Charco Neurotech CUE[1] User Testing Report

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Testing period: July – August 2020
Charco Neurotech

The aim of this study was to test the pre-production prototype of CUE[1] using Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) section III motor score, Timed Up and Go (TuG) test, and Timed Tapping test in an open-label non-clinical study. Using MDS-UPDRS section III as the primary outcome, the results indicated a positive response across all participants, with a mean improvement of 9 points. Additionally, the average reduction in time to complete tasks was 19% and 15% in the TuG and Timed Tapping test respectively. Questionnaire feedback from participants was also positive, indicating feasibility and acceptability of the device, and no adverse events were recorded.

1. Introduction

Charco Neurotech have now developed a professionally-made pre-production prototype which we wanted to trial with volunteers who live with Parkinson's disease. Since the last testing period, we have become certified to carry out MDS-UPDRS testing, the gold standard for quantifying Parkinson's disease symptoms where a qualified assessor subjectively scores different motor movements. This second round of testing had three major motivations; firstly, to identify whether the latest iteration also provided the benefits we saw with earlier prototypes; secondly, to assess the effect of the device by the gold standard of symptom assessment in Parkinson's disease, the MDS-UPDRS scale; and thirdly, to get further feedback and insight on the design, functionality and ease-of-use from PwP.

2. Methods

14 participants volunteered for this study. This consisted of 6 females and 8 males, all of whom have been diagnosed with Parkinson's disease. There was a range in the severity of their progression, with every participant between 1 and 4 on the Hoen & Yahr stage. All participants were examined and tested using the MDS-UPDRS section III (motor performance), a Timed Up and Go test, and a Timed Tapping test. These were performed at baseline (no intervention) and with the CUE[1] device activated (intervention) in various orders. With 4 out of 14 participants, multiple interventions were conducted for different stimulation intensities and carrier wave frequencies to provide personalised optimisation of the device. The examiners were non-blinded. The Timed Tapping task consisted of alternate tapping between two marked points for 60 seconds, 30cm apart, using the dominant index finger. The Timed Up & Go (TuG) tests were carried out from sitting with a 3-metre walk to and from a marker and a return to sitting. A feedback questionnaire was completed after the tasks, which contained sections on effectiveness, usability, and risk evaluation.

3. Results

3.1 MDS-UPDRS

12 participants underwent MDS-UPDRS assessment, and hence 24 assessments were taken. **A mean average of 9.3 points improvement was seen across the participants**. 3 of the 12 participants improved by more than 15 points, with the largest improvement being 19, and every participant improved by at least 3 points. See Figure 1 for each participant's difference with the intervention and Appendix A.1 for a table of scores for baseline vs. intervention.

The greatest differences were seen in UPDRS measures 3.4a, 3.6b, 3.14*, 3.16b, 3.17a, and 3.18, corresponding to Finger Tapping (Right Hand), Pronation-supination (Left Hand), global spontaneity*, Kinetic Tremor (Left Hand), Rest Tremor Amplitude (Right Hand), and constancy of rest tremor respectively (* marks the greatest difference).

