Peer Review File

Article information: https://dx.doi.org/10.21037/mhealth-21-16

Reviewer Comments

Comment 1:

The authors introduce an exciting web-based application for the acquisition and analysis of Archimedes spiral drawings on a computer screen. The authors provide enough data to demonstrate that this approach is entirely feasible for distinguishing normal and abnormal drawings. However, this application is far from validated in the traditional sense. The following important issues must be addressed in future studies.

The authors show that their approach is capable of distinguishing normal adults from abnormal adults. However, the data came from healthy volunteers and from computer simulations. Many types of movement disorders can produce abnormal spirals. These movement disorders include tremor, dystonia, myoclonus, chorea, ataxia, parkinsonism, corticospinal disease, and neuromuscular disease. The authors' methods need to be validated for each type of movement disorder.

Reply 1: We thank these reviewers for their kind reading of our text and their constructive criticism regarding the work left to do to encourage mainstream use of this application. We agree that the app requires further validation, specifically in measurement of its performance in several different patient populations.

Changes in the text: We have amended the Introduction (Line 73) and Discussion (Line 293) to emphasize that further validation of this application is required.

Comment 2: Distinguishing normal from abnormal is important, but many clinicians use spirography to assess clinical change with treatment or disease progression. Sensitivity to change will undoubtedly vary depending upon the spiral metrics and task protocol. This too needs to be examined.

Reply 2: We thank the reviewers for this keen insight. Disease progression or changes in treatment will certainly affect performance on spirography tasks. Future experiments will aim to understand how the application's sensitivity and specificity are affected by these variables. In the application and text's current, we hope that we have provided a starting point worthy of discussion in the public forum.

Changes in the text: We have amended our Introduction (Line 74) and Discussion (Line 295) to explain our intention to investigate this point further.

Comment 3: The authors used spiral metrics that have been previously published. The authors should explain why they did not examine spectral arc length, log dimensionless jerk, and spectral analysis for smoothness and rhythmicity.[1] The best spiral metrics

will likely depend on the type of movement disorder. Ultimately, the authors will need to compare their analysis results with expert clinical ratings.

Reply 3: We thank the reviewers for their reference and excellent suggestion. We read the referenced work with great interest and also refer to earlier work by the same group [3]. In our reading of the work, we understand these to be 3 powerful metrics for assessment of movement smoothness and rhythmicity. Their calculation and interpretation are optimally achieved through devices that provide both accelerometry and spatial coordinates through a gyroscope or similar tool. We note that the current application is unable to provide gyroscopic data, owing to its intended use when the iPad or digital tablet is stationary and fixed in position.

We note further 2 main limitations with regarding to movement smoothness analysis as discussed in [3], namely: 1) dependent on task ability and 2) dependent on the task itself. We tested our application in 20 total putatively healthy subjects whose ability to perform the task was observed after an instruction period. Further, none of these subjects have been diagnosed with a disorder, neurologic or otherwise, that may have impeded their ability to perform the task. Thus, the first major consideration with smoothness analysis – ability – would not be an issue for our task. Unfortunately, the second major limitation would apply in our case. Given that smoothness calculations are task-dependent, we cannot rule out the possibility that our use of different instructions for drawing the Archimedes spiral may affect the calculated metrics. Such technical bias would be enhanced in downstream analysis of principal components and distance between individual spiral metrics represented as vectors. As a result, we chose to proceed with calculation of first and second order smoothness metrics, both of which have been discussed extensively in earlier work for the analysis of Archimedes spirals. We were unable to confidently incorporate SPARC or log dimensionless jerk without prior knowledge of their use in the Archimedes spiral task. We chose instead to proceed only with metrics that had already been validated clinically in use with the Archimedes spiral task.

Changes in the text: None.

Comment 4: It is also important to consider the effect of normal aging and development. Tasks such as spiral drawing improve considerably with normal development,[2] and a decline in spirography with “normal aging” must also be examined.

Reply 4: We thank the reviewers for this keen insight. We have included this point in our discussion of the work, as also discussed above.

Changes in the text: We have amended our Introduction (Line 74) and Discussion (Line 295) to explain our intention to investigate this point further.

Comment 5: Finally, it would be helpful to clinicians if some jargon were removed or

defined. In particular, I am not sure what the authors mean by “digital workflow”, and it is also not clear what the authors mean by “technical replicate spirals”.

Reply 5: We thank the reviewer for this insight and apologize for the confusion. We understand how use of these terms may muddy our message.

Changes in the text: To communicate our intentions more clearly, we have replaced “digital workflow” with “tool and set of instructions for its use” (Line 68). We have also replaced “technical replicate spirals” with just “spirals”, as we hope the further description of the two tasks makes clear that each user drew five spirals per task.

References

[1] A. Melendez-Calderon, C. Shirota, S. Balasubramanian, Estimating Movement Smoothness From Inertial Measurement Units, Front Bioeng Biotechnol 8 (2020) 558771, https://doi.org/10.3389/fbioe.2020.558771.
[2] T.F. Lawerman, R. Brandsma, H. Burger, J.G.M. Burgerhof, D.A. Sival, A. the Childhood, S. Cerebellar Group of the European Pediatric Neurology, Age-related reference values for the pediatric Scale for Assessment and Rating of Ataxia: a multicentre study, Dev. Med. Child Neurol. 59 (10) (2017) 1077-1082, https://doi.org/10.1111/dmcn.13507.
[3] Balasubramanian, S., Melendez-Calderon, A., Roby-Brami, A. *et al.* On the analysis of movement smoothness. *J NeuroEngineering Rehabil* **12,** 112 (2015). https://doi.org/10.1186/s12984-015-0090-9.