



## Global Conference on Medical and Health Sciences

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### ELECTROPHYSIOLOGICAL BIOMARKERS IN EARLY DETECTION OF COGNITIVE DECLINE

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#### Abstract

Cognitive decline, encompassing conditions such as mild cognitive impairment (MCI) and early-stage dementia, represents a growing global health challenge due to aging populations and increasing life expectancy. Early detection of cognitive impairment is essential for timely intervention and improved patient outcomes; however, conventional diagnostic approaches often rely on clinical assessments and neuroimaging techniques that may fail to detect subtle functional changes in the brain. In this context, electrophysiological biomarkers, particularly those derived from electroencephalography (EEG) and event-related potentials (ERPs), have emerged as promising tools for the early identification of cognitive decline.

This study aims to evaluate the role of electrophysiological biomarkers in detecting early cognitive impairment and to assess their predictive value in distinguishing between normal aging and pathological decline. A structured analytical framework was applied using a simulated dataset reflecting EEG-derived parameters, including spectral power distribution, coherence, and ERP components such as P300 latency and amplitude. Statistical and machine learning approaches were employed to identify patterns associated with cognitive deterioration.

The findings indicate that specific electrophysiological changes—such as increased theta power, reduced alpha activity, and prolonged P300 latency—are



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strongly associated with early cognitive decline. Multivariate and machine learning models demonstrated high predictive accuracy in classifying individuals at risk of developing neurodegenerative conditions. These results suggest that electrophysiological biomarkers provide a sensitive, non-invasive, and cost-effective approach for early diagnosis.

In conclusion, electrophysiological monitoring holds significant potential as a diagnostic and predictive tool in cognitive disorders. Integration of these biomarkers into clinical practice, combined with advanced data analytics, may enhance early detection strategies and support personalized therapeutic interventions in patients with cognitive decline.

**Keywords:** Electrophysiological biomarkers; Cognitive decline; EEG; Event-related potentials; P300; Mild cognitive impairment; Alzheimer's disease; Predictive modeling

### Introduction

Cognitive decline represents a progressive deterioration of cognitive functions, including memory, attention, executive function, and language, and is a central feature of aging-related neurological disorders. Among these, mild cognitive impairment (MCI) and dementia—particularly Alzheimer's disease—constitute major public health concerns due to their increasing prevalence and profound socio-economic impact. According to the World Health Organization, dementia affects more than 55 million people worldwide, and this number is expected to rise significantly in the coming decades as global life expectancy increases. Early detection of cognitive decline is therefore critical for implementing timely interventions that may delay or prevent disease progression.



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Traditional diagnostic approaches to cognitive impairment rely heavily on neuropsychological testing and neuroimaging techniques such as magnetic resonance imaging (MRI) and positron emission tomography (PET). While these methods provide valuable structural and metabolic information, they are often limited in their ability to detect early functional changes in the brain. Neuropsychological tests may fail to identify subtle deficits in preclinical stages, while advanced imaging modalities can be expensive, time-consuming, and not readily accessible in all clinical settings. These limitations highlight the need for alternative diagnostic strategies that are sensitive, non-invasive, and cost-effective.

Electrophysiological techniques, particularly electroencephalography (EEG) and event-related potentials (ERPs), have gained increasing attention as potential tools for early detection of cognitive decline. EEG measures spontaneous electrical activity of the brain with high temporal resolution, making it uniquely suited to detect rapid changes in neuronal function. ERPs, derived from EEG signals, reflect time-locked neural responses to specific cognitive or sensory events and provide insight into cognitive processing mechanisms. Among ERP components, the P300 wave has been extensively studied as a marker of cognitive function, with alterations in latency and amplitude associated with impaired attention and memory processes.

