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# An EEG Study of Turning Freeze in Parkinson's Disease Patients: The Alteration of Brain Dynamic on the Motor and Visual Cortex

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***Abstract*— Freezing of gait is a very debilitating symptom affecting many patients with Parkinson's disease, leading to a reduced mobility and increased risk for falls. Turning is known to be the most provocative trigger for freezing of gait. However, the underlying brain dynamic changes associated with a turning freeze remain unknown. This study therefore used ambulatory EEG to investigate the brain dynamic changes associated with freezing of gait during turning. In addition, this study aimed to determine the most suitable EEG sensor location to detect freezing of gait during turning using our classification system. Data from four Parkinson's disease patients with freezing of gait was analysed using power spectral density and brain effective connectivity, comparing periods of successful turning with freezing of gait during turning. Results showed that freezing of gait during turning is associated with significant alterations in the high beta and theta power spectral densities across the occipital and parietal areas. Furthermore, brain effective connectivity showed that freezing during turning was associated with increased connectivity towards the visual area, which also had the highest accuracy to detect freezing episodes in the O1 regions by using power spectral density in our classification analyses. This is the first study to show cortical dynamic changes associated with freezing of gait during turning, providing valuable information to enhance the performance of future freezing of gait detection systems.**

## I. INTRODUCTION

Freezing of Gait (FOG) is a common gait deficit in persons with advanced Parkinson's disease (PD), often described by patients as a feeling of "being glued to the floor" [1]. This absence of forward progression disturbs balance and has been interconnected with an increase number in falls for PD patients resulting in injuries and creating a loss of independence for these patients. These physical and psychosocial consequences in turn reduce the quality of life for patients with PD, making FOG a highly important symptom to study [2]. This calls for the need for novel therapies that can aid in predicting a freeze and preventing falls.

Whilst many triggers of FOG have been described, the most precipitant is turning. In controlled timed-up-and-go (TUG) experiments, turning accounts for 48.4% of all witnessed FOG [3]. Turning is a complex motor task requiring both motor and cognitive processing to enable the correct selection, timing and scaling of movement. In addition, in PD patients with FOG the symptom can be exacerbated by emotion, attention and dopaminergic therapy, suggesting the existence of a complex pathophysiological process that not only involves the locomotor networks but also differing cortical areas and the basal ganglia system [3],[4],[5]. Despite advances in our understanding of FOG from recent neuroimaging work [6], the neurobiology specifically associated with turn provoked FOG remains unknown.

One method to advance our understanding of FOG would be through using surface ambulatory EEG techniques. Unlike neuroimaging studies this approach allows the potential to identify and detect FOG episodes during walking due to its ability to track the dynamic physiological changes throughout the brain in real time. The use of this portable measuring system allows the replication of an actual freezing event, allowing the patient to execute movements with timing and scaling as they would usually do outside of the testing environment. Being able to reflect actual gait planning whilst turning through the use of this system is a much more effective measurement of freezing which could allow for the prediction of FOG in a future treatment device.

Our group has developed a detection algorithm for recognizing FOG by analyzing energy power, entropy, correlation and brain effective connectivity (BEC) of EEG signals, providing valuable insights into the underlying brain mechanism [3],[7],[8]. However, these previous studies have focused on episodes of freezing that had mixed provocation factors. The current paper sought to analyse the EEG specifically associated with successful turning and turning associated with FOG.

As we have demonstrated from our previous studies, "classical" Power Spectral Density (PSD) and BEC are powerful methods for feature extraction from surface EEG recordings [7],[8]. Whilst we have established the role of PSD in analyzing FOG previously, BEC is a more recent and advanced approach, which might provide valuable insights into a better

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understanding of the complex physiological mechanisms of freezing in the brain. We hypothesized that there would be a distinct signal change (PSD and BCE) detectable by EEG comparing freezing whilst turning to successful turning with a loss of functional connectivity across the fronto-parietal networks processing visual information [9].

## II. METHODS

### A. Subjects and Task

Four patients diagnosed with idiopathic PD with significant FOG were recruited from the Parkinson's Disease Research Clinic at the Brain and Mind Research Institute, University of Sydney. The study was approved by The Human Research and Ethics Committee from the University of Sydney and all subjects read and signed written informed consent. They were assessed in the practically-defined "off" state following overnight withdrawal of dopaminergic therapy.

