# Detection of Freezing of Gait in Patients with Parkinson's Disease using Electroencephalography and Computational Intelligence

**By**

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# Certificate of Authorship/Originality

I, Aluysius Maria Ardi Handojoseno, certify that the work in this thesis has not previously been submitted for a degree, nor has it been submitted as part of the requirements of a degree, except as fully acknowledged within the text.

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*“Teach us to give and not to count the cost”*

*St. Ignatius Loyola*

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# Nomenclature

| | | |
|---|---|---|
| 3D-SSP | : | 3-dimensional Stereotactic Surface Projections |
| AD | : | Alzheimer Disease |
| ANN | : | Artificial Neural Networks |
| APSD | : | Auto-Power Spectral Densities |
| AR | : | Autoregressive |
| BA | : | Brodmann Area |
| BSS | : | Blind Source Separation |
| CPSD | : | Cross Power Spectral Density |
| CS | : | Centroid Scale |
| CWT | : | Continuous Wavelet Transform |
| DALY | : | Disability Adjusted Life Years |
| dDTF | : | Direct Directed Transfer Function |
| DNN | : | Dynamic Neural Network |
| DSM-IV | : | Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition |
| DTF | : | Directed Transfer Function |
| DWT | : | Discrete Wavelet Transforms |
| EEG | : | Electroencephalography |
| EMG | : | Electromyography |
| EOG | : | Electrooculography |
| ffDTF | : | Full Frequency Directed Transfer Function |
| FFT | : | Fast Fourier Transform |
| FI | : | Freeze Index |
| fMRI | : | Function Magnetic Resonance Imaging |
| FOG | : | Freezing of Gait |
| FOG-Q | : | Freezing of Gait Questionnaire |
| H&Y | : | Hoehn and Yahr |

| | | |
|---|---|---|
| ICA | : | Independent Component Analysis |
| MEG | : | Magnetoencephalography |
| MGAP | : | Microbe Genome Annotation Platform |
| MLP-NN | : | Multi Layer Perceptron Neural Networks |
| MMSE | : | Mini Mental State Examination |
| MRP | : | Movement-Related potentials |
| MSC | : | Magnitude Squared Coherence |
| MVAR | : | Multivariate Autoregressive |
| NFOG-Q | : | New Freezing of Gait Questionnaire |
| PCA | : | Principle Components Analysis |
| Pcc | : | Pearson's Correlation Coefficient |
| PD | : | Parkinson's Disease |
| PDC | : | Partial Directed Coherence |
| PLV | : | Phase Locking Value |
| PSD | : | Power Spectral Density |
| PSE | : | Power Spectral Entropy |
| PWF | : | Patient with PD with FOG |
| PWoF | : | Patient with PD without FOG |
| PWP | : | Patient with PD |
| RAS | : | Rhythmic Auditory Stimulation |
| ROI | : | Region of Interest |
| RT | : | Reaction Time |
| SCF | : | Spectral Centroid Frequency |
| sGPDC | : | Squared Generalized Partial Directed Coherence |
| SMA | : | Supplementary Motor Area |
| SPECT | : | Single Photon Emission Computed Tomography |
| TUG | : | Timed Up and Go |
| UPDRS | : | Unified Parkinson's Disease Rating Scale |
| VBM | : | Voxel-Based Morphometry |
| WCO | : | Wavelet Coherence |
| WCS | : | Wavelet Cross Spectrum |
| WE | : | Wavelet Energy |
| WEE | : | Wavelet Energy Entropy |
| WPLI | : | Weighted Phase Lag Index |
| WPS | : | Wavelet Power Spectrum |

# Abstract

Freezing of Gait (FOG) is a common movement disorder affecting patients with Parkinson's disease in the advanced stage. Patients often describe it as feeling like their feet are "glued to the floor" which suppresses their ability to start walking or to continue moving forward. It significantly affects patients' quality of life since the sudden and unpredictable characteristic of FOG is a common cause of falls and related injuries. It interferes with daily activities, and leads to a loss of independence. Freezing of gait is mainly perceived as an alteration in the pattern of movement, and the accelerometer, which senses movement, speed and direction, can be used as the main sensor in the detection of FOG in research studies.

Although the accelerometer has been successfully applied in the detection of FOG, it is only able to detect FOG as it occurs, which is often too late for prevention of injuries such as falls. The research in this thesis introduces electroencephalography (EEG) as a novel technique to address this problem. The EEG provides a window to see the transition episode *before* a freezing episode. Freezing of gait occurs as a result of complex, dynamic neurophysiology in the brain related to motor control as well as cognition and emotions, and the EEG signal can capture the electrical activity of the brain while this is occurring. In addition, scalp EEG has many other benefits, such as its portability, non-invasive nature, relative inexpensive cost and simple operation, whilst providing high precision in time measurements.

The study examined 16 patients (age 70.88 $\pm$ 6.92 years) with idiopathic Parkinson's disease and significant FOG, consisted of 9 patients at Hoehn and Yahr (H&Y) stages 2 and 2.5 - the early stages (56.25%), 5 patients at stage 3 - the moderate stage (31.25%), and

2 patients at stage 4 - the advanced stage (12.5%). This research studied the various features of EEG which can be used as indicators of FOG and aims to introduce the effective features as inputs for the FOG.

The first analysis was based on the classical power spectral density (extracted using Fast Fourier Transform) and its counterpart (extracted using wavelet transform). By using centroid frequency extracted from channel central zero (Cz) as input and artificial neural network as the classifier, the classification of two episodes (normal walking and 5 s transition before freezing) in the in-group was obtained with a sensitivity, specificity and accuracy of 77.0%, 74.1% and 79.5%, respectively.

The second analysis studied the cross correlation and coherence based features, aiming to improve the performance of the FOG detection and to obtain a better understanding of FOG. These features provide spatial properties of EEG which complement the time-frequency characterization gained from classical power spectral analysis.

Beyond correlation of two brain locations, in the third analysis, the brain connectivity dynamic analysis was explored further using the analysis of the causal influence between the brain locations of interest. A squared Generalized Partial Directed Coherence was used to evaluate this causal connectivity. This approach modelled effectively the inherently multivariate nature of neuronal networks. All the features were investigated with clinical EEG data. After the optimization using Independent Component Analysis and Bayesian regularization, and applying squared Generalized Partial Directed Coherence connectivity estimation, in the in-group the classifier achieved a sensitivity, specificity and accuracy of 89.1%, 91.2%, and 90.2% , respectively. The results in the out-group were relatively similar with a sensitivity, specificity and accuracy of 86.5%, 92.8% and 89.5%, respectively.

In addition, the physiology analysis provided the characterization of FOG. Beta oscillations in central lead were found to underlie the neural activity in transition to the freezing episode in power spectral measurement. In coherence study, pairwise frontocentral showed significant change, especially in the theta frequency. Effective connectivity also showed significant alteration on the causality measurement in this area. This finding lead

to the development of the predicted mechanism underlying FOG.

In summary, the techniques proposed in this dissertation contribute to the development of the detection system of FOG that can be used by patients with PD to improve their symptoms with satisfactory classification performance. In addition, the results of the experiment provide the electrophysiological signature of FOG in PD lead to novel insights into the pattern of spatiotemporal dynamic of the brain underlying this debilitating symptom of PD.