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The impact of dual tasking on cognitive performance in a Parkinson's disease cohort with and without freezing of gait: an EEG and behavioral based approach*

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Abstract— **Freezing of gait (FOG) is a common disabling gait disorder in late stage Parkinson's disease (PD), which can lead to falls and loss of independence. To date, the mechanisms causing FOG are still unknown and no treatment has proven to be effective. In this study, sixteen PD participants with and without clinically confirmed FOG symptoms were recruited, referred to as FOG+ and FOG-, respectively. All participants navigated through a customized virtual reality (VR) corridor by stepping in place (SIP) on a force plate while electroencephalography (EEG) data was recorded. The VR environment was combined with a cognitive, visual two-stimulus oddball response task, which was repeated while seated to allow for comparisons to the SIP condition. The VR environment proved to be a reliable tool to elicit FOG like symptoms in a clinical test environment. EEG recordings were compared between conditions (seated/SIP) within groups and behavioral performance was compared between groups and conditions for qualitative differences. In the seated condition FOG+ participants showed similar behavioral performance to FOG- participants, however, in the SIP condition the FOG+ group showed significantly decreased performance with longer reaction times and more target misses. Analysis of the EEG data revealed consistent visual responses to the stimuli, but an absence of the P3b component in stimulus-locked brain responses for FOG+ participants and both conditions. However, if data is response-locked, the P3b component is clearly visible for both conditions, supporting the theory that components related to decision making and motor preparation are present, but with variable delays.**

I. Introduction

Freezing of gait (FOG) is a highly disabling symptom in Parkinson's disease (PD), which leads to falls and hospitalizations and therefore to a decreased quality of life [1]. FOG occurs in up to 60% of all PD patients at some point in their disease course, incidence increasing with the stage of PD [2]. People with PD who show FOG symptoms experience the occasional inability to initiate or keep up a rhythmic stride pattern, feeling like their feet are "glued to the floor" [3] and are unable to move for differing time ranges, from seconds to minutes. FOG is commonly elicited by gait initiation, turning, walking through narrow spaces, doorways, dual tasking and anxiety, but can also occur when walking in open spaces [3]. Despite its prevalence, the underlying pathology of FOG is still unknown and no treatment has proven to be effective [3]. One of the difficulties of studying this condition is to induce FOG in a controlled clinical setting [4]. We have addressed this issue by using a virtual reality (VR) environment and a stepping in place (SIP) task, a similar model to that employed by [4]. The VR corridor contains narrow spaces and doorways designed to elicit FOG, and furthermore, a secondary cognitive, visual response task can be employed to add cognitive load to the SIP paradigm.

FOG+ participants are expected to show decreased gait and behavioral performance in this cognitive task while SIP compared to PD participants without FOG symptoms, subsequently called FOG-. More specifically this means that FOG+ participants exhibit FOG-like episodes and increased reaction times, as well as missing target responses in the visual response task. Furthermore, we hypothesize that clear ERPs can be recorded from both participant groups for the visual oddball task despite movement artefacts from SIP.

To date, little research has been reported on the study of FOG by means of electroencephalography (EEG) or local field potential (LFP) measurements. Only seven studies have been published, which have investigated FOG based on EEG/ LFP analysis with the first being published in 2012 [5]–[11]. To date there have been no publications investigating event-related potential (ERP) measurements during walking/SIP in a clinical population such as a PD cohort. This study aimed to investigate the influence of FOG on ERP components elicited by a speeded visual response oddball task as well as the influence on behavioral responses while simultaneously walking/SIP.

II. Methods

A. Participants

Sixteen participants with idiopathic PD were recruited from the Mater Misericordiae University Hospital Dublin, Ireland. Nine participants had been clinically confirmed to suffer from freezing (FOG+). Seven FOG- participants formed the disease matched control group in this study. Although a statistically significant age difference is existent ($p=0.0163$) between the two groups, no significant difference

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can be found regarding disease stage (p=0.3862), cognitive state (p=0.4166) or UPDRS motor scores (p=0.8282), providing two disease-matched groups. One FOG+ and one FOG- participant had to be excluded from analysis due to low signal-to-noise ratios in EEG recordings (analysis: FOG+ n=8, FOG- n=6).