The EEG were recorded from 32 Ag/AgCl scalp electrodes of Biosemi ActiveTwo system, band-passed filtered from 0.15 to 400 Hz, segmented to 1-s durations and digitized at 512 Hz. Only 8 location of interest were used based on previous finding of the affected location of the brain by FOG in a study using fMRI [10]: F3, Fz, F4 (motor planning and working memory), Cz (motor execution), P3, P4 (sensory integration), and O1, O2 (visual area). References was taken by averaging 2 EXG electrodes placed on the ear lobes.

The protocol consisted of several video-recorded TUG tasks that required subjects to walk 5 meters between a chair and a 0.6 x 0.6 m square target defined by a taped box on the floor. Subjects were asked to either make a right or a left turn (180 degrees or and 540 degrees) inside the taped box before returning to the chair. The video footage was labelled by two physicians specialized in movement disorders for the start and end of a turn and for periods of freezing of gait, defined as an absolute cessation or marked reduction of forward progression of the feet despite the intention to walk [1]. EEG data was extracted for periods of freezing of gait during turning (FT) and for periods of normal turning (NT), during which the subject was able to turn effectively inside the box during the TUG tasks. No distinctions were made between either left or right and 180 or 540 degrees turns to improve the power of the analyses.

### B. Feature extraction

In this study, 341 selected samples data (117 NT and 224 FT) were filtered using a band-pass (0.5-60 Hz) and band-stop (50Hz) Butterworth IIR. To eliminate differences in source strength due to variance in absolute measurement between electrodes and individual subject, a Z-transformation was applied. Five frequency bands were analysed, namely: theta (4-8 Hz), alpha (8-13 Hz), low beta (13-21 Hz), high beta (21-38 Hz), and gamma (38-60 Hz) [Fig. 1]. The beta frequency band was divided into high and low, based on previous findings showing that specifically high beta frequencies correlate with FOG [11]. A Wilcoxon Sum Rank Test with an alpha of 0.05 was used to investigate the power

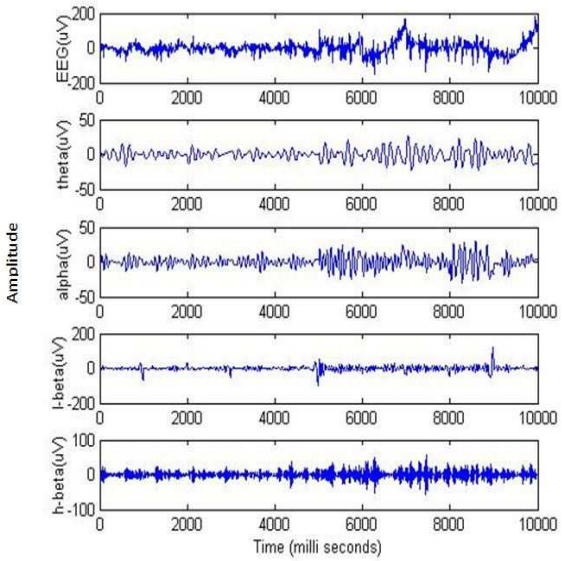


Fig. 1. Decomposition of EEG into four frequency bands in subject 1 shows the alteration of amplitude and frequency signals during a turning freeze (5001-1000 ms) as opposed to a normal turning (1-5000 ms)

spectral densities between periods of normal turning and periods of freezing turning. This feature was used as the main parameter for evaluating the significance of the electrode location during freezing turning.

Effective connectivity analysis was mapped between four brain regions (i.e. frontal, central, parietal, and occipital) by taking the mean of each related electrode in those regions and between electrode locations in subregions of interest, namely fronto-parietal regions (F3, Fz, F4, P3, P4) locations often associated with "executive-attention" and visual networks affected by in PD patients with FOG [12]. Squared generalized partial directed coherence (sGPDC) was used to describe the dynamics of the interactions between brain areas as it provides the best indication of FOG compare to several other methods [7].

