Author's response to reviews

Title: Screening for Parkinson's disease with response time batteries: A pilot study

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Dr. Louis notes that the diagnosis of Parkinson's disease can be based on imaging studies (e.g. positron emission tomography studies) under some circumstances, and so the statement that "the diagnosis of Parkinson's disease (PD) is entirely clinical" is not entirely accurate. I have added references to this literature in the first paragraph of the paper, and softened my original assertion.

Both Dr. Siderowf and Dr. Louis note that there is an established literature on the use of test batteries that include motor tasks, particularly the PD battery described by Montgomery et al. I have included references to this PD battery in the introduction, and in the discussion section - with particular attention to the sensitivity and specificity of the motor subtest of this battery. Given that the simple RT task described in the present manuscript demonstrates higher sensitivity and specificity than the motor subtest described by Montgomery et al., I believe that this underscores the importance of the data in our study.

Dr. Siderowf notes that there is an extensive literature on the use of reaction time tasks in PD. Rather than reviewing this literature (which almost universally supports a significant RT/MT difference between PD patients and controls), I have included a reference to an excellent review article by Gauntlett-Gilbert et al. within the introduction.

I have removed the positive and negative predictive values from the manuscript, in response to Dr. Louis' concerns about their utility (given the prevalence of the clinical outcome variable).

Dr. Siderowf notes that the sensitivity and specificity of the task presented in this paper is "not very good". I disagree with this comment - the sensitivity presented in this paper is 90% in the cross-validated sample, which is at least 20% better than the cross-validated sensitivity reported for the aggregate score on the Montgomery et al. PD battery (the sensitivity and specificity of their motor subtest is substantially lower), and the cross-validated specificity is 90%, which is equal to the specificity reported by Montgomery et al. I have, however, added comments to the discussion section that bear on Dr. Siderowf's concerns regarding the samples chosen for the paper (i.e. the fact that differential diagnostic conclusions may not be drawn from this sample).

In response to Dr. Louis' suggestion that the descriptive data for the sample might be presented in a more complete fashion, area graphs are presented for the UPDRS motor subscore of the UPDRS in each sample. This should give the reader a clearer impression of the sample composition on this measure. No statistics on disease duration were collected for these samples, as the UPDRS was considered more appropriate for assessing motor symptom severity. Similarly, participants were not evaluated with any measures that assessed the extent to which their PD was "tremor-dominant", and so it is not possible to speak to the extent to which the battery would be applicable to this population.

With regards to concerns about the approximate matching that was performed on the data, the individuals in these samples were randomly sampled from available participants within our clinic. IQ estimates, MMSE scores, and ages were assessed when admitting individuals to the study. This has been clarified in the method section.

Dr. Siderowf makes the excellent observation that differences between cued and uncued aspects of response time tasks might distinguish between PD patients and controls. As it happens, the effect size for this group difference is not sufficient to add meaningfully to the prediction equation (i.e. above and beyond
the group difference in speed).

Finally, Dr. Louis notes that it is unlikely that primary care physicians will use this battery, given its reliance on a special setup. While it is true that this may impact upon the speed with which motor speed batteries might be adopted in medical practices, it is also the case that previously validated motor function tests (e.g. Montgomery et al.) have utilized similarly complex equipment. As technology (both chronometric and computer) advances in this regard, it is likely that devices will become smaller and less expensive, and will allow this sort of testing to become more widespread. This is an excellent point, however, and I have added this to the discussion section.

I would like to thank both reviewers for their insightful comments, as their suggestions have strengthened this paper tremendously.