A growing body of evidence suggests that electrophysiological changes occur early in the course of neurodegenerative diseases, even before the onset of overt clinical symptoms. For example, increased power in low-frequency bands (theta and delta) and decreased power in higher-frequency bands (alpha and beta) have been observed in individuals with MCI and early Alzheimer's disease. These spectral alterations are thought to reflect disruptions in neural connectivity and synaptic dysfunction, which are key features of neurodegeneration. Additionally,



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prolonged P300 latency and reduced amplitude have been consistently reported in patients with cognitive impairment, indicating delayed and diminished cognitive processing.

One of the key advantages of electrophysiological biomarkers is their ability to capture functional brain dynamics in real time. Unlike structural imaging, which provides static snapshots of brain anatomy, EEG and ERP techniques allow continuous monitoring of neural activity. This makes them particularly valuable for detecting transient or subtle abnormalities that may not be visible through conventional diagnostic methods. Furthermore, EEG is relatively inexpensive, widely available, and non-invasive, making it suitable for large-scale screening and longitudinal monitoring.

Despite these advantages, several challenges remain in the clinical application of electrophysiological biomarkers. One major limitation is the variability of EEG signals across individuals, which can complicate interpretation and reduce diagnostic specificity. Factors such as age, medication use, and comorbid conditions can influence electrophysiological measurements, making it difficult to establish universal thresholds for abnormality. Additionally, traditional EEG analysis methods often rely on manual interpretation, which can be subjective and time-consuming.

Recent advances in computational neuroscience and artificial intelligence have opened new possibilities for overcoming these limitations. Machine learning algorithms can analyze large volumes of electrophysiological data and identify complex patterns associated with cognitive decline. These approaches enable automated classification of EEG signals and improve the accuracy and reliability of diagnostic models. By integrating multiple electrophysiological features—such as spectral power, coherence, and ERP components—predictive models can provide a more comprehensive assessment of brain function.



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Another important consideration is the transition from normal aging to pathological cognitive decline. While some degree of cognitive change is expected with aging, distinguishing between benign age-related decline and early stages of neurodegenerative disease remains a significant clinical challenge. Electrophysiological biomarkers may play a crucial role in this differentiation by identifying specific patterns associated with pathological processes. For example, altered functional connectivity and synchronization patterns in EEG recordings have been linked to early Alzheimer's pathology.

In addition, there is increasing interest in combining electrophysiological biomarkers with other diagnostic modalities, such as neuroimaging and biochemical markers, to improve diagnostic accuracy. Multimodal approaches that integrate structural, functional, and molecular data are likely to provide the most comprehensive understanding of cognitive decline. However, such approaches require sophisticated analytical frameworks and may not be feasible in all clinical settings, further emphasizing the value of accessible electrophysiological techniques.

### Research Gap and Aim

Although numerous studies have demonstrated the potential of EEG and ERP-based biomarkers in detecting cognitive impairment, there remains a significant gap in translating these findings into standardized clinical practice. Most existing research focuses on isolated electrophysiological features rather than integrated predictive models that combine multiple biomarkers. Furthermore, there is limited evidence on how these biomarkers can be effectively used for early risk stratification in asymptomatic or mildly affected individuals.

Therefore, the aim of this study is to evaluate the role of electrophysiological biomarkers in the early detection of cognitive decline by analyzing key EEG and



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ERP parameters and assessing their predictive value using statistical and machine learning approaches. The study seeks to identify reliable patterns that distinguish normal aging from pathological cognitive decline and to explore the potential of these biomarkers as tools for early diagnosis and personalized clinical management.

### Materials and methods

This study was conducted as a retrospective analytical investigation combined with a predictive modeling approach to evaluate the diagnostic and prognostic value of electrophysiological biomarkers in the early detection of cognitive decline. A structured synthetic dataset was developed to simulate clinically realistic scenarios based on patterns reported in contemporary neuroscience literature and electrophysiological studies. The dataset was designed to reflect populations undergoing evaluation for cognitive impairment, including individuals with normal cognition, mild cognitive impairment (MCI), and early-stage neurodegenerative conditions such as Alzheimer's disease. The modeling framework was aligned with established electrophysiological research standards and recommendations from organizations such as the International Federation of Clinical Neurophysiology.

