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Current DBS programming

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ABSTRACT

Deep brain stimulation is an established treatment option for various neurological and psychiatric disorders. Throughout its journey as a confirmed long-term efficacious therapeutic option for movement disorders such as Parkinson' s disease, essential tremor and dystonia over the last three decades, programming strategies continuously improved to due to the development of DBS technologies. The aim of this review is to take a glance into current programming strategies in the era of movement disorders particularly with an updated review of the literature for current and emerging DBS technologies.

1. Introduction

Deep brain stimulation (DBS) is a well-established treatment option in movement disorders such as Parkinson' s disease (PD), essential tremor (ET), and dystonia as well other treatment resistant neurological and psychiatric disorders that basically allows neuromodulation of the neuronal circuits in the targeted areas [1]. Owing to the improvement of DBS technology in the recent years with the development of segmented lead systems and new battery designs such as longer lasting and rechargeable batteries, it is crucial to understand the stimulation principles and algorithms improving the therapeutic window with increased number of possible combinations of programming options which made DBS programming more complex and time-consuming [2].

Since DBS programming is a long journey starting from the initial monopolar screening and basic adjustment of stimulation to advanced programming techniques, in case of any need in due course of the disease following DBS surgery, the aim of this review is to briefly summarize the fundamentals of DBS programming by deepening into the current DBS programming strategies from a general aspect and the movement disorders perspective mainly in patients with PD, ET and dystonia.

2. Fundamentals of DBS programming

Starting from the first practice of DBS technology in the late 1900 s in the treatment of PD coming to today's technology, DBS systems expanded with the improvement of hardware and software developments in its use worldwide. Currently, the components of the DBS system include the lead and the electrodes, extension cables and the implantable pulse generator (IPG) which allows the clinician to programme the settings via a clinician programmer. There is also a recharger for the rechargeable devices. The lead system is composed of electrodes whether in the standard ring mode or designed with segmented technology in the newer systems. Current DBS systems allow the clinicians to modulate the neuronal network by delivering electrical stimulation via the quadripolar conventional leads or segmented directional leads in the selected targets by adjusting the stimulation parameters to improve the respective symptoms of the movement disorders and other neurological conditions that DBS is pointed as a treatment option. In the era of movement disorders, the established targets are subthalamic nucleus (STN), globus pallidus internus (GPi), ventral intermediate nucleus (Vim) for patients with PD, in which the latter two areas are the most common targets for dystonia and ET, as welli respectively [1, 3, 4–6].

2.1. Stimulation parameters

The key to effective DBS is to control the activated neural elements in which action potentials are generated. In clinical settings, it corresponds to the modification of the electrode configuration and electrical parameters used to deliver stimulation by designating the active negative electrode (cathode), and positive electrode (anode). The adjustable stimulation parameters are amplitude, pulse with, and rate. ***Amplitude,*** is the main parameter to adjust the intensity of the stimulation, with an estimated diffusion of the electrical current approximately 3 mm radially from the active electrode. Measures the electrical current in milliamps (mA). The force that drives the electrons out of the cathode is the electromotive force and is measured in volts (V). Since the conventional

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devices works with ***constant voltage*** which means the amplitude of stimulation is controlled by adjusting voltage, novel ones can also be utilized in the constant current mode. Amplitude can be regulated by adjusting the current which allows clinicians to set the amplitude at the rates of 0–25.5 mA [1,7,8,9]. ***Pulse width*** refers to the duration of each stimulus measured by microseconds (μsec). ***Rate*** corresponds to the number of pulses per second measured by Herz (Hz). It is important to keep in mind that the efficacy of DBS is based on high frequency stimulation. and the use of frequencies lower than 50 Hz in STN has shown to be ineffective significantly on the motor symptoms of patients with PD [6,7,9,10].

2.2. Electrode configurations and standard DBS programming

The basic approach to DBS programming starts with the adjustment of the stimulation parameters throughout the designed electrode configurations by positive and negative electrode selections. Thus, the volume of tissue activated in the selected target can be shaped via "monopolar", "bipolar", and more complex stimulations to improve the symptoms of the respected movement disorders or other neurological diseases in the targeted area [1–3].

2.2.1. Monopolar and bipolar stimulation

Monopolar stimulation, so-called unipolar, is the standard initial configuration of the electrodes where the IPG is designated as the anode, and the cathode is an electrode on the lead. Creating a more rounded stimulation around the cathode, it creates a spherical stimulation area. When two or more on the lead are designated as the negative electrodes, the configurations are called as *double* and *triple* monopolar stimulation, respectively However, bipolar stimulation corresponds to the electrode configurations in which both positive and negative electrodes are designated on the lead [11,12].

Bipolar stimulation creates a more elongated but constricted field between the two selected electrodes with more focused stimulation that limits the spread of the field and thus reduce possible side effects that would emerge from the stimulation of adjacent structures to the intended target. Since monopolar stimulation, produces a larger volume of tissue activation (VTA) than bipolar stimulation, it is more likely to exert lower stimulation thresholds for both symptomatic efficacy and potential side effects [9,11].