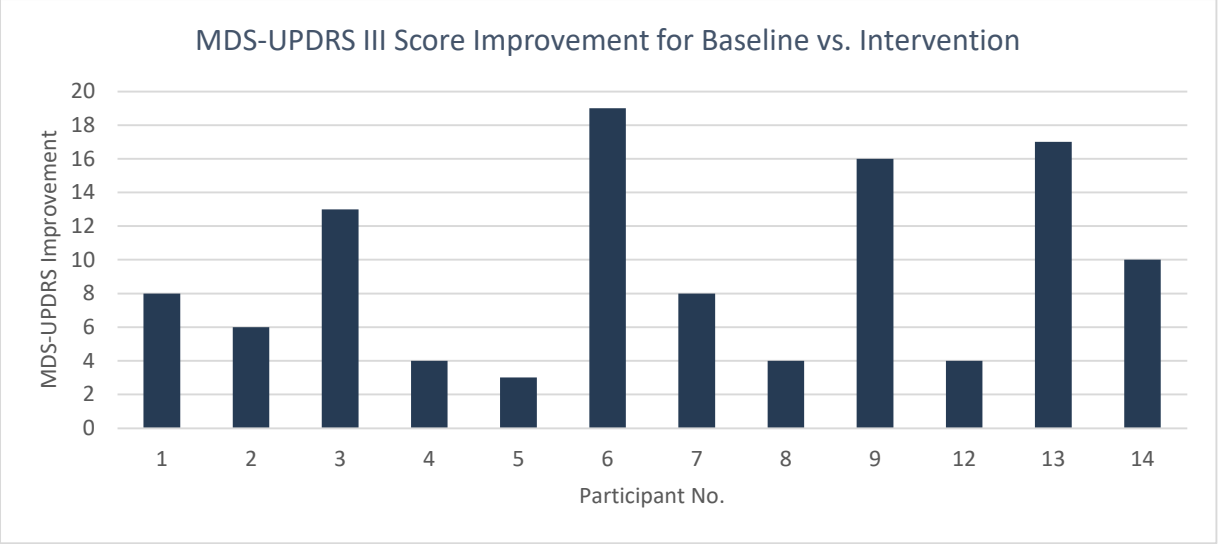

Figure 1. The improvement of MDS-UPDRS III score for each participant for when CUE[1] was activated vs. at baseline level.

3.2 Tasks

14 participants completed the TuG 3m task and 13 participants completed the Timed Tapping task for at least two conditions: the control and the intervention of CUE[1]. With 4 participants, multiple interventions were conducted for different stimulation intensities and carrier wave frequencies to find what worked best for them.

3.2.1 Timed Tapping

3 participants conducted the experiment for both hands, while the remaining 10 used their dominant hand only. **An average improvement of 19% was seen in the tapping task**. 1 out of 13 participants performed worse with the stimulation, with a decrease of 8% performance on the task, while the remaining 12 demonstrated improvement. The greatest improvement was 47.1%, and 9 of the 16 interventions (including the second hands from 3 of the participants) showed improvement above 10%. For the four participants who experimented with multiple vibrational settings, the average improvement from their optimal performance was 31.2%. Each participant's optimal performance was with a 1 second square wave condition. See Figure 2 for each participant's performance.

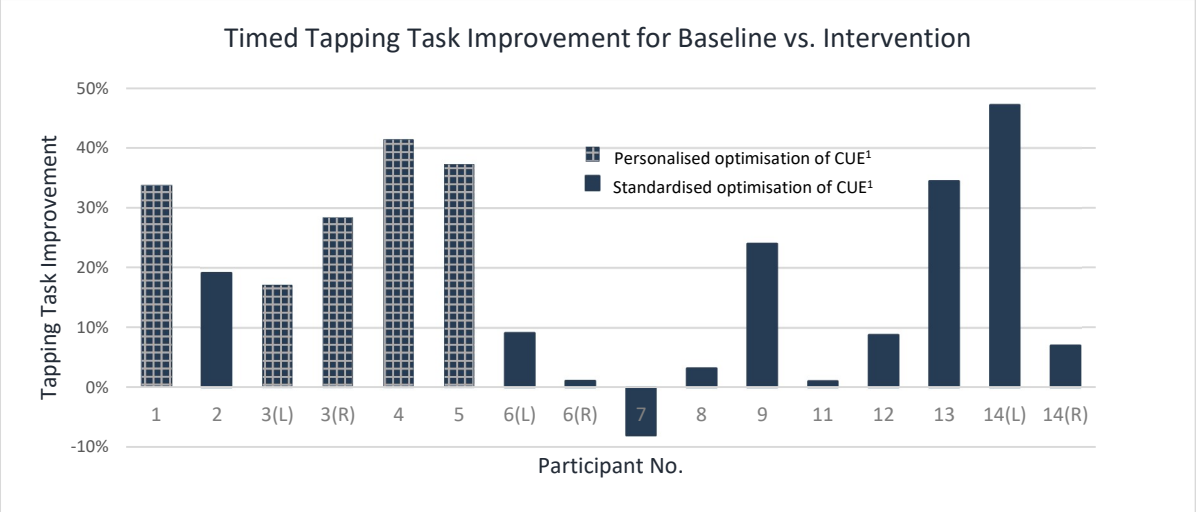

Figure 2. The improvement for the Timed Tapping task for each participant for when CUE[1] was activated vs. at baseline level.