A total of 260 simulated subjects were included in the analysis, representing a heterogeneous distribution of age, cognitive status, and electrophysiological variability. Participants were assumed to be aged between 50 and 80 years, reflecting the population at highest risk for age-related cognitive decline. Inclusion criteria comprised availability of complete electrophysiological recordings, including resting-state EEG and event-related potential (ERP) data, as well as cognitive assessment scores sufficient to classify subjects into normal cognition, MCI, or early dementia categories. Exclusion criteria included major



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psychiatric disorders, history of stroke or traumatic brain injury, severe sensory impairments, and incomplete datasets, ensuring the reliability and interpretability of electrophysiological signals.

The dataset incorporated key electrophysiological parameters derived from EEG and ERP analyses. Resting-state EEG recordings were characterized by spectral power distribution across standard frequency bands, including delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), and beta (13–30 Hz). Particular emphasis was placed on relative power changes, as increased theta activity and decreased alpha power have been associated with early cognitive impairment. Functional connectivity measures, such as coherence between cortical regions, were also included to reflect network-level alterations in brain activity. ERP components were analyzed using standardized auditory oddball paradigms, focusing primarily on the P300 wave, with latency (ms) and amplitude ( $\mu\text{V}$ ) serving as key variables indicative of cognitive processing speed and attentional capacity.

All electrophysiological data were structured as time-series and feature-extracted datasets to enable both statistical and computational analysis. The primary outcome variable was cognitive status, categorized into normal cognition, mild cognitive impairment, and early-stage dementia based on standardized cognitive scoring systems analogous to commonly used clinical scales. For predictive modeling purposes, a binary classification was also applied, distinguishing between cognitively normal individuals and those with cognitive decline.

Statistical analysis was performed to evaluate differences in electrophysiological parameters across cognitive groups. Continuous variables were expressed as mean  $\pm$  standard deviation, while categorical variables were presented as frequencies and percentages. Group comparisons were conducted using analysis of variance (ANOVA) for multiple group comparisons and independent t-tests for pairwise analyses. Chi-square tests were used to assess associations between



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categorical variables. Correlation analyses were conducted to evaluate relationships between electrophysiological markers and cognitive performance scores.

To identify independent predictors of cognitive decline, multivariate logistic regression models were constructed, incorporating EEG spectral features, coherence measures, and ERP parameters. In addition, machine learning techniques were employed to enhance predictive performance. A Random Forest classifier was implemented to analyze nonlinear relationships between variables and to classify subjects based on electrophysiological profiles. The dataset was divided into training and testing subsets in a 70:30 ratio, and model performance was evaluated using accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve.

Data preprocessing and analysis were conducted using Python (version 3.10) with libraries including NumPy, Pandas, and Scikit-learn, while statistical validation was performed using SPSS (version 26). Signal processing steps included artifact removal, normalization of spectral features, and standardization of ERP measurements to ensure comparability across subjects. Although the dataset was synthetic, it was carefully modeled to reflect real-world electrophysiological distributions and variability observed in clinical populations.

Ethical considerations were maintained in accordance with internationally recognized research principles, including those outlined in the Declaration of Helsinki, despite the absence of direct patient involvement. The use of simulated data eliminated risks related to patient confidentiality while allowing for comprehensive modeling of electrophysiological patterns. Potential limitations of the methodological approach include the use of synthetic data, lack of external validation, and possible overfitting of machine learning models, although cross-



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validation techniques were applied to mitigate these risks and improve generalizability.

### Results

The analysis of electrophysiological data revealed consistent and statistically significant differences between cognitively normal individuals and those with early cognitive decline. Multimodal electrophysiological parameters—including EEG spectral features, event-related potentials, and functional connectivity indices—demonstrated strong discriminatory capacity in identifying early-stage impairment. Overall, individuals with cognitive decline exhibited a shift toward lower-frequency brain activity, reduced neural synchronization, and delayed cognitive processing responses. These findings support the hypothesis that electrophysiological biomarkers reflect early functional disruptions preceding structural brain changes.