Based on the concept of Granger causality, partial directed coherence (PDC) described the exclusive directional flow of information from the activity in the region of interest (ROIs) $s_j(n)$ to the activity in $s_i(n)$ [13]. The squared generalized PDC is a modification of PDC to increase its sensitivity, create an absolute strength of the coupling score, make it scale-invariant, emphasize the sources, and defined as [14]:

$$sGPDC_{j\to i}(f) = \frac{(\frac{1}{\sigma_i}\left|\bar{A}_{ij}(f)\right|)^2}{\sum_{k=1}^{N}\frac{1}{\sigma_k^2}\bar{A}_{kj}(f)\bar{A}^*_{kj}(f)}. \qquad (1)$$

This connectivity measures were obtained using the Nuttall Strand methods to estimate multivariate autoregressive models of time series, a frequency domain representation of the existing multivariate relationships between simultaneously analyzed time series. A short data sliding windows that tracts fast changes in the brain signals with a size of 128 points (256 ms) was consecutively shifted by 32 points (64 ms) to calculate a cross-spectral power density matrix, which allowed us to translate time domain into a frequency domain. Schwarz's Bayesian Criterion (SBC) was then used

to estimate the model order $p$, which was used due to its superiority over other methods [15].

The statistical significance of nonzero PDC values at each frequency domain was obtained using a bootstrap approach based on a Theiler algorithm to discriminate between noise induced randomness and as a deterministic measurement of data connectivity. The MVAR model coefficients were drawn from 20 different signal realizations, with a 99% level of significance being employed as the rule for rejecting a value that occurred by chance.

### C. Statistical Test and Classification

The mean, maximum and minimum values of PSD from each electrode's location in each EEG frequency band were taken to evaluate their strength in detecting FOG. Only features with a $p$-value of $<0.05$, as computed by the non parametric Wilcoxon Sum Rank Test were chosen for this test. A three layer Back Propagation Neural Networks with 4 to 5 hidden nodes were used as a classifier with early stopping that helped prevent over-fitting and improved generalization. Using Levenberg Marquardt's algorithm, 59% of the data were trained, validated and tested by 25% and 19 % of the total data. The prediction of sensitivity, specificity and accuracy were measured based on mean squared prediction errors. The average and standard deviation of 20 training and testing data were recorded for further analysis.

## III. RESULT AND DISCUSSION

Table 1 shows the power spectral density results between periods of normal turning and periods of freezing turning, with smaller $p$-values indicating stronger feature differences between the two conditions. The strongest significant differences between the two conditions were found in the beta bands of the occipital areas O1 and O2 ($p \leq 0.0001$). In addition, these results also showed that the parietal areas P3 and P4 were significantly affected by freezing in the theta, alpha, and high beta frequency bands ($p \leq 0.0005$).

This finding is supported by the inter-region BEC analysis [Fig. 2(A)], in which we found a significant increase of information flow toward the occipital areas from the three other areas (P $\rightarrow$ O, C $\rightarrow$ O, F $\rightarrow$ O). This indicates the freezers are 'over-relying' on visual information during a turning freeze. One can argue that patients adopt this strategy to compensate for a loss of kinaesthetic feedback [16], and especially during a FOG episode their feedback from the muscles and joints are a lot different than what they expected. Therefore freezers might need to use more of their visual system to gain information about what is happening so that Cz is able to come up with a motor plan again [16]. As an addition, the trouble of integrating visual information into a motor plan often associated with parietal regions, which were also significantly affected in all the frequency bands of interest except low beta [17]. Finally, the decreased information flow between the frontal regions (F3, Fz and F4) and right parietal regions P4 [Figs. 2(B) and 3] could indicate a loss of attention [18].