3.2.2 TuG 3m

Three participants demonstrated freeze-of-gait episodes while the TuG 3m task was being conducted. Their task improvement data was not included in the average. **An average improvement of 15% was seen in the TuG-3m task**. 1 out of the 11 participants performed worse with the stimulation, with a slower time by 9%, while the remaining 10 demonstrated improvement. All four participants that experimented with multiple vibrational settings- 1, 3, 4 and 5- demonstrated an increase in performance for the 1-second square wave condition versus the 'optimised' condition. The greatest improvement was 30.7%, and 7 of the 11 participants showed improvement above 10%. See Figure 3 for each participant's performance.

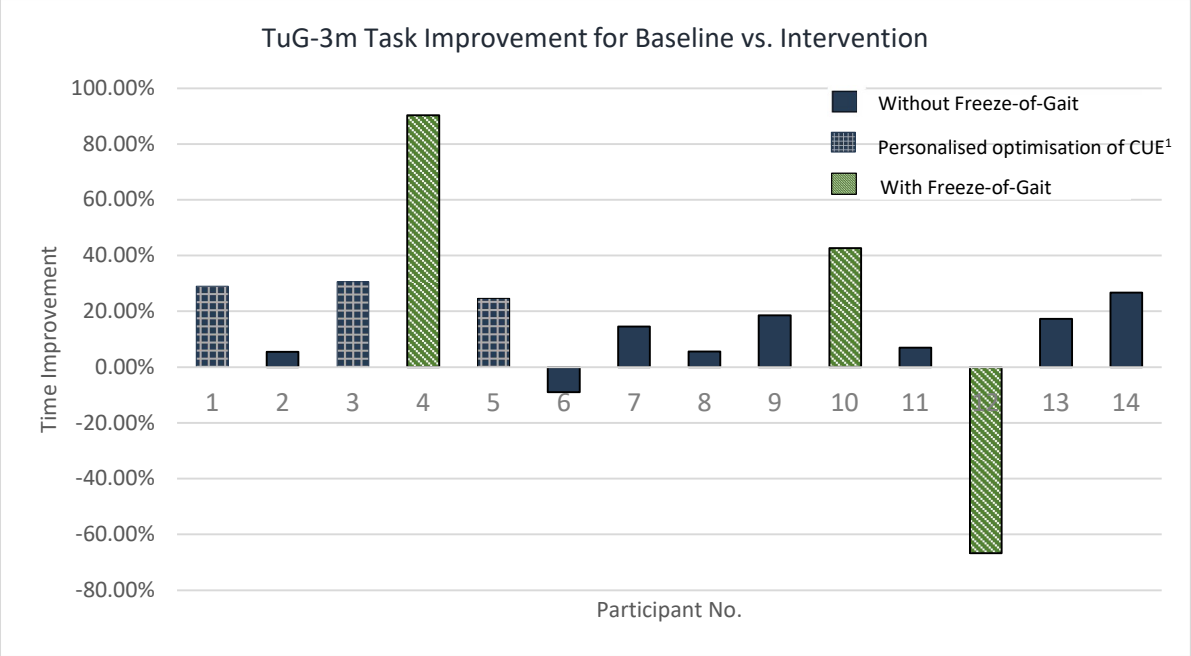

Figure 3. The improvement of time for the Timed Up & Go 3-metre task for each participant for when CUE[1] was activated vs. at baseline level.

3.3 Questionnaire

11 participants completed the feedback questionnaire covering efficacy, usability and risk. Efficacy results demonstrated that 100% of participants believed the device 'can' help them or 'maybe' able to help them. When asked to elaborate, those that said 'maybe' said that they would like to use the device for a longer period before definitively saying that the device could help them. 100% of participants said they would use it again.

From a usability perspective, 55% of participants were able to activate the device fully and 36% to some extent. 9% were not able to activate the device at all. This feedback was very important, and as a result a key functionality change was later made to the device by simplifying the activation process from a triple click to a single-click of the button. Furthermore, 90% were able to access the adhesive and 82% were able to apply the adhesive independently. 91% liked the look of the device. See Figure 4 for a summary of the results. A risk assessment (see Figure 5) was also conducted, with 100% of participants saying the device did not cause pain, discomfort, intrusion, or noise.

