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Directional Deep Brain Stimulation

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Abstract

Innovations in the field of deep brain stimulation (DBS) are introduced recently, considering that the fundamentals of DBS remained significantly unchanged over 25 years. Technological advances involve not only DBS hardware but also new patterns of stimulation, brain imaging and pathophysiological pathways. Every effort is done to obtain the best outcome for the patient with the lower adverse effects rates.

Keywords: Deep brain stimulation; Neural activation; Parkinson's disease; Current controlled stimulation; Current steering

Introduction

The basic goal of DBS is to stimulate targeted brain regions eliciting a therapeutic response while minimizing stimulation of non-target brain regions (responsible for side effects). Stimulation is delivered by an implanted pulse generator (IPG) through annular electrode contacts implanted in subcortical structures. Direct stimulation of the target may be hindered by inaccurate electrode placement or by limitations in the IPG/electrode to generate the necessary electric field (generally in a spherical mode until recently) for optimal therapeutic benefit. Traditional DBS technology relies on voltage-controlled stimulation with a single source; however, recent engineering advances are providing current-controlled devices with multiple independent sources. These new stimulators deliver constant current to the brain tissue, irrespective of impedance changes that occur around the electrode, and enable more specific steering of current towards targeted regions of interest. Subcortical structures can shift by an average 2 mm (4 mm in rare occasions) over the course of a DBS surgery. While small, these deviations in electrode placement may limit the ability of the stimulators to selectively activate the target brain region [1].

DBS lead design

There are many novel electrode contact designs, arising from the need to obtain an electric field conformed to the variable anatomy in the brain target of interest.

The "Vercise" lead (Boston Scientific) is realized with a multi-lumen structure with the best of an eight contact span (15.5 mm) and spacing (0.5 mm) which may lead to improved durability and longevity of the entire system, thus minimizing the risk of replacement procedures. Its use allows independent current settings for each of the eight contact of the lead and stimulation with pulse width below 60 μs, offering independent frequency adjustments in separate areas along a single lead [2].

The "DirectSTIM" (Aleva Neurotherapeutics) is a novel quadripolar lead of four rings. Each ring consists of three independent compartments with its own orientation (0°, 120°, 240°) allowing independent stimulation in a given direction, so-called current-steering.

The "SureSTIM" (Sapiens) consists of 32 contacts distributed around the lead that may be activated group-wise. This system allows for true sculpting of the field of stimulation to maximise symptom relief and avoid side effects.

The "Infinity" (St. Jude Medical) is a cylindric quadripolar lead with the middle two contacts sectorised into three independent and adjustable directional electrodes [3].

New patterns of stimulation

The progress in lead technology is due by necessity to stimulate optimally the targets without spread to adjacent structures. From a general point of view, nuclei for DBS like subthalamic nucleus (STN) and ventral intermediate nucleus (VIM) are difficult to target and anatomical variability is to be considered on MRI to prevent stimulation side effects [4,5]. The need to deliver stimulation in a tailored fashion is the basis of development of a new generation of leads and stimulation mode.

Interleaving stimulation mode

A new IPG from Medtronic, FDA- and CE-approved, called ACTIVA PC or ACTIVA RC, is able to deliver independent and alternated stimulation of two contacts in the quadripolar DBS lead with different values for voltage and pulse width but with the same frequency. In this way structures adjacent to the target may be stimulated with different amplitudes when classical modalities are no efficient on the symptoms. This technique of neuromodulation has been applied in the subthalamic nucleus for Parkinson's disease (PD) [6], in the globus pallidus internus (GPi) for dystonia [7] and in the STN and the ventrolateral thalamus for PD and essential tremor [8]. These experiences, however, are not conclusive for objective clinical benefits superior to the classical method of stimulation. The disadvantages related to the interleaved stimulation mode are the premature battery depletion and inability to change the frequency of stimulation.

