also induced dyskinesia. B: By shifting the current more dorsally (84% on contact #2, 16% on contact #3, at 2.0 mA) motor symptoms improved further without driving dyskinesia. C: Additional activation of contact 1 (10% on contact #1, 75% on contact #2, 15% on contact #3, at 2.0 mA) reduced apathy possibly by affection of the limbic portion of the STN. After fixation of the electrodes at the burr hole we saw mild lead deviation of the electrode which resulted in a final lead location 2 mm too rostrally. Still the patient did benefit from an excellent clinical effect as described in the manuscript so that the electrode location did not have to be corrected. The rostral location might explain the proximity of contact #1 to the limbic portion of the STN. D: Activation of contact 4 located in the zona incerta resulted in further improvement of tremor and dyskinesia. The Boston Scientific GUIDE DBS System was used to generate the figure. This system locates the lead in the anatomy through the following steps: A pre-operative MRI is fused to a post-operative CT. The Morel atlas [7] is registered to the pre-operative MRI. An automated algorithm locates the lead in a post-operative CT.

Table 1
Activated contacts (left), distribution of current (middle) and possible pathophysiological mechanism of action (right) in our patient with Parkinson's disease and multiple source deep brain stimulation of the subthalamic nucleus. Note, that the different distribution of current is targeting different anatomical structures and, clinically, different clinical symptoms.

Number of contact (from ventral to dorsal)	Percentage of current applied to the tissue	Possible mechanism of action
1	10% current stimulation (0.6 mA)	We assume that the improvement of apathy was due to the stimulation of the limbic portion of the STN [3]
2	50% current stimulation (3 mA)	Monopolar review identified this contact as the best single therapeutic contact, and a major part of the current is delivered through this contact for good overall motor outcome
3	10% current stimulation (0.6 mA)	We stimulated through this contact to reshape the field and maintain the clinical effect of contact #2 without driving dyskinesia side effects.
4	30% current stimulation (1.7 mA).	We assume that the further improvement in tremor and dyskinesia was due to the stimulation of the zona incerta (tremor) [4] and pallidofugal fiber-tracts (dyskinesia) [5] crossing the white matter located dorsal to the STN.

to combine those optimal settings - we decided to deliver simultaneous and independent stimulation through the 4 contacts (Fig. 1D). Overall current amplitude on the right STN lead was then at 5.9 mA (pulse width of 60 μ s and frequency of 130 Hz remained unchanged). We were able to simply reshape the electrical field along the 4 contacts and fractionalize the current as shown in Table 1. Of course our topographic explanations of the observed effects are merely hypothetical since we neither have proof that the zona incerta or the limbic portion of the STN are in fact affected by stimulation nor that affection of these areas would reliably lead to the observed changes. L-dopa dose reduction was remarkable – decreased by 70%, 3 months after the surgery and by 100% today. The UPDRS motor score improved from 45 points without therapy to 15 points with DBS. Over two years later in January 2013, the patient was still reporting excellent results from current steering, with clear speech, good gait, excellent postural reflex, no rest tremor, and only tiny action tremor.

This is the first report of the effects of multiple source current steering in human. As we could show in previous studies, pathological activity in PD patients is clustered along the STN and ZI, thus, customized stimulation on different contacts is reasonable [6]. In former times stimulating multiple contacts might have been limited by the high amounts of current used consequently shortening battery life. With the rechargeable system used in this case study, battery depletion and reduced battery life was

not a clinically relevant restriction. Current steering based on a precise monopolar review led to a good reduction of all motor symptoms while minimizing side effects. The current steering stimulation strategy was successful in improving motor scores and distinct therapeutic benefits on dyskinesia, tremor, and apathy without causing unwanted side effects. Of course the majority of PD patients can be sufficiently treated with a simple monopolar voltage or current stimulation. A robust comparison of the clinical effects achievable by single source systems (voltage or current) to the clinical effects achievable by current steering with multiple independent current sources has not been performed. However, when more contacts need to be activated (as in the case described) programming opportunities of conventional systems are limited to timing-based strategies (e.g., sequential interleaving of two fields) or a limited current-control mode. In sum, the effective degrees of freedom for DBS programming are higher with the Vercise™-system. If this will result in better performance of DBS in PD has to be shown in future studies.

Conflict of interest

All authors report no conflict of interest.

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