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Programming Deep Brain Stimulation for Tremor and Dystonia: The Toronto Western Hospital Algorithms

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A R T I C L E I N F O

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A B S T R A C T

Background: Deep brain stimulation (DBS) is an effective treatment for essential tremor (ET) and dystonia. After surgery, a number of extensive programming sessions are performed, mainly relying on neurologist's personal experience as no programming guidelines have been provided so far, with the exception of recommendations provided by groups of experts. Finally, fewer information is available for the management of DBS in ET and dystonia compared with Parkinson's disease.
Objective/hypothesis: Our aim is to review the literature on initial and follow-up DBS programming procedures for ET and dystonia and integrate the results with our current practice at Toronto Western Hospital (TWH) to develop standardized DBS programming protocols.
Methods: We conducted a literature search of PubMed from inception to July 2014 with the keywords "balance", "bradykinesia", "deep brain stimulation", "dysarthria", "dystonia", "gait disturbances", "initial programming", "loss of benefit", "micrographia", "speech", "speech difficulties" and "tremor". Seventy-six papers were considered for this review.
Results: Based on the literature review and our experience at TWH, we refined three algorithms for management of ET, including: (1) initial programming, (2) management of balance and speech issues and (3) loss of stimulation benefit. We also depicted algorithms for the management of dystonia, including: (1) initial programming and (2) management of stimulation-induced hypokinesia (shuffling gait, micrographia and speech impairment).
Conclusions: We propose five algorithms tailored to an individualized approach to managing ET and dystonia patients with DBS. We encourage the application of these algorithms to supplement current standards of care in established as well as new DBS centers to test the clinical usefulness of these algorithms in supplementing the current standards of care.

Introduction

Tremor is the most common movement disorder characterized by the involuntary and rhythmic muscle contraction of one or more body segments [1]. Essential tremor (ET), in particular, has an overall estimated prevalence of 4.6% among people over 65 years [2], with more than 50% of patients having a suboptimal control of their tremor with conventional drug treatments [3,4]. An alternative method of managing drug-resistant ET patients is deep brain stimulation (DBS) of the ventralis intermedius (Vim) nucleus of the thalamus. Vim DBS has demonstrated excellent outcomes and an acceptable adverse effect profile [5–7]; however, problems in balance and speech, especially following bilateral procedures, as well as decay of stimulation benefit over time in up to 73% of patients have been found [8,9]. With the exception of an expert-opinion paper on the initial programming and long-term management [8], no guidelines are available for the management of stimulation-induced side effects and long-term decay of benefit.

Abbreviations: CCS, current-constant stimulation; CT, computed tomography; DBS, deep brain stimulation; ET, essential tremor; GPi, globus pallidus pars interna; IPG, internal pulse generator; MICC, multiple independent current control; MRI, magnetic resonance imaging; MS, multiple sclerosis; PD, Parkinson's disease; TWH, Toronto Western Hospital; VCS, voltage-constant stimulation; Vim, ventralisintermedius nucleus of the thalamus; VPL, ventro-postero-lateral thalamic nucleus.

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Dystonia is a complex movement disorder characterized by the variable combination of sustained involuntary postures and more rapid movements that may occur in isolation or in combination with other neurological symptoms [10]. Surgery has completely revolutionized the management of dystonia [11] as DBS of the globus pallidus pars interna (GPi) is effective for the treatment of generalized, segmental and focal dystonia, although there is little evidence for its benefit in non-isolated dystonia [12]. Postoperative early management of patients with dystonia differs from that in patients with ET or Parkinson's disease (PD) due to delayed improvement of symptoms following initiation of DBS. Accordingly, optimization of DBS in dystonia may be time consuming for both the physician and the patient. Furthermore, GPi DBS may also induce a wide spectrum of side effects including slowness of fine movements as well as speech and gait difficulties [13].

With the exception of the recommendations provided by Movement Disorders Society task force for DBS, i.e., expert opinion papers [13,14], there are no formal guidelines for the postoperative management of dystonia patients, particularly with respect to the management of side effects.

The lack of systematic algorithms to guide programming causes inconsistent and inefficient stimulation adjustments, as well as numerous or unnecessary patients' visits [15]. These issues compel us to find ways to improve the efficiency of programming sessions in ET and dystonia, aiming at ameliorating the quality of care for DBS patients. In order to develop standardized protocols and algorithms, we present the results of a review of the available literature on the initial and follow-up DBS programming as well as our practice at Toronto Western Hospital (TWH).