Multi-independent current controlled stimulation mode

In 2014 CE approved a new DBS lead and device from Boston Scientific named VERCISE with the ability to target multiple nuclei

along the trajectory by multiple source constant current. Lead is made of eight contacts spanning 15.5 mm. The rationale of this kind of stimulation consists of independent current setting (amplitude, pulse width and frequency) for each of eight contacts of the lead referred to as" multi-independent current controlled" (MICC) stimulation mode. Another advantage of this new system is the possibility to stimulate with pulse widths below 60 μs, not available with other devices. There are, in fact, two multicentre studies that evaluated the effects of short pulse widths (<60 μs) in deep brain stimulation of the subthalamic nucleus for Parkinson's disease [9-11] and in a case of phantom limb pain [12]. Disadvantages are the impossibility for true field shaping and true selective directional steering and the MRI-incompatibility of the system.

Adaptive/close-loop stimulation

Traditional DBS systems - called open loop DBS (OLDBS) - stimulate continuously and the parameters are set according to the variable clinical state of patients, especially during fluctuations in patients with movement disorders, or according to their cognitive/psychological states. Adaptive DBS (aDBS) consists of closed-loop (CLDBS), real-time changing of stimulation parameters according to the patient's clinical state. The advantages of this kind of stimulation could be the reduced battery usage and less expensive therapy in a personalised fashion. A closed loop deep brain stimulation (CLDBS) system automatically adjusts stimulation parameters by the brain response in real time. A challenge with CLDBS is to achieve an optimal control of the symptoms modulating stimulation on the variations of an internal or external biomarker in a biofeedback loop. One of these biomarkers is represented by the oscillations in the beta frequency range (around 20 Hz), a product of synchronisation across neurons of the cortical-basal ganglia circuitry. For example, in patients with advanced Parkinson's disease, when medications are working, beta oscillations of STN disappear, but when akinesia and rigidity are predominant, beta oscillations are present in LFP recordings. CLDBS may deliver stimulation "on demand", only when system performance is compromised by pathologically exaggerated synchronization in the beta band [13]. Little et al, using a brain-computer interface able to detect the beta activity from the STN of PD patients, measured a significant improvement in UPDRS with adaptive DBS as opposed to continuous DBS with half the energy expenditure required in standard DBS [14]. Alternative neurochemical feedback for close-loop stimulation involves detection of neurotransmitters like dopamine and serotonin in animal models, revealing an important step toward the development of a closed-loop DBS system for human application [15].

Advances in IPG technology

The problems related to the IPGs are the relatively short duration (5-7 years), the need to surgical replacement with a greater risk of infections and the design that may often create discomfort to the patient. To resolve these issues, Medtronic introduced in 2008 the first rechargeable DBS device, so-called Activa RC, with a lifespan improved until 9 years. However, the patient every week has to charge the system to prevent depletion. After the third depletion of battery the IPG becomes unresponsive and it has to be surgically replace. To avoid this problem, Boston Scientific introduced in the Vercise IPG a new technology, named Zero-Volt, to guarantee no damages of the battery in case of depletion too. As to the design, Brio by St. Jude Medical represents the smallest rechargeable IPG with a volume of 18 cc. To offer a better cosmetic result, the presence of an enhanced antenna allows the IPG implant deeper up to 2.5 cm but a complete depletion of battery is often the main cause of surgical reposition.

Advances in imaging

The new instruments of brain imaging in view of DBS are represented by using diffusion tensor imaging (DTI) to better visualize targets and to suggest potential "new" targets for trials in DBS or the novel WAIR sequence to target VIM in indistinguishable cases [16,17]. Tractography helps in targeting somatosensory fibres in DBS to visualize the laterality of the thalamus and to avoid placement of the lead in the internal capsule. High Tesla MRI is the future to visualize basal ganglia, discriminating each component of tfhe nuclei. Structural imaging should be used not only preoperatively but also during the procedure, in the refinement phase of DBS targeting. The possibility to perform DBS surgery in a dedicated MRI suite allows immediate verification and real time correction of the lead with safety and efficacy [18].

Conclusions

DBS novel technologies are under development to provide clinicians with new tools making targeting, programming and overall management easier. These technologies vary in focus but converge to provide safer and more accurate positioning of electrodes with a subsequent optimization of therapeutic benefit. Future advances and improvements in neuroimaging are likely to personalize approaches for surgical treatment such as tailored DBS based on symptoms, potential for progression, and co-morbidities. DBS procedures continue to be refined, in order to reduce errors and side effects, improving patient comfort and optimizing successful outcomes.

