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Reply to letter to the editor "Adaptive DBS in Parkinson's disease: Headlines, perspectives and challenges"

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We thank the Editor for the opportunity to reply to the Letter to the Editor by Pina-Fuentes et al. [1], concerning our recent article on neural closed loop or adaptive DBS (aDBS) [2]. Our study adds to a growing body of scientific evidence that aDBS in patients with Parkinson's disease (PD) is safe, tolerable, efficacious, and efficient. These promising attributes have been demonstrated in studies when aDBS was performed in the acute setting, days after implantation of DBS leads [3–8], and in the chronic setting, after years of clinical DBS (cDBS) [2,9–11]. Such studies have been reported in a single person and in larger cohorts, using either externalized leads and stimulators or implanted leads and neurostimulators. Similar results have been seen using single and dual threshold control policy algorithms. We foresee that the research in aDBS will accelerate as neurostimulator systems that can concurrently sense and stimulate become more widely available, and we agree with the authors that the use of quantitative metrics of motor behavior allows finer resolution of outcomes than clinical rating scales.

Studies to date have emphasized different priorities: some studies, using externalized systems, tested the superiority of aDBS over cDBS regarding motor behavior, or adverse effects [2–4]; some have tested the ability of aDBS to adapt to concurrent use of medication [6–8] and others tested safety, tolerability and feasibility of chronically implanted systems using either kinematic or neural control variables [2,9,11]. Among all the studies a common finding has been efficacy of aDBS compared to no DBS, and greater efficiency compared to cDBS.

Despite the encouraging results of early feasibility studies in the acute or chronic setting and in single cases or larger cohorts, much is yet to be determined regarding optimizing aDBS for motor and non-motor features of PD and other neuropsychiatric diseases. A greater understanding of neural and behavioral signals obtained during activities of daily living, will provide functionally relevant control variables for aDBS and will be the infrastructure for future aDBS systems. Preliminary investigations of these control variables are already taking the field beyond using the average power of the resting state beta band to drive aDBS [12]. Technological advances incorporated into the new investigative aDBS system (Summit™ RC + S, Medtronic Inc, FDA IDE required), make it possible to use temporal features of the filtered local field potential (LFP) signal as a neural control variable (such as beta burst duration). It will be possible to adapt both frequency and intensity in control policy algorithms, and to perform bilateral, independently controlled aDBS over longer periods of time in freely moving PD people, to address critical needs, such as freezing of gait.

Pina-Fuentes et al. suggest that a limitation of the studies of aDBS, published to date, is that the LFP recordings are made from electrodes (contacts) distant from that used to stimulate. We would clarify that in our aDBS protocols the recording electrodes are the ones immediately dorsal and ventral to the stimulating electrode and the recording is in bipolar mode (the potential difference between the pair of electrodes is recorded), which means that the LFP recorded from this bipolar pair includes and surround the active electrode rather than being distant from it. We would suggest that obtaining LFP feedback from a larger volume of the target structure surrounding the stimulation electrode may be helpful, especially as many optimized cDBS configurations require stimulation through two of three active electrodes. Further technological advances in directional leads that are capable of concurrent sensing and stimulation, will allow more research into the use of more localized sensing and stimulation fields in different regions of the target structure.

While it is encouraging to observe improved efficacy of short periods of aDBS to cDBS, most large outcome studies of cDBS have demonstrated remarkable efficacy regarding motor outcomes over many years, and we do not think this should be the sole focus of implementing aDBS at this early stage We suggest that there is a lot of work still to be done before we can determine whether aDBS has superior efficacy over current cDBS paradigms and whether this is in the degree of motor improvement or in the sustainability of movement, the adaptation to concurrent medical therapy or changing states of activity, and/or the adverse effect profile.

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Conflicts of interest

Dr. Bronte-Stewart is a member of a clinical advisory board from Medtronic. Ms. Velisar has no conflicts of interest.