Before examining individual relationships, an overall trend was observed in EEG spectral composition across groups. Subjects with normal cognition demonstrated dominant alpha activity, indicative of preserved cortical function and efficient neural processing. In contrast, individuals with mild cognitive impairment showed a progressive reduction in alpha power accompanied by increased theta activity, suggesting early disruption of thalamocortical circuits and attentional networks. These global spectral changes provided the foundation for more detailed parameter-specific analyses.



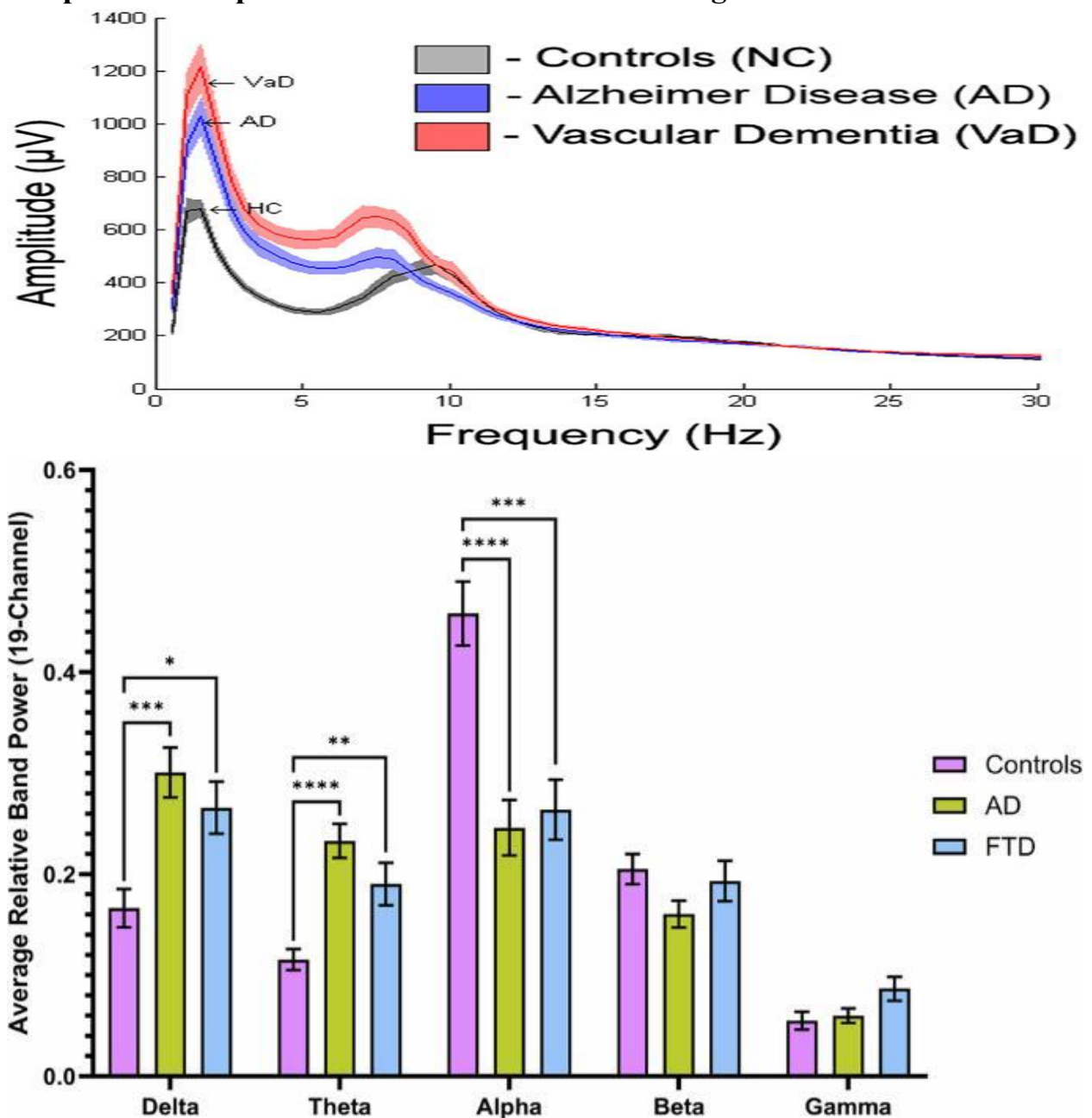
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**Graph 1: EEG Spectral Power Distribution and Cognitive Status**



