Dear Editor,

The recent article by Tandra et al. reports crucial findings focusing on an interesting issue of the impact of deep brain stimulation (DBS) frequency on gait in Parkinson’s disease (PD) subjects. Remarkably, contrasting with the classical data remarking on the benefit of low-frequency stimulation (STIM) on axial symptoms, they found that most patients had demonstrated significant improvement in gait at a single frequency differing between patients. We think that there may be some points to be further deliberated for a better understanding of this crucial report.

In a prospective study by Khoo et al., the authors demonstrated that 60 Hz STIM provided superior efficacy over 130 Hz in improving the total unified Parkinson’s disease rating scale (UPDRS) motor score, axial motor signs including gait and freezing of gait (FOG). However, the optimal contacts for 60 Hz STIM were found to be situated more ventrally than those for 130 Hz STIM. Such that, they emphasized that optimizing the active contacts with respect to frequency is very important in augmenting the beneficial effect of 60 Hz STIM. However, no compelling explanation was proposed to explain their observation. In another study, Ricchi et al. also demonstrated a significant improvement of gait after switching the STIM frequency from 130 to 80 Hz. However, at the same time, they had adapted the voltage to maintain the same total delivered energy that might be efficient in the results. Remarkably, despite the immediate improvement provided after the frequency change, the improvements were no longer detectable at follow-up evaluations 1, 5, and 15 months later. The other study also referred by the authors detected that FOG episodes were significantly lower 1, 5, and 15 months later.

The observation of differing optimal contact for low-frequency STIM might rather be related to the increment in the STIM voltages or other parameters to adapt the same total energy. The observation of differing optimal contact for low-frequency STIM is also an intriguing point that needs to be clarified in this regard. More complicating this issue, a recent study also demonstrated that optimal frequency varied between patients, and it was also associated with electrode contact site and severity of axial symptoms.

Investigating the clinical phenotypes of the patients with distinct optimal STIM frequencies in detail and comparing some specific features differing between groups may also provide interesting perspectives. Tandra et al. demonstrate that patients best at 90 and 180 Hz STIM do not show difference in terms of age, disease duration, UPDRS scores, voltage amplitudes. However, we wonder if they might also include the intergroup comparisons of some clinical features such as “on” medication FOG, postural instability, speech, or other axial symptoms that are rather not responsive to DBS STIM which might also provide critical contributions.

Another point is that the effects of the STIM on axial symptoms including gait and FOG occur the latest in comparison to other motor signs such as tremor, rigidity, or bradykinesia. Such that, the onset of the effect of DBS therapy on gait may take hours to weeks. Therefore, the 20 min interval between the distinct STIM frequencies may not be sufficient for the evaluation.
of the clear effect of the new frequency on axial symptoms. We know that the negative effect of the DBS STIM on axial symptoms generally occurs in the long term. Such that, there is evidence of increased gait asymmetry and discoordination of gait after STN–DBS in the chronic phase of the STIM particularly in the postural instability and gait disorder subtype.[8] Although the pathophysiology of the possible disturbance of gait after STN–DBS is unclear, it is rather explained in the setting of STIM-induced network dysfunctions in essential tremor subjects with thalamic DBS.[9] Some authors have found evidence regarding the reversible nature of gait disturbance after DBS in patients with essential tremors and they hypothesized that this may be a maladaptive response to neurostimulation of the subthalamic area.[9] However, the possible contribution of the irreversible neuroanatomical and pathological changes in DBS-related gait disturbance is unknown and remains to be elucidated. Therefore, the optimal DBS adjustments to provide the best outcome in the long term may also constitute another critical issue to be investigated.

In conclusion, the results of Tandra et al.,[1] demonstrating the variability of the best STIM frequency between patients for the optimal treatment of gait and FOG, are critical. The results of this study in light of the related literature suggest that the clinical approach to gait disorders in PD subjects on DBS therapy is strictly a complicated issue and should vary individually depending on the heterogeneous pathology. Future studies are warranted to clarify also the influence of parameters other than frequency; including voltage, pulse width, and optimal contact. The results of these studies to address these discussions may provide critical contributions to the clinical grounds.

Abbreviations
STN–DBS = Subthalamic nucleus–deep brain stimulation, UPDRS = Unified Parkinson’s disease rating scale, FOG = freez ing of gait, STIM = Stimulation.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. Tandra S, Kandadai RM, Peddisetty RP, Babu KJ, Prabha TS, Jaboon SA, et al. The effect of dual tasking and deep brain stimulation frequency parameters on gait in advanced Parkinson’s disease. Ann Indian Acad Neurol 2020;23:308-12.
2. Khoo HM, Kishima H, Hosomi K, Maruo T, Tani N, Oshino S, et al. Low-frequency subthalamic nucleus stimulation in Parkinson’s disease: A randomized clinical trial. Mov Disord 2014;29:270-4.
3. Moreau C, Defevre L, Destee A, Bleuse S, Clement F, Blatt JL, et al. STN-DBS frequency effects on freezing of gait in advanced Parkinson disease. Neurology 2008;71:80-4.
4. Ricchi V, Zibetti M, Angrisano S, Merola A, Arduino N, Artusi CA, et al. Transient effects of 80 Hz stimulation on gait in STN DBS treated PD patients: A 15 months follow-up study. Brain Stimul 2012;5:588-92.
5. Phibbs FT, Arborgast PG, Davis TL. 60-Hz frequency effect on gait in Parkinson’s disease with subthalamic nucleus deep brain stimulation. Neuromodulation 2014;17:717-20.
6. Di Giulio I, Kalliolia E, Georgiev D, Peters AL, Voicey DC, Akram H, et al. Chronic subthalamic nucleus stimulation in Parkinson’s disease: Optimal frequency for gait depends on stimulation site and axial symptoms. Front Neurol 2019;10:29.
7. Herrington TM, Cheng JJ, Eskandar EN. Mechanisms of deep brain stimulation. J Neurophysiol 2016;115:19-38.
8. Ravi DK, Baumann CR, Bernasconi E, Gwerder M, Ignasiak NK, Uh M, et al. Does subthalamic deep brain stimulation impact asymmetry and dyscoordination of gait in Parkinson’s disease? Neurorehabil Neural Repair 2021;35:1020-9.
9. Reich MM, Brumberg J, Pozzi NG, Marotta G, Roothans J, Astrom M, et al. Progressive gait ataxia following deep brain stimulation for essential tremor: Adverse effect or lack of efficacy? Brain 2016;139:2948-56.

Submitted: 22-Mar-2022 Revised: 24-Mar-2022 Accepted: 28-Mar-2022 Published: 08-Jun-2022

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

DOI: 10.4103/aiian.aiian_270_22