Resting-State Electroencephalogram Biomarkers of Cognitive Impairment in Parkinson's Disease: A Theory-Driven Predictive and Interpretable Modeling Study

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Parkinson's Disease (PD) is a chronic neurodegenerative disorder affecting ~12 million worldwide, causing >329,000 deaths annually, with 80% of cases strongly influenced by cognitive impairment and PD dementia (PDD). Cognitive dysfunction eventually impacts ~80% of individuals with PD, with an 8-year cumulative PDD prevalence of ~78% and mortality rates 3–4× higher than controls. Current subjective cognitive assessment is insensitive, detecting only ~25% of mild impairment cases. This study presents a novel, theory-driven machine learning framework, leveraging biological resting-state electroencephalogram (EEG) features and model interpretability to detect cognitive impairment in PD. Resting-state EEG recordings from 149 participants (100 PD, 49 healthy controls) were analyzed. Cognitive status was assessed using the MoCA. EEG signals (2–5 minutes) were preprocessed and decomposed into neurophysiologically and statistically significant spectral (1-45 Hz), time–frequency, connectivity, entropy, and microstate-based features using PSD, FFT, DWT, and functional connectivity metrics. These features correspond to cognitive domains and known neural processes, such as frontal control, network coupling/synchronization, slowing rhythms, and microstate instability. Predictive models were trained to distinguish impaired from unimpaired subjects. Repeated 5×5-fold cross-validation had a mean AUC of 0.81 and an accuracy of 73% using 5 features. The maximum fold-level performance was an AUC of .96 with 85% accuracy. Interpretability analyses revealed the frequency bands, cortical regions, and network interactions driving predictions, showing that theory-driven EEG features can be biologically interpretable biomarkers of cognitive impairment in PD with translational relevance.

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