TABLE I. GROUP MEAN DEMOGRAPHICS AND CLINICAL TEST SCORES; ONLY IN THE ANALYSIS INCLUDED PARTICIPANTS ARE REPRESENTED

	FOG+	FOG-
Number of included participants	8	6
Gender (male %)	100	50
Age (years)	69 ± 5.4	59 ± 7.2
Years since diagnosis	11 ± 9.0	6 ± 2.9
Years since symptom onset	13 ± 8.9	8 ± 3.5
NFOGQ Total	16 ± 5.4	0 ± 0
H&Y Total	2 ± 0.5	2 ± 0.2
UPDRS III Total	31 ± 14.0	29 ± 15.8
MOCA Total	25 ± 2.5	26 ± 3.0
FAB	16 ± 1.7	17 ± 1.5
BDI Total	2 ± 2.4	2 ± 1.8

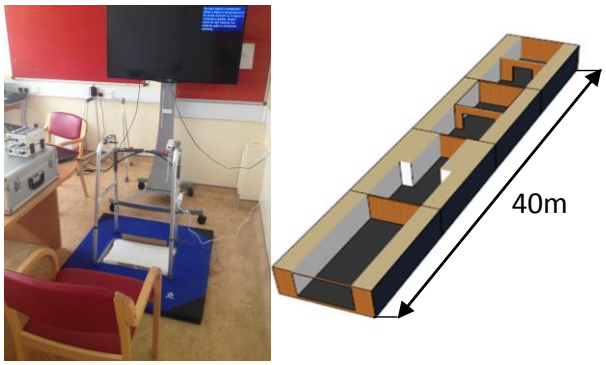

Figure 1: Experimental set-up (left) showing the Wii board with surrounding safety mat and Zimmer frame in front of the large screen TV; behind the Wii board is a chair for participant's to rest and the EEG equipment is placed on the table on the left; The virtual reality corridor overview (right) shows the four sections with 10m each

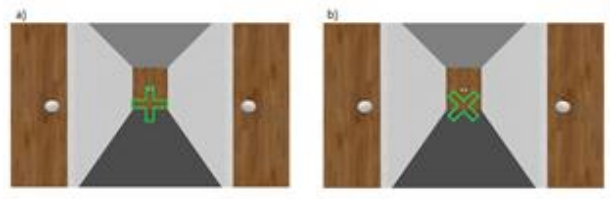

Figure 2: a) Standard and b) target stimuli of visual response task

Preceding experimentation, all PD participants underwent an extensive clinical and neurophysiological assessment, considering their disease severity (Hoehn & Yahr =H&Y), drug treatment, cognitive ability (Montreal Cognitive Assessment =MOCA, Frontal Assessment Battery =FAB), mental state (Beck Depression Inventory =BDI), motor ability (Unified Parkinson's Disease Rating Scale, part III =UPDRSIII), and impact of FOG on daily living (New Freezing of Gait Questionnaire =NFOGQ). TABLE I shows the participants' demographics and average test scores. All tests were rated unblinded by the same neurologist specialized in movement disorders and potential participants were excluded from testing if they had an acquired traumatic brain injury, MOCA test scores below 23 or if they were physically unable to carry out the response task while SIP. Furthermore, all participants gave written informed consent prior to experimentation and the study was approved by the Ethical Review Committee of the Mater Misericordiae University Hospital, Dublin.

