Non-invasive intervention for motor signs of Parkinson's disease: the effect of vibratory stimuli

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In recent years there has been a renewed interest in the use of peripheral vibration to ameliorate some of the motor symptoms of Parkinson's Disease (PD). The possibility that peripheral vibration can improve patients' motor symptoms is exciting as the intervention is non-invasive and low cost. However, there remains little published scientific research to support some of the claims. Previously we demonstrated that vibration at 80 Hz at the wrist for 30s prior to movement onset improved motor performance in a variety of manual tasks both in healthy controls and in PD patients (1). Here we report the results of testing whether a wearable haptic device ("The Emma Watch") developed by Microsoft Research (2), that delivers constant vibratory stimuli at the wrist, significantly improves motor function of the stimulated upper limb in patients with PD.

The Emma watch delivers constant vibration at 200Hz through six small electromagnetic mechanical stimulators, three on each side of the wrist. The vibration frequency is modulated by a lower frequency, either 20bpm (beats per minute) or 60bpm. These modulation parameters were based on the parameter that improved motor function in the first tested PD patient (60bpm) and on a parameter that did not (20bpm). Here we tested whether the Emma watch could improve motor function in 16 PD patients (11 women, mean age = 63 years, range 52-72 years,

UPDRS III RUL 7±3**, disease duration was 10.5 ± 6 years, average daily dose of Levodopa was 500mg**). Idiopathic PD was diagnosed according to the UK PD Society Brain Bank criteria (3) and further confirmed by abnormal dopamine transporter (DaT) SPECT. None of the subjects were on any non-PD medications **(psychotropic medications)** that could affect the measurements performed. All patients were assessed in the ON state, which was evaluated an hour after taking levodopa and 2 hours of taking dopamine agonists. The study was approved by the local institutional ethics committee and written informed consent was obtained from all participants.

Motor performance was assessed through three different tasks:

A) a nine-peg hole test (4); B) a STAR tracing task; C) a SPIRAL tracing task. For A) subjects were instructed to place nine pegs into nine holes as quickly as possible while they were timed with a stop watch. Subjects performed B) and C) using an inking digitizer pen on a WACOM Intuos Pro L digitizing tablet with 8192 pressure levels and a resolution of 5080 lines per inch. An in-house Windows application recorded WACOM data (pen x/y coordinates and pressure level) into a log file along with the beginning and end timestamps for each task.

For both tracing tasks (STAR and SPIRAL) subjects were instructed to trace the figure on a sheet of paper placed on top of tablet surface as precisely and quickly as possible. Participants were instructed to complete the STAR task starting from the centre going to the edge and then back, beginning with the line at 90 degrees (up) and then moving clockwise. The SPIRAL task

started from the centre. Each set of 3 tasks was repeated in three different conditions in a randomized order: absence of vibratory stimuli (NoVib); during 200Hz vibration with 60bpm modulation (200Hz60bpm); during 200Hz vibration with 20bpm modulation (200Hz20bpm). The order of the tasks was randomized across participants so there was no order effect.. Each task and each condition was repeated three times.

The nine-hole peg test was performed both with Emma Watch (NoVib, 200Hz60bpm, 200Hz20bpm) and an electromagnetic mechanical stimulator (80 Hz vibratory stimuli) used in the previous study (1).

The following dependent variables were recorded for each motor task:

-Nine peg hole test: corrected mean completion time of the test (seconds)

- For the STAR tracing task and SPIRAL tracing task: the average of the absolute error from the target at every time point.

For the nine-hole peg test, a repeated-measures ANOVA with one factor Condition with four levels (noVib, 200Hz60bpm, 200Hz20bpm and 80Hz) revealed a significant main effect of the condition on the mean completion time of the nine-peg hole test, ($F(3, 45) = 3.8$, $p = 0.016$ $Eta2 = 0.202$, Fig1a). Post-hoc pairwise comparisons revealed a significant difference between mean completion time between 80 Hz and NoVib ($p<0.01$, $t(15) = -3.58$). These results replicated the previous study using the same device and task (1). There was evidence of a significant

difference between mean completion time between 200Hz60bpm and NoVib (one-tailed predicted direction; p=0.05, t(15) = 1.713). There was no significant difference between the mean completion time between 80Hz and 200Hz60bpm (p=0.36, t(15) = 0.941). There was no significant difference between mean completion time 200Hz20bpm and NoVib, (p = 0.69, t(15) = 0.412). Therefore, for the nine-hole peg test we firstly replicated our previous result and provided preliminary evidence that continuous vibration with the Emma watch at 200Hz60bpm improved motor performance.

For the STAR tracing tasks, a repeated measures ANOVA factor condition with three levels (noVib, 200Hz60bpm, 200Hz20bpm) showed a main effect of condition ($F(2,30) = 3.65$, $p = 0.037$, eta2 = 0.19, Fig1b). The Emma watch reduced error in the 200Hz60bpm compared with both noVib and 200Hz20bpm (one-tailed tests; $t(15)=1.86$, $p=0.041$ and $t(15)=2.03$, $p=0.03$ respectively).