TABLE I

CORRELATION ANALYSIS OF NORMALIZED POWER SPECTRAL DENSITY BETWEEN NORMAL TURNING AND FREEZING TURNING

| Lead | Freq. | Normal Turning | Freezing Turning | $p$-value |
|---|---|---|---|---|
| F3 | $\theta$ | 0.0324 ± 0.0183 | 0.0291 ± 0.0177 | 0.1029 |
| | $\alpha$ | 0.0231 ± 0.0124 | 0.0210 ± 0.0117 | 0.1036 |
| | low $\beta$ | 0.0116 ± 0.0060 | 0.0108 ± 0.0051 | 0.2980 |
| | high $\beta$ | 0.0044 ± 0.0060 | 0.0044 ± 0.0024 | 0.0010 |
| Fz | $\theta$ | 0.0296 ± 0.0129 | 0.0267 ± 0.0136 | 0.0349 |
| | $\alpha$ | 0.0214 ± 0.0092 | 0.0194 ± 0.0093 | 0.0366 |
| | low $\beta$ | 0.0110 ± 0.0049 | 0.0102 ± 0.0043 | 0.1669 |
| | high $\beta$ | 0.0035 ± 0.0019 | 0.0041 ± 0.0021 | 0.0131 |
| F4 | $\theta$ | 0.0506 ± 0.0281 | 0.0462 ± 0.0303 | 0.0318 |
| | $\alpha$ | 0.0355 ± 0.0180 | 0.0328 ± 0.0199 | 0.0244 |
| | low $\beta$ | 0.0169 ± 0.0071 | 0.0160 ± 0.0080 | 0.0397 |
| | high $\beta$ | 0.0054 ± 0.0062 | 0.0052 ± 0.0028 | 0.0645 |
| Cz | $\theta$ | 0.0271 ± 0.0114 | 0.0230 ± 0.0110 | 0.0017 |
| | $\alpha$ | 0.0198 ± 0.0084 | 0.0169 ± 0.0075 | 0.0033 |
| | low $\beta$ | 0.0105 ± 0.0047 | 0.0094 ± 0.0036 | 0.0779 |
| | high $\beta$ | 0.0040 ± 0.0023 | 0.0048 ± 0.0024 | 0.0020 |
| P3 | $\theta$ | 0.0330 ± 0.0152 | 0.0264 ± 0.0108 | $\leq$0.0001 |
| | $\alpha$ | 0.0238 ± 0.0095 | 0.0200 ± 0.0070 | 0.0001 |
| | low $\beta$ | 0.0125 ± 0.0041 | 0.0120 ± 0.0034 | 0.4643 |
| | high $\beta$ | 0.0058 ± 0.0036 | 0.0082 ± 0.0044 | $\leq$0.0001 |
| P4 | $\theta$ | 0.0292 ± 0.0136 | 0.0234 ± 0.0106 | 0.0002 |
| | $\alpha$ | 0.0213 ± 0.0093 | 0.0176 ± 0.0070 | 0.0005 |
| | low $\beta$ | 0.0116 ± 0.0046 | 0.0107 ± 0.0036 | 0.0967 |
| | high $\beta$ | 0.0061 ± 0.0042 | 0.0079 ± 0.0042 | $\leq$0.0001 |
| O1 | $\theta$ | 0.0455 ± 0.0321 | 0.0492 ± 0.0318 | 0.1645 |
| | $\alpha$ | 0.0328 ± 0.0190 | 0.0381 ± 0.0193 | 0.0013 |
| | low $\beta$ | 0.0200 ± 0.0080 | 0.0284 ± 0.0120 | $\leq$0.0001 |
| | high $\beta$ | 0.0217 ± 0.0192 | 0.0359 ± 0.0222 | $\leq$0.0001 |
| O2 | $\theta$ | 0.0455 ± 0.0240 | 0.0425 ± 0.0255 | 0.1391 |
| | $\alpha$ | 0.0330 ± 0.0139 | 0.0335 ± 0.0156 | 0.4778 |
| | low $\beta$ | 0.0198 ± 0.0067 | 0.0255 ± 0.0110 | $\leq$0.0001 |
| | high $\beta$ | 0.0183 ± 0.0142 | 0.0302 ± 0.0190 | $\leq$0.0001 |

Freq.: Frequency

In the classification analysis where we used input from one channel at a time [Table 2], the occipital channel appeared to be providing the best information for detecting a turning freeze with the sensitivity and accuracy of testing data being 74.61 % and 68.63 %, higher relatively to the classification result obtained from the other locations of interest. These results support the previous finding of the significant alteration of power spectral and information flow in the visual cortex.

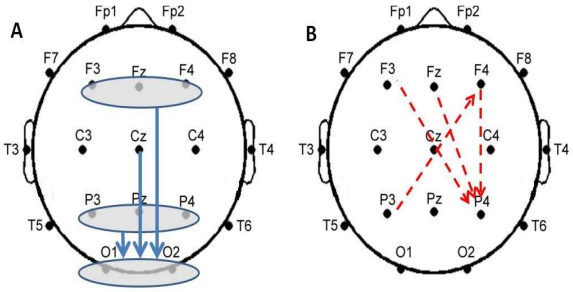


Fig. 2. The significant alteration of information flow during turning freezing (A) between region and (B) intra-frontoparietal region estimated using sGPDC causality. The regional analysis reveals an increase of information flow to occipital area while the fronto-parietal analysis shows a decrease of information flow affected right region of parietal and frontal.