Methods

We conducted a review on the following topics: 1) initial programming for ET and dystonia; and 2) follow-up stimulation adjustments for ET (addressing balance and speech impairment as well as decay of stimulation benefit) and dystonia (addressing micrographia and gait and speech impairment). Multiple searches of the literature on PubMed in English language from inception to July 2014 were undertaken using the following keywords: "balance", "bradykinesia", "deep brain stimulation", "dysarthria", "dystonia", "gait disturbances", "initial programming", "loss of benefit", "micrographia", "speech", "speech difficulties", and "tremor". A total of 179 papers were retrieved. Additional articles were also recovered from recent reviews and reference lists of relevant publications. In total, 76 papers were taken into account for this review after excluding those not focused on movement disorders, preclinical studies and duplicated data. Results from the studies related to ET and dystonia and considered to build the algorithms are summarized in Table 1.

Essential tremor

Initial programming

Available data and management

Studies evaluating the effect of different stimulation parameters in ET showed that tremor control is usually achieved by increasing the amplitude to 2 V or 3 V and is further improved by 30% with longer pulse widths (90–120 µsec); the frequency-response curve shows an inverse linear relationship between tremor magnitude and frequency between 45 and 100 Hz and a flat floor between 130 and 185 Hz [16–19]. In addition, monopolar stimulation provides a stronger effect than bipolar stimulation [16].

The main goal of the first programming visit after the surgery is to determine the amplitude threshold for clinical benefits and side effects (i.e., the therapeutic window) for each of the electrode contacts [8]. There is debate on the timing of first programming visit [8] and current practices among centers vary. For instance, stimulation initiation has been reported the day after [6] or 4–10 weeks after surgery [15]. Similarly to PD, the improvement in tremor after surgery due to the insertional effect (i.e., the transient effect produced by the mechanical placement of the electrode) along with the different electrode impedances due to the insertion trauma-related anti-inflammatory response may lead to an incorrect estimation of thresholds when programming is performed soon after surgery. The latter may have important clinical implications when using voltage-constant stimulation (VCS) since the current delivered to the tissue is inversely proportional to the electrode impedance [34]. A recent study showed a continuous decrease of therapeutic impedance within 10 years in PD patients with subthalamic nucleus (STN) DBS [35]. Clinicians should be aware of such reduction over time, since declining impedance goes along with a substantial enlargement of the local volume of tissue activated when VCS is applied. As such, during programming it may be useful to establish a security distance (e.g., of about 0,3V) below the threshold for permanent side effects (i.e., muscle spasms) to avoid their reappearance in case of spontaneous variation of impedance. On the other hand, current-constant stimulation (CCS), which dynamically adjusts the current to adapt to changes in impedances of the tissue-electrode interface, might offer the advantage of a more stable stimulation when the programming is performed soon after the surgery [36].

The clinical effect of any programming algorithm is closely related to the electrode location. Thus, checking electrodes placement postoperatively using either approved magnetic resonance imaging (MRI) or stereotactic computed tomography (CT) protocols is strongly advised since it may be helpful to both point to which contact may be the most effective and envisage the source of potential side effects [37]. Post-operative neuroimaging is also helpful in ruling out potential surgical complications (e.g., bleedings or infections). Before starting the programming, the impedance for each of available contacts using standard stimulation parameters is recorded [38] to rule out hardware problems and to be used as a reference when troubleshooting future technical issues [39]. Then, the therapeutic window for each contact is determined by means of stepwise increase of amplitude (0.5V) using a monopolar configuration [i.e., the internal pulse generator (IPG) is the anode and the contact is the cathode] and keeping both the pulse width (60 µsec) and the frequency constant (130 Hz) [8,39]. Amplitude is further increased to determine the threshold for side effects, which can be *somatosensorial* (paresthesia, taste changes) or *motor* (muscle spasms and cerebellar signs like limb ataxia, cerebellar gait, postural instability and dysarthria).

Ideally, initial programming should take place in the off drug condition to gain a better understanding of stimulation efficacy [8]. However, tremor patients undergoing DBS have usually minimal improvement from medications. The target to determine the benefit of stimulation is the action tremor (postural and kinetic) in the contralateral upper limb. Postural tremor can be assessed with the arms outstretched or elbow bent (wing-beating position). Kinetic tremor can be assessed with the finger-to-nose maneuver or asking the patient to draw a spiral, drink water from a cup or pour water from a glass to another one [8], and is the principal target of stimulation adjustments. Since tremor may spontaneously fluctuate and is further influenced by fatigue or anxiety, it is important to try to keep these assessments as consistent as possible and switch the stimulation off regularly to monitor the baseline tremor. Likewise, it is also useful to keep the patient blinded to the stimulation amplitude and compare settings, switching from one to the other or repetitively ramp up specifically at the border of maximum benefit/occurrence of side effects to get a sharp border [8].