B. Experimental set-up

Participants navigated through a custom designed VR corridor by stepping in place (SIP) on a force plate (Nintendo Wii balance board). Simultaneously, brain activity was recorded with a 128 active electrode system (BioSemi B.V.). The VR corridor consists of four different sections of equal lengths which are separated by sliding doorways and contain several narrow passages and open doorways (see Figure 1). For this study, the VR environment was augmented by a secondary task to add cognitive load to the SIP-task. This consisted of a visual go/no-go response task requiring participants to respond by pressing a button when presented with the target stimulus (20%), but not when presented with the standard stimulus (80%) (Figure 2). Stimuli were presented for 0.5s with a randomized inter-stimulus interval between 0.25s and 0.75s. For comparison of brain responses during the response task, the visual go/no-go response task was performed while SIP (3x100s trials) and while seated (1x300s trial). In the seated paradigm participants received the visual flow of progressing through the corridor to keep the visual information consistent.

C. Analysis

EEG analysis: All files were processed using FASTER[1] [12], an objective and automated application of independent component analysis (ICA) for artefact removal (ocular and muscular artefacts), ensuring unbiased and objective rejection of components.

Subsequently, the continuous data was band pass filtered for 1-30Hz and epoched to the triggers of standard stimuli, target stimuli and button responses. Epoch lengths were set to 800ms, with 100ms pre-stimulus and 700ms post-stimulus content for stimulus locked ERPs and 500ms pre-stimulus and 300ms post-stimulus content for response-locked epochs. Data was baseline corrected to a 40ms pre-stimulus interval. The number of channels was reduced to three regions of interest (ROI) with six electrodes over occipital scalp, six electrodes over central scalp and three electrodes over frontal scalp. A threshold of ±100μV was applied in order to automatically detect channels containing artefacts in each epoch. Epochs with more than five bad channels were rejected. The electrodes were averaged for each ROI in order to increase the signal to noise ratio. Furthermore, epochs were averaged across all trials of each paradigm for the different trigger types and data was re-referenced offline to the frontal electrode average due to greater ERP amplitudes compared to an overall electrode average reference.

[1] The FASTER software tool and its manual are available online at http://sourceforge.net/projects/faster/

III. Results

All but one FOG+ participant showed motor arrests while SIP throughout the experiment, whereas none of the FOG- participants exhibited these FOG-like events.

A. Behavioral results

Table II provides an overview of reaction times and target misses for both participant groups (FOG+/ FOG-) as well as both conditions (sitting/ SIP). In the seated response task, reaction times did not differ significantly for FOG+ and FOG- (Mann-Wilcoxon test: p=0.121). However, in the SIP condition reaction times differed significantly between groups (Mann-Wilcoxon test: p=0.005) with FOG- showing a tendency towards shorter reaction times in the SIP condition, whereas FOG+ exhibited longer reaction times, though each not reaching statistical significance. The number of missed targets was not statistically different between FOG+ and FOG- for the sitting condition (p=0.093). However, for the SIP condition the number of missed targets differed significantly between FOG+ and FOG- (p=0.008).

TABLE II. Group means for the reaction times and number of missed targets in the visual response task per condition

	Reaction time [s]		# of missed targets	
	FOG+	FOG-	FOG+	FOG-
Sitting	1.05 ± 0.17	0.57 ± 0.04	4.38 ± 1.52	1.00 ± 0.33
SIP	1.15 ± 0.17	0.53 ± 0.03	11.63 ± 2.99	1.83 ± 0.80

B. EEG results

The lack of distinguishable ERP components for FOG+ in Figure 3 emphasizes the need for response-locking of ERPs when investigating the N2 and P3b component in this cohort.