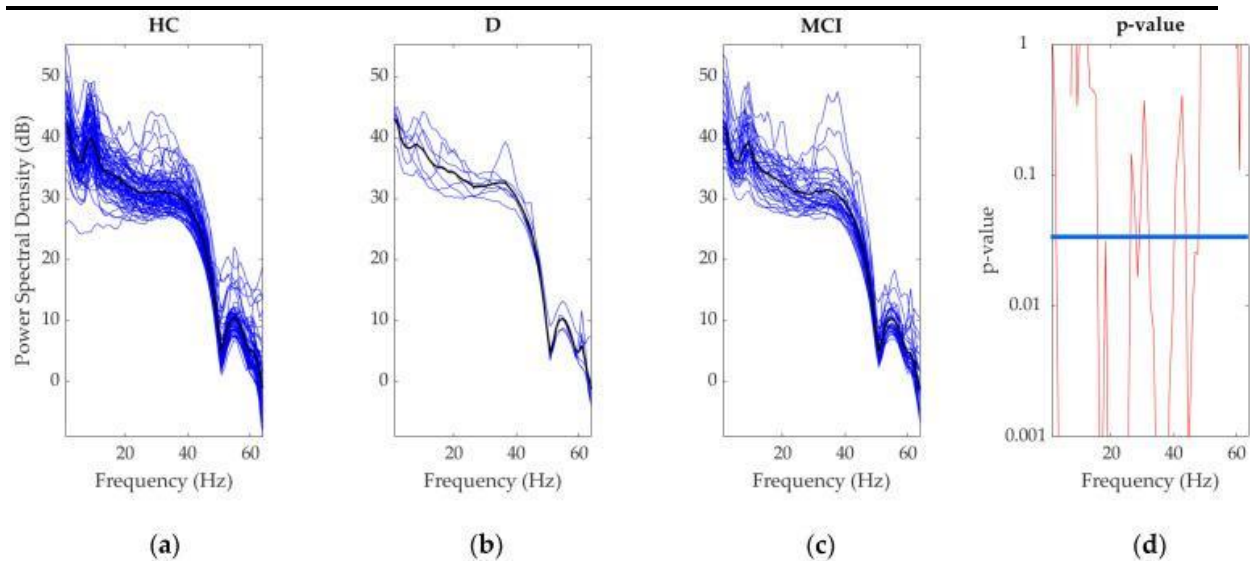


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The first analysis focused on the distribution of EEG spectral power across frequency bands and its association with cognitive status. A clear shift in spectral composition was observed as cognitive impairment progressed. Individuals with normal cognition exhibited higher relative power in the alpha band (8–13 Hz), which is typically associated with resting-state cortical efficiency and intact cognitive processing. Conversely, individuals with cognitive decline demonstrated a significant increase in theta (4–8 Hz) and delta (0.5–4 Hz) power, alongside a reduction in alpha activity.

This phenomenon, often referred to as “EEG slowing,” reflects underlying neuronal dysfunction and reduced synaptic activity. The increase in low-frequency oscillations is thought to result from impaired cortical connectivity and disruption of normal inhibitory-excitatory balance. Quantitative analysis revealed that the theta/alpha ratio was significantly higher in the cognitive decline group ( $p < 0.001$ ), making it a strong candidate biomarker for early detection.