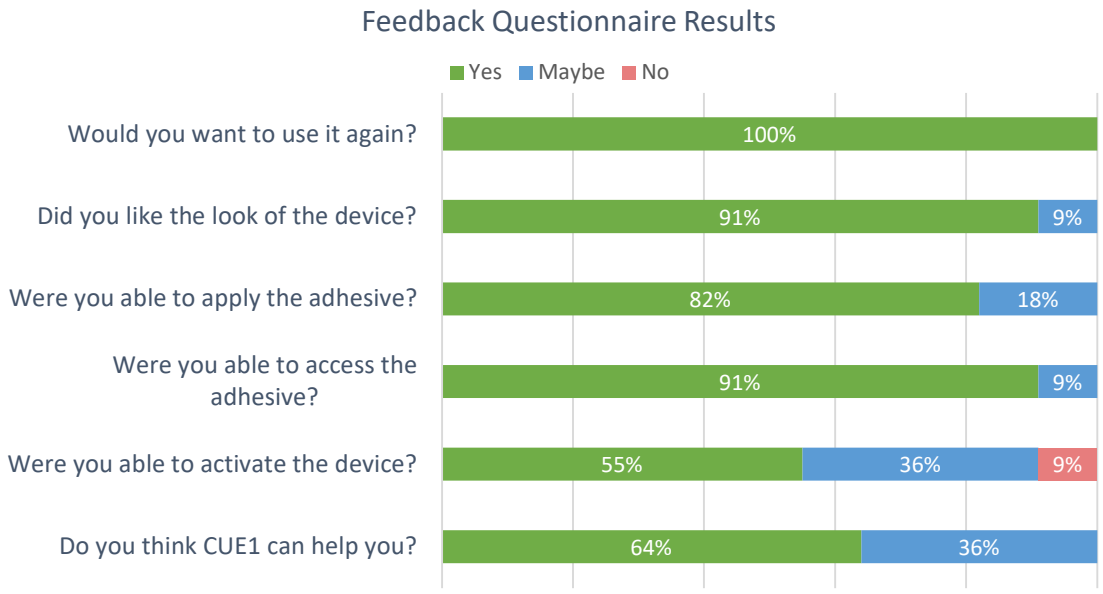

Figure 4. The efficacy and usability results from the feedback questionnaire.

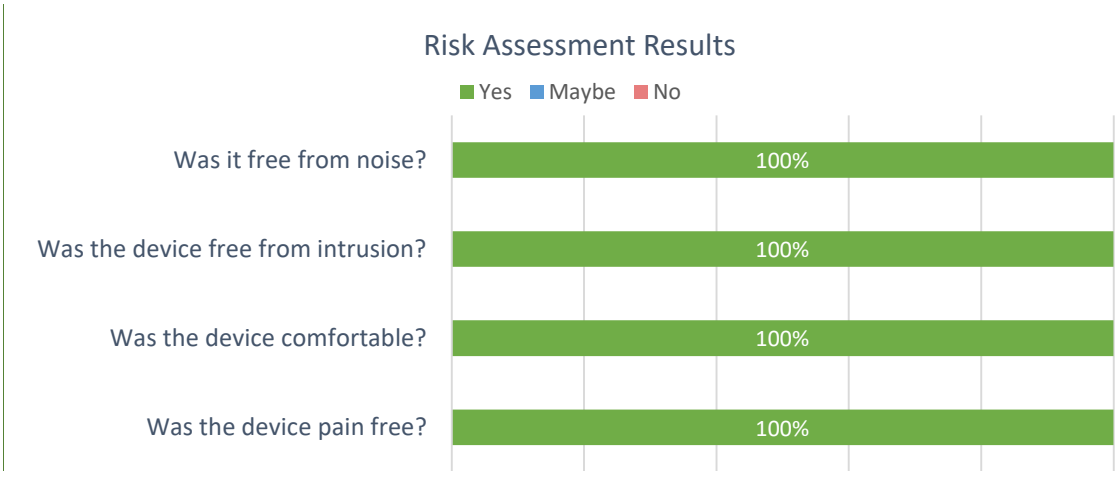

Figure 5. The risk assessment results from the feedback questionnaire.