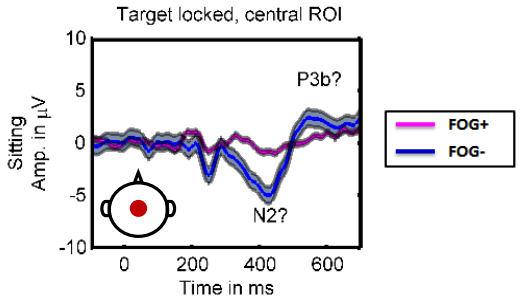

Figure 3: Group means for target locked ERPs for central ROI, showing no distinguishable ERPs for FOG+ in the seated condition, and thus, the need for response-locking

Both participant groups exhibited P1, N1 and P2 ERP components, which are different from baseline activity. However, the N2 component is not clearly distinguishable for FOG+ in the occipital ROI for stimulus-locked ERPs (see Figure 4-left). The well-researched P3b component is not detectable in the stimulus-locked ERPs. However, once EEG data is response-locked to the button press, the P3b component was clearly distinguishable (0-200ms) for both groups and across conditions with a steep slope around the reaction time (0ms) (see Figure 4-right).

Results of a detailed statistical analysis of the individual ERP components across conditions and within groups can be viewed in [23]. Statistical analysis across groups was not conducted due to low sample sizes.

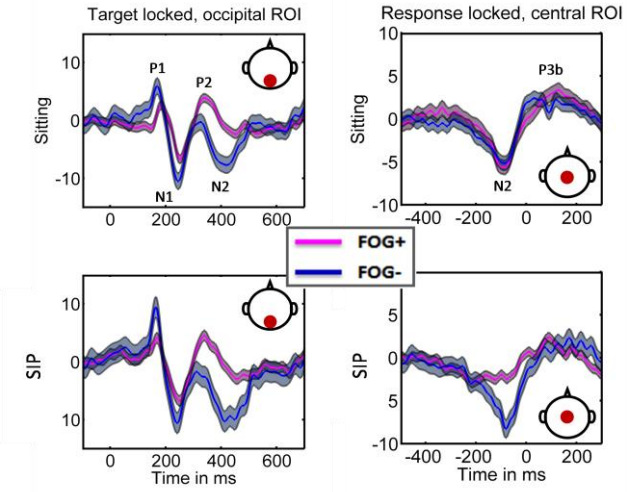

Figure 4: Group means for target locked ERPs for occipital ROI (left) and response locked ERPs for central ROI (right) for FOG+ (pink) vs. FOG- (blue); shown in grey are the standard errors; the red dots in the scalp figure show the location of the depicted electrode average

IV. Discussion

A. Behavioral data discussion

An increased number of missed targets and increased reaction times for the response task while SIP for the FOG+ group indicates that the challenges arising from dual tasking has a different impact on FOG+ than FOG- participants. FOG+ participants may have limited resources for processing tasks, which leads to decreased performance in at least one of the dual tasks (SIP or response task scores), whereas FOG- participants can perform two tasks without a dual-task cost.

The results from this study for FOG- participants are at odds with previous publications, which report deteriorating task performance when dual tasking for young, healthy participants [13], older adults [14] and data cohorts with neurological diseases such as Parkinson's disease [15], [16]. However, this difference could be due to low sample sizes. The impact of dual tasking appears to be greater for elderly and especially participants with neurological diseases [17]. This may potentially be due to increased attentional effects, since the seated response task was carried out in one block of 300s instead of three 100s trials as for the SIP condition. Results for FOG+ participants, however, are consistent with literature showing poorer behavioral performance in the SIP condition [18].

B. EEG data discussion

Previous studies have reported the feasibility of high-density EEG recordings during walking in healthy, young individuals [19–21]. Both groups in the current study displayed overall similar morphology of the early (prior to 250ms) ERP components across conditions, agreeing with

existing literature that ERPs are not considerably affected by SIP/ walking [19, 20]. This also supports the feasibility of EEG based studies to further investigate the underlying pathology of FOG.

The need for response-locking of EEG data to detect the P3b component for both participant groups is probably an indicator for a random onset of activity related to the P3b component within and across participants. It has been recently reported by [22] that the P3b component is more distinguishable in older adults when it is response-locked since stimulus-locked ERPs do not account for delays in processing of information and differing reaction times across and within participants.