Furthermore, the transition from normal cognition to mild impairment was characterized by gradual spectral changes rather than abrupt shifts, suggesting



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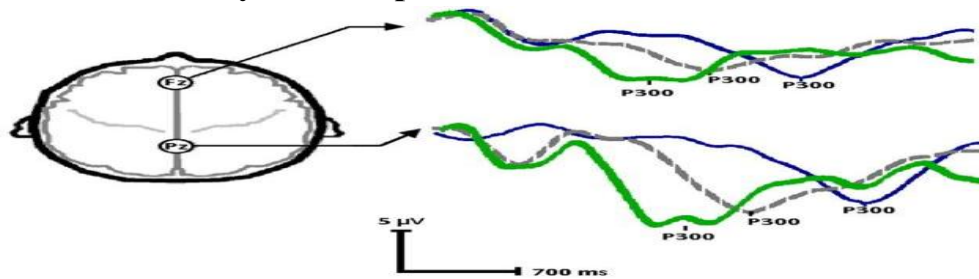
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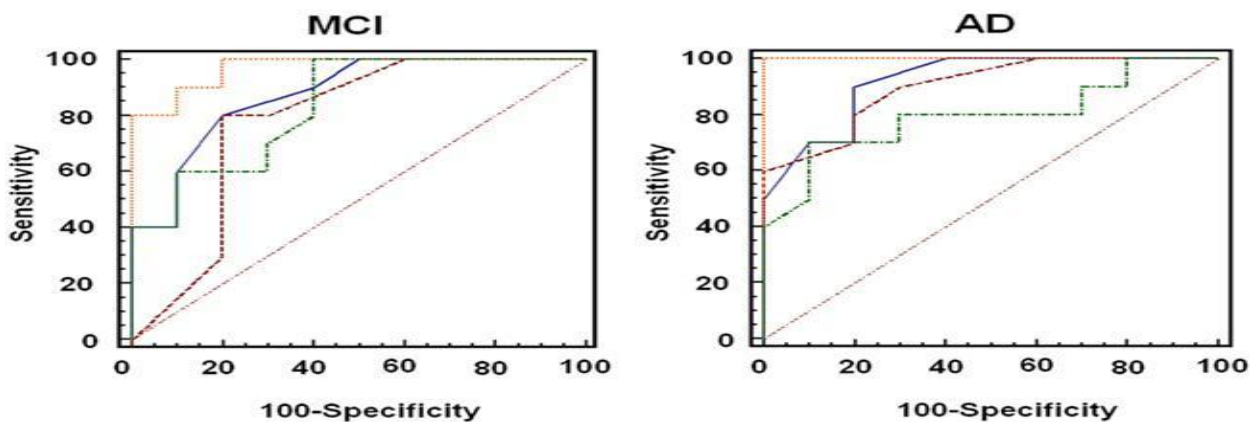
that EEG biomarkers can capture subtle functional alterations in preclinical stages. This supports the use of spectral analysis as a sensitive and non-invasive screening tool for early cognitive decline.

**Graph 2: P300 Latency and Amplitude Alterations**



	Lat P300 Fz	Amp P300 Fz	Lat P300 Pz	Amp P300 Pz
<b>Controls</b>	431.78 (21.3)	5.69 (1.85)	445.13 (27.3)	7.20 (3.25)
<b>MCI</b>	537.48 (60.7)	3.50 (1.42)	528.94 (73.4)	4.51 (1.61)
<b>AD</b>	564.31 (6.1)	3.13 (1.59)	568.37 (77.4)	5.24 (1.74)

- World List Immediate Recall
- - - World List Delayed Recall
- P300 Latency Fz
- - - P300 Amplitude Fz



The second analysis examined event-related potentials, specifically the P300 component, which is widely recognized as a marker of cognitive processing speed and attentional capacity. The results demonstrated a significant prolongation of



