Author’s response to reviews

Title: Physical Therapy and Deep Brain Stimulation in Parkinson Disease: Protocol for a Pilot Randomized Controlled Trial

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Reviewer #1: This manuscript describes the protocol for pilot study examining the safety, feasibility, and efficacy of an 8-week physical therapy intervention compared to standard of care for individuals with Parkinson's Disease receiving Subthalamic nucleus deep brain stimulation (STN-DBS). Overall, the manuscript is well-written and focuses on an important area of study. However, there are a number of issues that, if addressed, would greatly strengthen this manuscript:

We thank Reviewer 1 for their thoughtful comments. We believe that addressing the reviewer’s comments has significantly improved the manuscript. Our detailed responses are italicized below.

1. Page 4, line 16-17 - there appears to be some words missing from this sentence "Postural and may be detrimental to overall function…..

Response: Thank you for pointing this out. We believe removing this sentence will ease reading and does not take away from the message that postural instability is a problem for people with DBS. Later in the paragraph, we mention that postural instability and gait difficulty may increase risk for falls, which clarifies our point that postural instability and gait problems may be detrimental to function.

2. On page 6, authors indicate "Furthermore, the standard of care for STN-DBS does not include PT". What is the evidence of this? Where is the citation for this statement?
Response: Thank you for your comment. This statement was based on knowledge of the current clinical practice paradigm in people with PD. The current standard of care for PT in people with PD is to wait until gait and balance problems develop or until the person is falling to refer to PT. Nijkrake and colleagues (Nijkrake MJ et al., Mov Disord. 2009) indicate that allied healthcare, which includes PT is not often utilized among people with PD suggesting lack of uniformity in the referral process. We also looked at the “Guide to Deep Brain Stimulation Therapy” published by the National Parkinson’s Foundation. This document, developed for patients, indicates people with DBS can resume exercise soon after surgery, but there is no indication that they will be referred to a physical therapist for specialized treatment. We have added this citation (NPF Guide) to the manuscript.

3. The methods and design section is very thin on recruitment and randomization procedures. Authors are advised to consult the Consort Extension checklist for pilot and feasibility studies (http://www.equator-network.org/reporting-guidelines/consort-2010-statement-extension-to-randomised-pilot-and-feasibility-trials/) to ensure sufficient details for this pilot study are reported.

Response: Thank you for this comment. We added information about the randomization procedures for this study in the first paragraph of the Methods/Design section. We believe this increases transparency and will facilitate reproducibility.

4. It is not clear if Intervention participants will receive the Standard of care plus the Physical therapy intervention or just the physical therapy intervention. I'm assuming the former, and if so, authors should be explicit about this.

Response: Both groups will receive the standard of care, which we considered adjustment of medication and stimulation parameters on an as needed basis. We now clarify this within the manuscript.

5. It is not clear how authors will determine from this pilot study whether there is sufficient evidence to move forward with a larger scale trial in terms of safety and feasibility outcomes. What is the specific % of sessions/exercises that should be completed across intervention participants which would indicate sufficient feasibility to move forward with a larger scale RCT? How many adverse events will determine that the intervention is sufficiently safe to move forward, given that there is not enough power to determine statistical significance for adverse events?

Response: Thank you for raising this point. We hypothesize that participants will complete at least 80% of prescribed intervention sessions. This value for adherence to the intervention is comparable to what has been found in other studies. A citation for a review paper that discusses this was added. With respect to adverse events, we have clarified how these will be assessed within the manuscript. We will monitor serious adverse events and non-serious adverse events. We will determine whether these are directly or not directly related to the intervention. We set
the threshold for not moving on with a larger trial if there is greater than 1 serious adverse event that is directly related to the intervention. We chose greater than 1 because it is possible that 1 serious adverse event may be due to chance, but more than that would be unacceptable.

6. What statistic are authors using for effect size? What effect size calculations — please provide more detail regarding how this was determined.

Response: We used Cohen’s f for the effect size. 0.25 is classified as a medium effect size (Cohen, J. (1969). Statistical power analysis for the behavioural sciences. New York: Academic Press. – p 348). We arbitrarily chose this effect size given the lack of preliminary data on the efficacy of PT for people with DBS. We felt at least a medium effect size for the efficacy measures would offer preliminary support to move on to a larger trial.