V. Conclusion

The VR environment proves to be a very efficient and reliable method to induce FOG like symptoms in a controlled fashion in PD participants with FOG, providing a platform for further experiments on the pathology of FOG. This study was the first of its kind, investigating ERPs during locomotion in a clinical population.

FOG+ participants demonstrated decreased behavioral performance for the SIP condition while simultaneously performing a secondary cognitive task compared to the cognitive only task in the sitting condition. Additionally, data shows the need for response-locking of ERPs in order to detect late ERP components, such as the P3b, due to differing on-set times as a result of delays in information processing and/or differing reaction times in this cohort.

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References

[1] B. R. Bloem, J. M. Hausdorff, J. E. Visser, and N. Giladi, "Falls and freezing of gait in Parkinson's disease: a review of two interconnected, episodic phenomena.," *Mov. Disord.*, vol. 19, no. 8, pp. 871–84, Aug. 2004.

[2] N. Giladi, T. A. Treves, E. S. Simon, H. Shabtai, Y. Orlov, B. Kandinov, D. Paleacu, and A. D. Korczyn, "Freezing of gait in patients with advanced Parkinson's disease.," *J. Neural Transm.*, vol. 108, no. 1, pp. 53–61, Jan. 2001.

[3] J. G. Nutt, B. R. Bloem, N. Giladi, M. Hallett, F. B. Horak, and A. Nieuwboer, "Freezing of gait: moving forward on a mysterious clinical phenomenon.," *Lancet Neurol.*, vol. 10, no. 8, pp. 734–44, Aug. 2011.

[4] J. M. Shine, E. Matar, S. J. Bolitho, V. Dilda, T. R. Morris, S. L. Naismith, S. T. Moore, and S. J. G. Lewis, "Modeling freezing of gait in Parkinson's disease with a virtual reality paradigm.," *Gait Posture*, vol. 38, no. 1, pp. 104–8, May 2013.

[5] J. M. Shine, A. M. A. Handojoseno, T. N. Nguyen, Y. Tran, S. L. Naismith, H. Nguyen, and S. J. G. Lewis, "Abnormal patterns of theta frequency oscillations during the temporal evolution of freezing of gait in Parkinson's disease," *Clin. Neurophysiol.*, Oct. 2013.

[6] A. Singh, A. Plate, S. Kammermeier, J. H. Mehrkens, J. Ilmberger, and K. Bo, "Freezing of gait-related oscillatory activity in the human subthalamic nucleus," vol. 3, pp. 25–32, 2013.

[7] W. Thevathasan, A. Pogosyan, J. a Hyam, N. Jenkinson, T. Foltynie, P. Limousin, M. Bogdanovic, L. Zrinzo, A. L. Green, T. Z. Aziz, and P. Brown, "Alpha oscillations in the pedunculopontine nucleus correlate with gait performance in parkinsonism.," *Brain*, vol. 135, no. Pt 1, pp. 148–60, Jan. 2012.

[8] J. B. Toledo, J. López-Azcárate, D. Garcia-Garcia, J. Guridi, M. Valencia, J. Artieda, J. Obeso, M. Alegre, and M. Rodriguez-Oroz, "High beta activity in the subthalamic nucleus and freezing of gait in Parkinson's disease.," *Neurobiol. Dis.*, vol. 64C, pp. 60–65, Dec. 2013.

[9] P. D. Velu, T. Mullen, E. Noh, M. C. Valdivia, H. Poizner, Y. Baram, and V. R. de Sa, "Effect of visual feedback on the occipital-parietal-motor network in Parkinson's disease with freezing of gait.," *Front. Neurol.*, vol. 4, no. January, p. 209, Jan. 2014.

[10] A. M. A. Handojoseno, J. M. Shine, T. N. Nguyen, Y. Tran, S. J. G. Lewis, H. T. Nguyen, and S. Member, "The detection of Freezing of Gait in Parkinson's disease patients using EEG signals based on Wavelet decomposition.," *Conf. Proc. IEEE Eng. Med. Biol. Soc.*, vol. 2012, pp. 69–72, Jan. 2012.