For the SPIRAL tracing tasks there was no main effect of condition ($F(2,30) = 0.91$, $p = 0.41$, eta2 = 0.06, Fig1c). However, The Emma watch did show reduced error in the 200Hz60bpm compared with 200Hz20bpm (one-tailed tests; $t(15)=2.05$, $p=0.029$) but not when compared with noVib (one-tailed test; $t(15)=0.75$, $p=0.23$)

Our study aimed to test the impact of the non-invasive intervention device “Emma watch” on motor performance in PD patients. We found that 200Hz peripheral vibration at 60bpm

modulation applied during the performance of different tasks of a total of 16 PD patients on medication improved performance related to movement speed as well as precision of performance on our tracing motor control tasks. In contrast, peripheral vibration at 200Hz with 20bpm had no significant effect on motor performance. These data, although preliminary, are consistent with the idea that vibrotactile stimulation can improve motor function in patients with PD but further work is required now to establish these findings and investigate the relationship further.

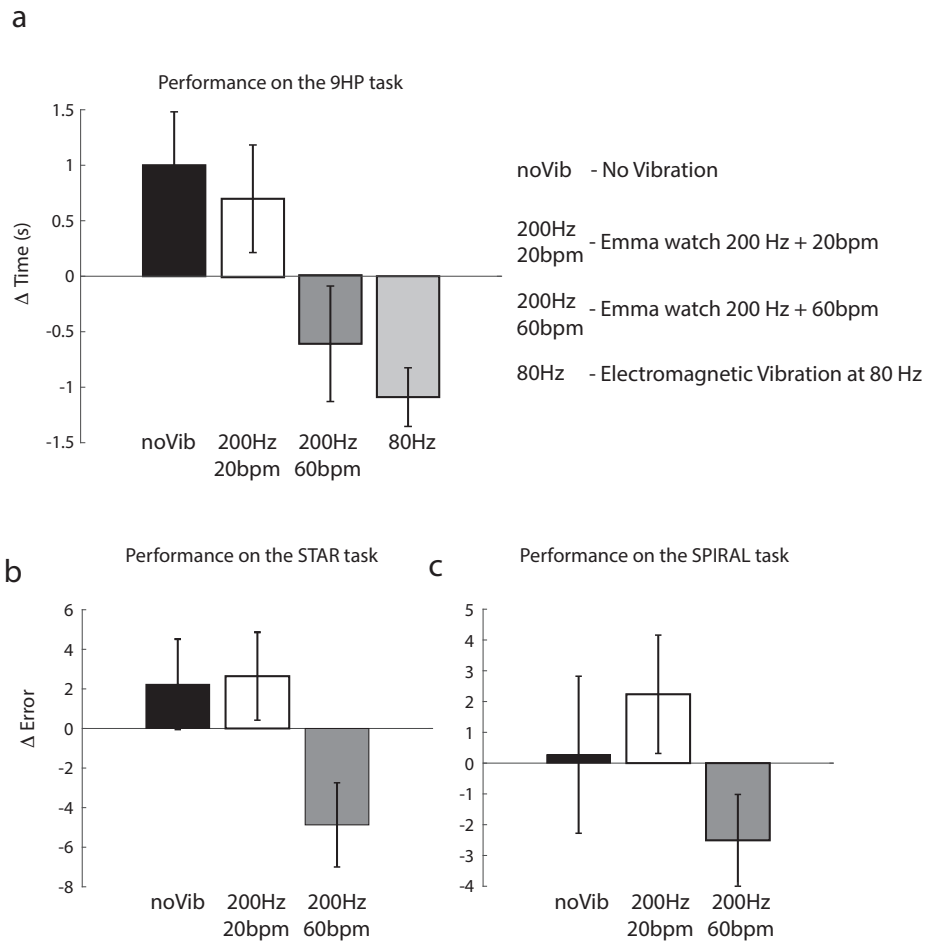

Figure 1 shows the averaged data for the 3 different task tested in this study: a) 9 HP task, b) STAR task and c) SPIRAL task. The bars show the difference from the mean across all conditions for each task (i.e. if there was no modulation the bars would be at zero thus removing the between subject variance). Error bars are the SEM.

1. Macerollo A, Palmer C, Foltynie T, Korlipara P, Limousin P, Edwards M, Kilner JM. High-frequency peripheral vibration decreases completion time on a number of motor tasks. Eur J Neurosci. 2018; 48:1789-1802.
2. "The invention that helped me write again" (2016, Dec 7). Retrieved from https://www.bbc.co.uk/news/av/magazine-38208814/the-invention-that-helped-me-write-again.
3. Hughes, A. J., Daniel, S. E., Kilford, L., & Lees, A. J. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992, 55: 181-184.
4. Oxford Grice, K., Vogel, K. A., Le, V., Mitchell, A., Muniz, S., & Vollmer, M. A. Adult norms for a commercially available Nine Hole Peg Test for finger dexterity. Am J Occup Ther 2003, 57: 570-573.