References

1. Chaturvedi A, Foutz TJ, McIntyre CC (2012) Current steering to activate targeted neural pathways during deep brain stimulation of the subthalamic region. Brain Stimul 5: 369-377.
2. Hariz M (2014) Deep brain stimulation: new techniques. Parkinsonism Relat Disord 20: 192-196.
3. Ughratdar I, Samuel M, Ashkan K (2015) Technological Advances in deep brain stimulation. J Parkinsons Dis 5: 483-496.
4. Richter EO, Hoque T, Halliday W, Lozano AM, Saint-Cyr JA (2004) Determining the position and size of the subthalamic nucleus based on magnetic resonance imaging results in patients with advanced Parkinson disease. J Neurosurg 100: 541-546.
5. Daniluk S, Davies GK, Ellias SA, Novak P, Nazzaro JM (2010) Assessment of the variability in the anatomical position and size of the subthalamic nucleus among patients with advanced Parkinson's disease using magnetic resonance imaging. Acta Neurochir (Wien) 152: 201-210.
6. Wojtecki L, Vesper J, Schnitzler A (2011) Interleaving programming of subthalamic deep brain stimulation to reduce side effects with good motor outcome in a patient with Parkinson's disease. Parkinsonism Relat Disord: 17: 293-294.
7. Kovacs N, Janszky J, Nagy F, Balàs I (2012) Changing to interleaving stimulation might improve dystonia in cases not responding to pallidal stimulation. Mov Disord 27: 163-165.
8. Baumann CR, Imbach LL, Baumann-Vogel H, Uhl M, SarntheinJ, et al. (2012) Interleaving deep brain stimulation for a patient with both Parkinson's disease and essential tremor. Mov Disord 27: 1700-1701.
9. Steigerwald F, Reese R, Matthies C, Volkmann J (2013) Increased Therapeutic Window with Shorter Pulse Widths (< 60 μs) of Deep Brain Stimulation in Parkinson's Disease. Mov Disord 28: 1281.
10. Carcieri S, Zhao Y, Van Dyck N, Volkmann J (2013) Study design of a double-blind, randomized, controlled trial (RCT) evaluating the effects of short pulse width in deep brain stimulation (DBS) of the subthalamic nucleus for Parkinson's disease (CUSTOM-DBS). Mov Disord 28: 438.

11. Timmermann L, Jain R, Zhao Y, Brucke T, Seijo F, et al. (2013) VANTAGE trial: a prospective, multi-center trial evaluating deep brain stimulation with a new multiple-source, constant-current rechargeable system (VERCISE) in Parkinson's disease. Neurology 28: 173.
12. Sims-Williams HP, Selbi WR, Javed S, Pickering AE, Patel NK (2013) Two birds, one stone: single electrode dual target stimulation for the treatment of phantom limb pain. Stereotact Funct Neurosurg 91: 264.
13. Little S, Brown P (2014) The functional role of beta oscillations in Parkinson's disease. Parkinsonism Relat Disord, 20: 544-548.
14. Little S, Pogosyan A, Neal S, Zavala B, Zrinzo L, et al., (2013) Adaptive deep brain stimulation in advanced Parkinson disease. Ann Neurol 74: 449-457.
15. Chang SY, Kimble CJ, Kim I, Paek SB, Kressin KR, et al. (2013) Development of the Mayo Investigational Neuromodulation Control System: toward a close-loop electrochemical feedback system for deep brain stimulation. J Neurosurg 119: 1556-1565.
16. Vassal F, Coste J, Derost P, Mendes V, Gabrillargues J, et al. (2012) Direct stereotactic targeting of the ventrointermediate nucleus of the thalamus based on anatomic 1.5-T MRI mapping with a white matter attenuated inversion recovery (WAIR) sequence. Brain Stimul 5: 625-633.
17. Miocinovic S, Parent M, Butson CR, Hahn PJ, Russo GS, et al. (2006) Computational analysis of subthalamic nucleus and lenticular fasciculus activation during therapeutic deep brain stimulation. J Neurophysiol 96: 1569-1580.
18. Zrinzo L, Yoshida F, Hariz M, Thronton J, Foltynie T, et al. (2011) Clinical safety of brain magnetic resonance imaging with implanted deep brain stimulation hardware: large case series and review of the literature. World Neurosurg 76: 164-172.