[11] A. M. A. Handojoseno, J. M. Shine, T. N. Nguyen, Y. Tran, S. J. G. Lewis, H. T. Nguyen, and S. Member, "Using EEG spatial correlation, cross frequency energy, and wavelet coefficients for the prediction of Freezing of Gait in Parkinson's Disease patients.," *Conf. Proc. IEEE Eng. Med. Biol. Soc.*, vol. 2013, pp. 4263–6, Jan. 2013.

[12] H. Nolan, R. Whelan, and R. B. Reilly, "FASTER: Fully Automated Statistical Thresholding for EEG artifact Rejection.," *J. Neurosci. Methods*, vol. 192, no. 1, pp. 152–62, Sep. 2010.

[13] T. Szturm, P. Maharjan, J. J. Marotta, B. Shay, S. Shrestha, and V. Sakhalkar, "The interacting effect of cognitive and motor task demands on performance of gait, balance and cognition in young adults.," *Gait Posture*, vol. 38, no. 4, pp. 596–602, Sep. 2013.

[14] U. Lindenberger, M. Marsiske, and P. B. Baltes, "Memorizing while walking: increase in dual-task costs from young adulthood to old age.," *Psychol. Aging*, vol. 15, no. 3, pp. 417–36, Sep. 2000.

[15] B. R. Bloem, V. V Valkenburg, M. Slabbekoorn, and J. G. van Dijk, "The multiple tasks test. Strategies in Parkinson's disease.," *Exp. brain Res.*, vol. 137, no. 3–4, pp. 478–86, Apr. 2001.

[16] G. Yogev, N. Giladi, C. Peretz, S. Springer, E. S. Simon, and J. M. Hausdorff, "Dual tasking, gait rhythmicity, and Parkinson's disease: which aspects of gait are attention demanding?," *Eur. J. Neurosci.*, vol. 22, no. 5, pp. 1248–56, Sep. 2005.

[17] G. Yogev-Seligmann, J. M. Hausdorff, and N. Giladi, "The role of executive function and attention in gait.," *Mov. Disord.*, vol. 23, no. 3, pp. 329–42; quiz 472, Feb. 2008.

[18] J. Spildooren, S. Vercruysse, K. Desloovere, W. Vandenberghe, E. Kerckhofs, and A. Nieuwboer, "Freezing of gait in Parkinson's disease: the impact of dual-tasking and turning.," *Mov. Disord.*, vol. 25, no. 15, pp. 2563–70, Nov. 2010.

[19] P. De Sanctis, J. S. Butler, B. R. Malcolm, and J. J. Foxe, "Recalibration of inhibitory control systems during walking-related dual-task interference: a mobile brain-body imaging (MOBI) study.," *Neuroimage*, vol. 94, pp. 55–64, Jul. 2014.

[20] K. Gramann, J. T. Gwin, N. Bigdely-Shamlo, D. P. Ferris, and S. Makeig, "Visual evoked responses during standing and walking.," *Front. Hum. Neurosci.*, vol. 4, p. 202, Jan. 2010.

[21] S. Debener, F. Minow, R. Emkes, K. Gandras, and M. de Vos, "How about taking a low-cost, small, and wireless EEG for a walk?," *Psychophysiology*, vol. 49, no. 11, pp. 1617–21, Nov. 2012.

[22] S. P. Kelly and R. G. O'Connell, "The neural processes underlying perceptual decision making in humans: Recent progress and future directions.," *J. Physiol. Paris*, Sep. 2014.

[23] S. M. Waechter, "A study of freezing of gait in Parkinson's disease based on mobile electroencephalography coupled with gait data in a virtual reality environment", MSc, Trinity College Dublin, Trinity College Library Dublin, 2014