Parkinsonism and Related Disorders 58 (2019) 85–86

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Correspondence

Hybrid deep brain stimulation system to manage stimulation-induced side effects in essential tremor patients

ARTICLE INFO

Keywords:
Pulse width
Therapeutic window
Essential tremor
Medtronic
Boston scientific
Hybrid system

Deep brain stimulation (DBS) of the ventral intermedius thalamic nucleus (VIM) is an established treatment for essential tremor (ET) [1]. Stimulation-related improvement is thought to be caused by stimulation of small axons within the target whereas side effects are caused by stimulation of large, more distant, fibers [2].

Chronaxie, a measure of the excitability of neural elements, reflects the interdependence of stimulus amplitude and pulse width (PW). Large axons have a lower chronaxie (i.e. more excitability) than small axons. Therefore, it is postulated that pulse width (PW) reduction widens the therapeutic window of DBS by preventing higher amplitudes from depolarizing larger axons [3].

We report two ET patients in whom the use of short PW resulted in an increased therapeutic window. Patients initially carried Medtronic (Minneapolis, USA) implantable pulse generators (IPG) but in spite of multiple adjustments they had suboptimal therapeutic stimulation due to side effects. Given the theoretical effect of PW lower than 60μs (not possible with Medtronic IPG), patients consented to undergo an IPG change to a Boston Scientific IPG (Marlborough, USA). A Vercise M8 Adapter Kit was used to connect the new IPG with existing Medtronic electrodes 3387.

Patients were assessed before and after IPG change using Fahn-Tolosa-Marin tremor rating scale of the stimulated side; side effects were assessed with visual analogue scale, videotaped motor examination and gait analysis.

Both patients signed written consent to being videotaped for publication. The study (retrospective chart review for case report) was approved by our local ERB.

Patient 1 is a 73-year-old woman with ET for 35 years who underwent DBS 2.5 years ago with moderate improvement of tremor. DBS was not optimized due to paraesthesia and muscle pulling of the right leg, affecting gait at 3V/60μs/130Hz (corresponding to a current of 3.7mA and charge density [4] of 2.66 μC/cm^2/phase) (Fig. 1). After switching to the Boston Scientific IPG, the same contact was identified as the best therapeutic stimulation. Paraesthesia was reported at 3.6mA/60μs/130Hz. With 5.5mA/30μs/130Hz a better tremor improvement was obtained without paraesthesia and mild pulling of the leg (Fig. 1, Video 1). Three months later, she retained ongoing benefit and stimulation was increased to 3.0mA/30μs/220Hz (charge density of 1.49 μC/cm^2/phase) with further improvement of tremor and tolerable side effects.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.parkreldis.2018.07.013.

Patient 2 is a 74-year-old man with ET for 23 years who underwent DBS 17 years ago with marked initial benefit. However, over time he developed dysarthria and hemi-body paraesthesia with increasing stimulation resulting in suboptimal tremor control (3.8V/60μs/180Hz, corresponding to a current of 4.76 mA and charge density of 4.76 μC/cm^2/phase). After switching to the Boston Scientific IPG, tremor and speech improvement with only mild paraesthesia was observed at 8.5mA/30μs/180Hz (charge density of 4.23 μC/cm^2/phase; Fig. 1, Video 2).

Supplementary video related to this article can be found at https://doi.org/10.1016/j.parkreldis.2018.07.013

Our report supports the safety and feasibility of using the Vercise M8 Adapter Kit in order to connect Boston Scientific IPGs to Medtronic electrodes. Both patients tolerated the procedure without any adverse event.

Furthermore, this preliminary clinical experience also confirmed the theoretical utility of low PW in improving tremor control without stimulation-induced side effects. In addition, since a lower charge density was seen after the IPG changes we can also hypothesize a longer battery life with the new settings. Recently, two acute double-blinded studies in Parkinson disease patients confirmed a widened therapeutic window with lower PW stimulation [4,5]. Both studies also showed reduced energy consumption based on the calculation of the total charge delivered per pulse. Similar findings were reported in three ET patients in another study [3].

The main limitation of our study is the open-label nature of

Abbreviations: FTM-TRS, Fahn-Tolosa-Marin tremor rating scale (right side of body); VAS, Visual Analogue Scale; IPG, Implantable pulse generator; DBS, Deep brain stimulation

https://doi.org/10.1016/j.parkreldis.2018.07.013
Received 31 May 2018; Received in revised form 10 July 2018; Accepted 22 July 2018