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References

[1] Piña-Fuentes D, van Dijk JMC MB. Adaptive DBS in Parkinson's disease: headlines, perspectives and challenges. Brain Stimul 2019 May 8. https://doi.org/10.1016/j.brs.2019.04.014. pii: S1935-861X(19)30206-2.

[2] Velisar A, Syrkin-Nikolau J, Blumenfeld Z, Trager MH, Afzal MF, Prabhakar V, et al. Dual threshold neural closed loop deep brain stimulation in Parkinson disease patients. Brain Stimul 2019. https://doi.org/10.1016/j.brs.2019.02.020.

[3] Little S, Pogosyan A, Neal S, Zavala B, Zrinzo L, Hariz M, et al. Adaptive deep brain stimulation in advanced Parkinson disease. Ann Neurol 2013;74:449–57. https://doi.org/10.1002/ana.23951.

[4] Little S, Tripoliti E, Beudel M, Pogosyan A, Cagnan H, Herz D, et al. Adaptive deep brain stimulation for Parkinson's disease demonstrates reduced speech side effects compared to conventional stimulation in the acute setting. J Neurol Neurosurg Psychiatry 2016;87:1388–9. https://doi.org/10.1136/jnnp-2016-313518.

[5] Little S, Beudel M, Zrinzo L, Foltynie T, Limousin P, Hariz M, et al. Bilateral adaptive deep brain stimulation is effective in Parkinson's disease. J Neurol Neurosurg Psychiatry 2016;87:717–21. https://doi.org/10.1136/jnnp-2015-310972.

[6] Rosa M, Arlotti M, Ardolino G, Cogiamanian F, Marceglia S, Di Fonzo A, et al. Adaptive deep brain stimulation in a freely moving parkinsonian patient. Mov Disord 2015;30:1003–5. https://doi.org/10.1002/mds.26241.

[7] Rosa M, Arlotti M, Marceglia S, Cogiamanian F, Ardolino G, Fonzo AD, et al. Adaptive deep brain stimulation controls levodopa-induced side effects in Parkinsonian patients: DBS Controls Levodopa-Induced side effects. Mov Disord 2017;32:628–9. https://doi.org/10.1002/mds.26953.

[8] Arlotti M, Marceglia S, Foffani G, Volkmann J, Lozano AM, Moro E, et al. Eight-hours adaptive deep brain stimulation in patients with Parkinson disease. Neurology 2018;90:e971–6. https://doi.org/10.1212/WNL.0000000000005121.

[9] Malekmohammadi M, Herron J, Velisar A, Blumenfeld Z, Trager MH, Chizeck HJ, et al. Kinematic adaptive deep brain stimulation for resting tremor in Parkinson's disease: letters: new observations. Mov Disord 2016;31:426–8. https://doi.org/10.1002/mds.26482.

[10] Piña-Fuentes D, Little S, Oterdoom M, Neal S, Pogosyan A, Tijssen MAJ, van Laar T, Brown P, van Dijk JMC, Beudel M. Adaptive DBS in a Parkinson's patient with chronically implanted DBS: a proof of principle. Mov Disord 2017 Aug;32(8):1253–4. https://doi.org/10.1002/mds.26959. Epub 2017 Jun 7.

[11] Swann NC, de Hemptinne C, Thompson MC, Miocinovic S, Miller AM, Gilron R, Ostrem JL, Chizeck HJ, Starr PA. Adaptive deep brain stimulation for Parkinson's disease using motor cortex sensing. J Neural Eng 2018 Aug;15(4). https://doi.org/10.1088/1741-2552/aabc9b. 046006.

[12] Anidi C, O'Day JJ, Anderson RW, Afzal MF, Syrkin-Nikolau J, Velisar A, et al. Neuromodulation targets pathological not physiological beta bursts during gait in Parkinson's disease. Neurobiol Dis 2018;120:107–17. https://doi.org/10.1016/j.nbd.2018.09.004.

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