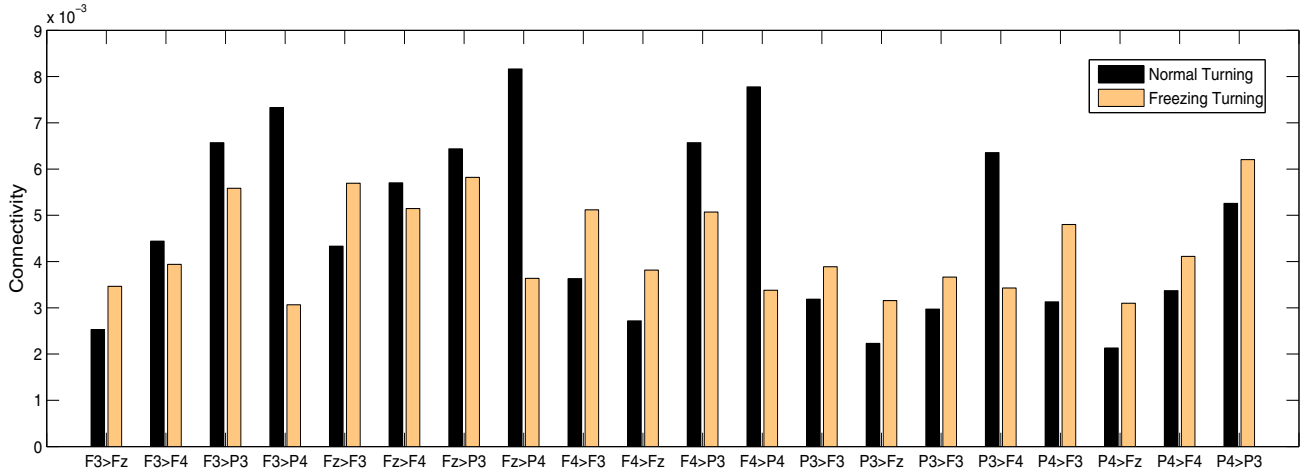


Fig. 3. Frontoparietal sGPDC causality.

TABLE II

CLASSIFICATION RESULTS OF PSD FEATURES USING MLP-NN IN DETECTING TURNING FREEZING

| Lead | Training | | | Testing | | |
|---|---|---|---|---|---|---|
| | Sens % | Spec % | Acc % | Sens % | Spec % | Acc % |
| F3 | 65.32 | 50.79 | 70.98 | 63.78 | 48.99 | 66.27 |
| Fz | 69.51 | 47.14 | 64.22 | 68.22 | 48.38 | 62.35 |
| F4 | 71.00 | 44.99 | 69.02 | 67.74 | 43.65 | 65.39 |
| Cz | 66.79 | 57.65 | 69.80 | 60.40 | 47.72 | 60.00 |
| P3 | 61.62 | 51.92 | 70.39 | 60.92 | 48.07 | 66.27 |
| P4 | 68.90 | 53.75 | 70.00 | 69.98 | 44.20 | 69.22 |
| O1 | 76.88 | 50.62 | 71.08 | 74.61 | 48.43 | 68.63 |
| O2 | 66.27 | 53.84 | 66.37 | 64.61 | 50.56 | 62.35 |

Sens: Sensitivity; Spec: Specificity; Acc: Accuracy

## IV. CONCLUSIONS

While frontoparietal processing is known to be associated with directing attention and integrating visual information into a motor plan, in this study we found that the occipital area was more affected during a turning freeze. The results of a classification system using data from one location only also suggests that this visual cortex region is the optimal reference location for the detection of a turning freeze, whilst also providing possible insights into the neural processes underlying freezing of gait during turning. Further studies using larger cohorts of patients are needed to further validate this finding. Using combination of input data from different locations instead of using a single channel can be expected to increase the performance of the system. Finally, the application of this novel observation in more advanced feature extraction and classifier systems will provide a better performance of the FOG detection system.

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