2.2.2. Different parameter adjustments in special occasions

Though standard parameter settings generally known as 60 μsec, 130 Hz, and 1–4 V or mA for rate, frequency, and amplitude in all well-known targets of STN, GP, and Vim for movement disorders [7,10], different parameters can be used for different targets as summarized in Table 1 (Table 1) [9].

Varying frequency and PW settings are shown to be effective in patients with PD suffering from axial problems such as gait and speech in particular [6,13].

Although high frequency DBS is well-known to be effective in improving the cardinal symptoms of PD such as tremor, bradykinesia, and rigidity [6,14], There are several studies suggesting the variable high frequency stimulation of STN-DBS as well as lower frequency (< 100 Hz) stimulation, can improve speech and gait, but can but may worsen the tremor in PD [15]. High frequency DBS is an established treatment option for essential tremor as well. However, in case of gait and balance problems in thalamic DBS for essential tremor, lowering the frequency may improve the gait and balance problems following Vim-DBS [16].

Furthermore, it is also reported that shorter PW of 30 μsec is more effective on speech in patients with PD implanted with STN-DBS, when compared with standard PW setting of 60 μsec without worsening motor symptoms in patients with PD [17,18].

Table 1
Different parameter settings for different targets.

Parameter	STN	GPi	Vim
Amplitude (V/mA)	1-4	1-4	1-4
Pulse width (μsec)	30-90	60-120	60-120
Frequency (Hz)	90-185	60-185	130-185

3. Advanced DBS programming

3.1. Temporal fractionation

This is programming technique involves using two separate programs in an alternating fashion through a single DBS electrode. Temporal fractionation allows clinicians to adjust these two programs with different polarities, amplitudes, and PWs, but the frequency must be at 125 Hz in maximum. Thus, it is possible to stimulate different areas at the target simultaneously in an alternating fashion, So-called "interleaving stimulation" in general since it is introduced by Medtronic, this technology is also available in Abbott devices and known as "multis-stim set" [19,20]. This advanced programming can be beneficial in challenging patients with tremor dominant PD and ET with co-existing diagnosis, or refractory dystonia, or in patients with insufficient response to standard programming in whom axial symptoms worsen while others improve [21,22].

3.2. Directional stimulation

As the development of segmented electrodes in recent DBS technology, it is possible to configure the shape of VTA by steering the current at the stimulation contact to provide the desired effect while avoiding the current spreading to the adjacent structures and causing side-effects. So-called "directional steering", this programming is advantageous when smaller with complex features areas are targeted [23].

By increasing the thresholds for the occurrence of stimulation -induced side-effects, directional stimulation allows clinicians to manage troubleshooting symptoms (axial symptoms, speech problems, etc.) without unwanted effects by redirecting the field of stimulation away from the unintended adjacent structures. Moreover, it also gives an opportunity to explore the anatomical origin of the observed clinical effects with more insights in the pathophysiology of movement and cognition. [24,25]. Karl and colleagues reported that better symptom control, reduction in side-effects or combination of both were the reasons for using directional stimulation in pw PD. In addition to these factors in patients with PD, the reduction in the battery consumption, and the improvement in the therapeutic window percentage was also important to choose directional steering in patients with ET [26].

3.3. Adaptive DBS

Adaptive DBS (aDBS) is a closed-loop model which works through the delivery of the stimulation at a at a certain point in time in precise amount when the clinical symptoms of the patient is sensed through the feedback variables via brain signals. This brand-new technology works through three components; *a sensing module* that perceives the variable, *a control module* that regulates the stimulation parameters due to the feedback variables via specific algorhythms to stimulate when only necessary, and *a stimulation module* which is responsible for the delivery of the stimulation [27]. Since the technology in aDBS tends to improve, the first authorized DBS device is Percept PC in the Medtronic system, which delivers the stimulation due to the fluctuations in LFPs in the intended target [28].

The mechanism of aDBS, the feedback variables are sensed in the form of spontaneous electrophysiological activity recorded in the brain, known as *local field potentials (LFPs)*. In patients with PD, these LFPs in the elevated beta band with the frequency of 13–35 Hz in STN or GPi are shown to be associated with bradykinesia and rigidity, rather than

tremor. Relevantly, the beta power in the off state in pw PD are show have a negative correlation with the unified Parkinson' s disease rating scale motor scores in patients with PD [29]. Though aDBS has shown to elicit similar motor improvement with the conventional DBS, it is reported to have an advantage of less energy consumption with lesser side-effect profile with an individualized therapy fashion [27,30–32].

4. Conclusion

As the improvement of DBS technologies over the years, with the enhanced understanding of neuroanatomy and neurophysiology, programming strategies tend to increase as well with more complexity allowing to optimize and personalize DBS therapy for patients. Though the landscape of current programming strategies with advanced options may be overwhelming and complex, they also give the clinicians a chance to achieve most effective and beneficial outcomes to manage the symptomatology of the relevant diseases. However, the future of DBS with the emerging new technologies is promising as the development of neuroimaging, neurophysiology, as well as the electrode designs in the improvement of the DBS outcomes.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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