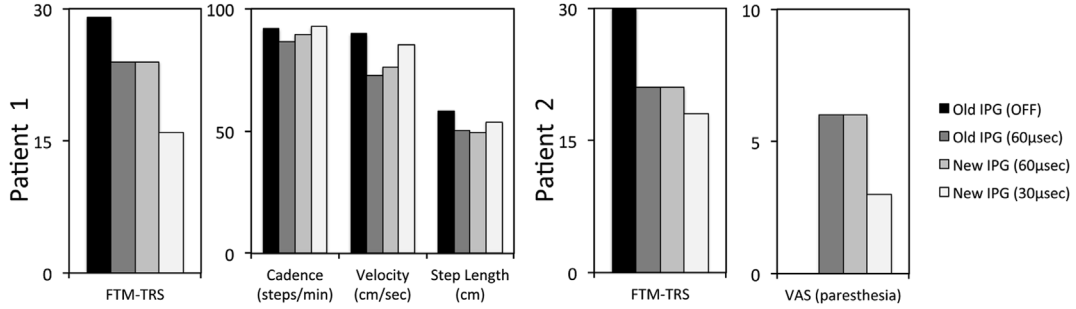

Fig. 1. Patient 1. FTM-TRS (left panel) and gait analysis (right panel, by Zeno Walkway, Prokinetics) during four conditions: before IPG change with DBS off and on (Medtronic, 3.0V/60µs/130Hz, equivalent current: 3.7mA, charge density: 2.66 µC/cm^2/phase) and after IPG change (Boston Scientific) with settings inducing best tremor control with minimal side effects (3.0mA/30µs/220Hz, charge density: 1.49 µC/cm^2/phase).
Patient 2. FTM-TRS (left panel) and VAS assessing para
esthesia (right panel) during four conditions: before IPG change with DBS off and on (Medtronic, 3.8V/60µs/180Hz, equivalent current: 4.8mA, charge density: 4.76 µC/cm^2/phase) and after IPG change (Boston Scientific) with settings inducing best tremor control with minimal side effects (8.5mA/30µs/180Hz, charge density: 4.23 µC/cm^2/phase).

assessment, requiring further controlled studies exploring the long-term effect of shortened PW stimulation. Nevertheless, we have reported the safety and benefits of using the Vercise M8 Adapter Kit in creating a hybrid system when a short PW is needed, thus avoiding the need for major revision surgery.

Authors' roles

DS: execution of the study, analysis and interpretation of the data, writing the first draft.

AML: interpretation of the data, critiques and final approval of the version to be published.

AF: conceptualization of the study, interpretation of the data, revising the manuscript and final approval of the version to be published.

Author disclosures

AML and AF are in the advisory board of Boston Scientific and received honoraria and research support by the same company.

Financial disclosures (past 12 months)

DS has nothings to disclose.

AML is consultant for Medtronic, Abbott, Boston Scientific and Functional Neuromodulation.

AF has received grant support from the University of Toronto, the McLaughlin Centre and the Michael J. Fox Foundation; he received speaking honoraria from UCB pharma, Medtronic, Boston Scientific, Abbvie, Novartis, Chiesi pharmaceutical, Ipsen and TEVA; he is in an advisory board for Abbvie and Ipsen and provided consultancies for UCB pharma, Medtronic, Boston Scientific, and Abbvie.

Acknowledgements

None.

References

[1] A. Fasano, G. Deuschl, Therapeutic advances in tremor, Mov. Disord. 30 (2015) 1557–1565.
[2] M. Reich, F. Steigerwald, A. Sawalhe, R. Reese, K. Gunalan, S. Johannes, R. Nickl, C. Matthies, C.C. McIntyre, VolkmannJ. Short pulse width widens the therapeutic window of subthalamic neurostimulation, Ann. Clin. Translat. Neurol. 2 (4) (2015) 427–432, https://doi.org/10.1002/acn3.168.
[3] U. Akbar, R.S. Raike, N. Hack, C.W. Hess, J. Skinner, D. Martinez-Ramirez, S. DeJesus, M.S. Okun, Randomized, blinded pilot testing of nonconventional stimulation patterns and shapes in Parkinson's disease and essential tremor: evidence for further evaluating narrow and biphasic pulses, Neuromodulation 19 (2016) 343–356, https://doi.org/10.1111/ner.12397.
[4] W. Bouthour, J. Wegrzyk, S. Momjian, J. Peron, V. Fleury, E. Tomkova Chaoui, J. Horvath, C. Boex, C. Luscher, P.R. Burkhard, P. Krack, A. Zacharia, Short pulse width in subthalamic stimulation in Parkinson's disease: a randomized, double-blind study, Mov. Disord. 33 (1) (2018 Jan) 169–173, https://doi.org/10.1002/mds.27265.
[5] F. Steigerwald, L. Timmermann, A. Kühn, A. Schnitzler, M.M. Reich, A.D. Kirsch, M.T. Barbe, V. Visser-Vandewalle, J. Hübl, C. van Riesen, S.J. Groiss, A.S. Moldovan, S. Lin, S. Carcieri, L. Manola, J. Volkmann, Pulse duration settings in subthalamic stimulation for Parkinson disease, Mov. Disord. 33 (1) (2018 Jan) 165–169, https://doi.org/10.1002/mds.27238.

Derrick Soh[a], Andres M. Lozano[b,c], Alfonso Fasano[a,c,*]
[a] *Morton and Gloria Shulman Movement Disorders Centre and the Edmond J. Safra Program in Parkinson's Disease, Toronto Western Hospital, UHN, Toronto, Ontario, Canada*
[b] *Division of Neurosurgery, Department of Surgery, Toronto Western Hospital, University of Toronto, Canada*
[c] *Krembil Research Institute, Toronto, Ontario, Canada*
E-mail addresses: alfonso.fasano@uhn.ca, alfonso.fasano@gmail.com (A. Fasano)

[*] Corresponding author. University of Toronto, Krembil Research Institute, Movement Disorders Centre, Toronto Western Hospital, 399 Bathurst St, 7McL412, Toronto, ON, M5T 2S8, Canada.