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Thalamic Deep Brain Stimulation and Gait in Orthostatic Tremor

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1. Research project: A. Conception, B. Organization, C. Execution;
2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
3. Manuscript: A. Writing of the first draft, B. Review and Critique.

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Keywords

Deep Brain Stimulation; Orthostatic Tremor; Gait Analysis; Vim

Orthostatic tremor (OT) is a rare hyperkinetic disorder of weight-bearing limbs, characterized by postural unsteadiness when standing and a high-frequency tremor of 13–18 Hz (1–3). Neuroimaging studies in OT have demonstrated a role of the cerebello-thalamo-cortical network (4). The role of thalamic connections, implicated in the response to ventral intermediate nucleus deep brain stimulation (Vim-DBS) in OT patients (5), remains unclear.

Eight years ago, we reported a 74-year-old woman after undergoing bilateral Vim-DBS for medication-resistant OT (5). She had failed clonazepam (10 mg/day), valproate (500 mg/day), and primidone (225 mg/day). Before surgery her upright stationary posture was <30 seconds and she required assistance for standing and walking. After Vim-DBS, the latency between rising and symptom onset increased from 30 seconds to 5 minutes, but moderate gait and postural disability persisted, gradually worsening over years despite numerous attempts of optimizing DBS settings. She reported imbalance and a tendency to fall backwards. The neurological examination revealed wide-based gait but nerve conduction studies did not show signs of peripheral neuropathy.

In order to examine the long-term efficacy of Vim-DBS in OT and study the heretofore-unexamined Vim-DBS efficacy on gait, we performed a gait analysis-assisted assessment of DBS settings (Supplementary Material). Spatio-temporal gait parameters, dynamic stability index, and coefficient of variation of step length and swing phase (6) were analyzed in three different conditions: 1) DBS-OFF; 2) DBS-ON at baseline (Left: contact 2–/case+, 3.9Volts, 90µsec, 185Hz; Right: contact 9–/case+, 3.9Volts, 90µsec, 185Hz); 3) and optimized DBS-ON.

The active contacts were confirmed (14.2 mm [left] and 12.0 mm [right] lateral to mid-commissural point; 7.2 mm [left] and 4.9 mm [right] anterior to posterior commissure, and 2.3 mm [left] and 0.3 mm [right] superior to anterior-posterior commissural plane), while a reduction of stimulation intensity (decreasing voltage by 0.3Volts and pulse width by 30µsec bilaterally) was found to be associated with objective and subjective gait improvements.

Both optimized and baseline DBS-ON conditions improved gait velocity and step length, reducing the spatial and temporal variability of gait when compared to DBS-OFF (Figure 1). However, the baseline DBS-ON condition, which resulted to be supra therapeutic, was associated with a worsening of dynamic balance in the medio-lateral and antero-posterior axes, as measured by step width and dynamic stability index.

These data suggest that Vim-DBS may exert a complex and multifaceted modulation of gait in OT, with two main stimulation-dependent outcomes: 1) improvement of OT symptoms, which may result in increased gait velocity and step length; and 2) potential induction of gait ataxia, which may result in increased stride width and time spent on double support.

The complexity of these Vim-DBS-mediated outcomes has been described in essential tremor (7), where the suppression of tremor usually correlates with an improvement of ataxic gait, while a supra-therapeutic stimulation may result in re-emergence of ataxia.

While these single-case observations need to be confirmed in larger studies, we suggest that the OT impairs gait in part by the persistence of high-frequency tremor on weight-bearing limbs during the single-support phase of walking (Figure 1). An integrated clinical/gait analysis approach may be necessary to assist the optimal programming of Vim-DBS stimulation parameters to effectively modulate the severity of OT symptoms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1. Changes in gait parameters according to Vim-DBS settings

Note the improvement in gait velocity (a), cadence (b), and step length (c) between DBS OFF and DBS ON, with a further amelioration with the optimization of stimulation parameters. The dynamic stability index (d) worsened between DBS OFF and DBS-ON-st, but it substantially improved after optimization of DBS settings (ON-opt). The variability (CV) of steps (e), as measured by the CV of swing time and step length, significantly improved in both DBS ON conditions. Stride width (f) significantly worsened between DBS OFF and suprathreshold DBS (ON-st), with a partial recovery after returned to optimized DBS settings (ON-opt).

Surface EMG recording of Tibialis Anterior during walking (g): the characteristic OT tremor activity at 15–16Hz alternatively switches from one weight-bearing limb to the other. The swing phase of gait lead to a brief, sudden disappearance of tremor that immediately reappears when the foot touches the soil.

DBS OFF: Deep brain stimulation turned OFF; DBS ON-st: Deep brain stimulation turned on with supra-threshold settings (Left Vim: contact 2–/case+, 3.9Volts, 90µsec, 185Hz; Right Vim: contact 9–/case+, 3.9Volts, 90µsec, 185Hz); DBS ON-opt: Deep brain stimulation turned on with optimized settings (Left Vim: contact 2–/case+, 3.6Volts, 60µsec, 185Hz; Right Vim: contact 9–/case+, 3.6Volts, 60µsec, 185Hz); CV: coefficient of variation