4. Discussion

These results indicate positive effects of CUE[1] as measured by movement assessments and tasks in a non-randomised, open-label non-clinical study. The mean MDS-UPDRS motor score improvement of 9 points across participants is significantly higher than the quoted minimally clinically significant MDS UPDRS III score of 3.25[1], and 11 out of 12 participants had greater improvements than this. The difference in the means were also statistically significant at a 95% confidence interval ($p = 0.00013$), with a score of MDS UPDRS III score of 2.2 being statistically significant. All 12 participants hence had a statistically significant score.

In comparison to task results from the first round of Charco Neurotech's user testing[2], results from this round demonstrate statistical consistency. The average improvement in the Timed Tapping task was 18% from the first round, compared to 19% in this round. TuG 3-metre tasks were not completed in the first round of testing, however normal 3-metre walking tasks showed a 5% improvement in the first round. Given that the TuG-3m showed an average of improvement of 19%, it may be possible that the standing and sitting portion of the task was responsible for the majority of the improvement.

Results also indicated that, for the four participants that tried multiple vibrational settings, the 1-second square-wave setting was the most effective variation of the 'optimised setting'. This could be for a number of reasons. Firstly, the 1-second square-wave setting was tested chronologically after the 'optimised setting', and hence the task performance improvement could be due to a short-term learning factor of the task, or also a cumulative lasting effect of previous stimulation from the other testing conditions. The findings do suggest that more users could potentially refine the 'optimised setting' parameters. It is also appreciated that the optimal settings may be different for individuals using the device. The CUE[1] has therefore been developed to have adjustable settings through a companion application to allow users to personalise their dosage.

Correlations ran between the improvements across the 3 different measurements were inconclusive, with correlation coefficients ranging from -0.22 to 0.47. A full breakdown of improvements per participant can be seen in the Appendix A.2.

5. Conclusion

An average improvement of 9.3 points above baseline was seen in the MDS-UPDRS Section III scores with the CUE[1] intervention, which is significantly higher than a clinically relevant difference of 3.25 points. The tapping task saw an average performance improvement of 19% and the TuG 3m task saw an average performance improvement of 15% when considering the freezing-of-gait conditions. This user testing hence provides promising evidence that CUE[1] is providing effective treatment of movement symptoms in People with Parkinson's. Results will still need to be reproduced in a clinical setting before its effectiveness can be authenticated, but this report provides strong motivation for selection of this device for clinical trial.

[1] Horváth, K., Aschermann, Z., Ács, P., Deli, G., Janszky, J., Komoly, S., ... & Kovács, N. (2015). Minimal clinically important difference on the Motor Examination part of MDS-UPDRS. *Parkinsonism & related disorders*, *21*(12), 1421-1426.
[2] https://charconeurotech.com/wp-content/uploads/2020/11/Charco_Usertestingresults_2020.pdf

A. Appendix

A.1 MDS-UPDRS Section III table for baseline vs. intervention

Participant No.	1	2	3	4	5	6	7	8	9	12	13	14	μ^*
UPDRS-Baseline	12	22	31	37	14	46	16	19	25	49	32	44	**28.9**
UPDRS-Intervention	4	16	18	33	11	27	8	15	9	45	15	34	**19.6**
Difference	8	6	13	4	3	19	8	4	16	4	17	10	**9.3**

* μ denotes the average.

A.2 Improvements across the 3 measurements per participant

No.	Timed Tapping	MDS-UPDRS Section III	Timed Up & Go 3m
1	33.75%	8	29.05%
2	19.08%	6	5.49%
3	22.72%	13	30.67%
4	41.38%	4	90.33%*
5	37.25%	3	24.67%
6	5.10%	19	-9.00%
7	-8.04%	8	14.50%
8	3.17%	4	5.62%
9	23.97%	16	18.53%
10	N/A	N/A	42.72%*
11	1.03%	N/A	6.93%
12	8.75%	4	-66.67%*
13	40.79%	17	17.27%
14	7.02%	10	26.67%

* denotes cases of Freeze-Of-Gait while task was being performed.