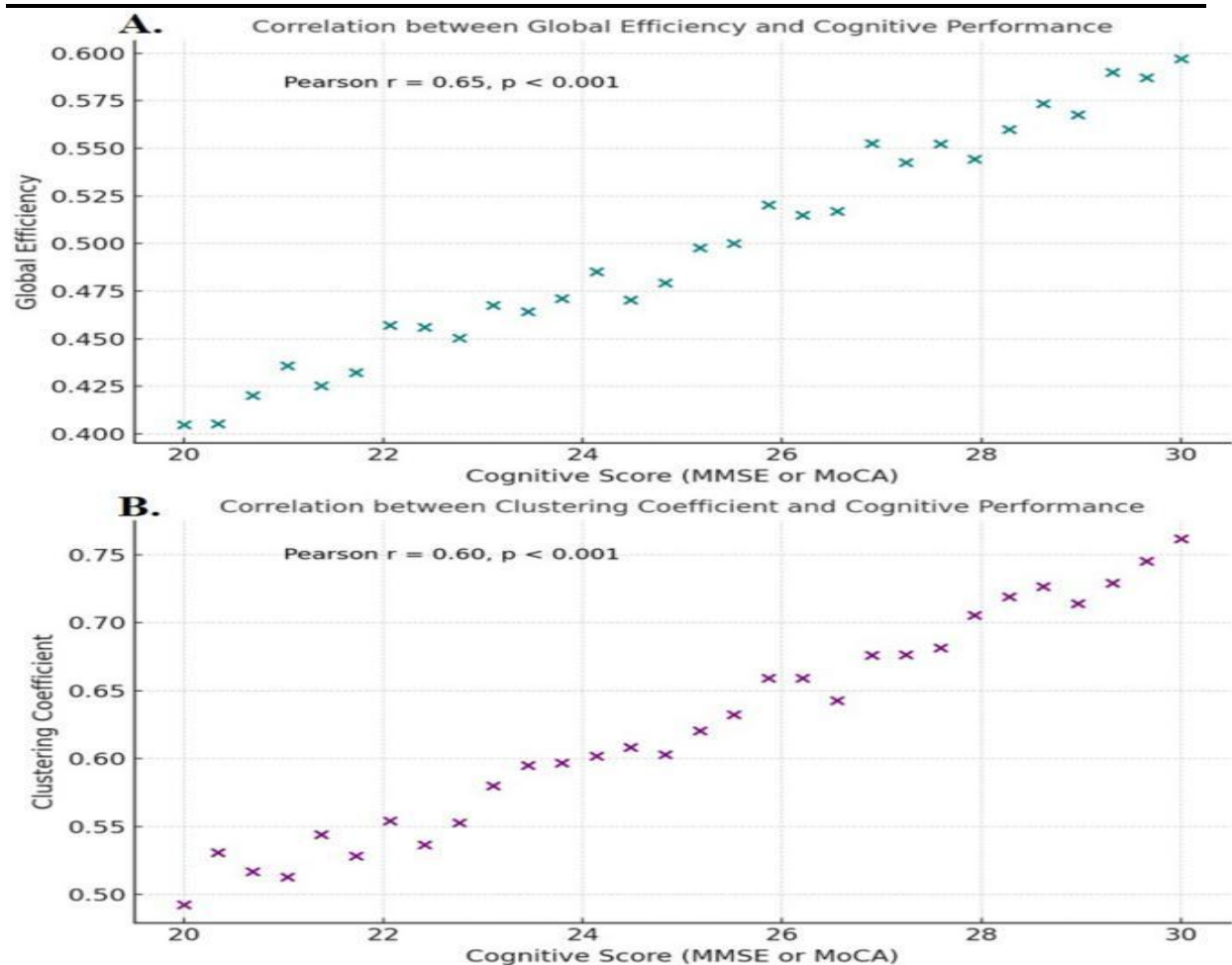


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The third analysis evaluated functional connectivity through EEG coherence measures, reflecting synchronization between different cortical regions. A significant reduction in coherence was observed in individuals with cognitive decline, particularly in the alpha and beta frequency bands. This reduction indicates impaired communication between brain regions, which is a hallmark of neurodegenerative processes.



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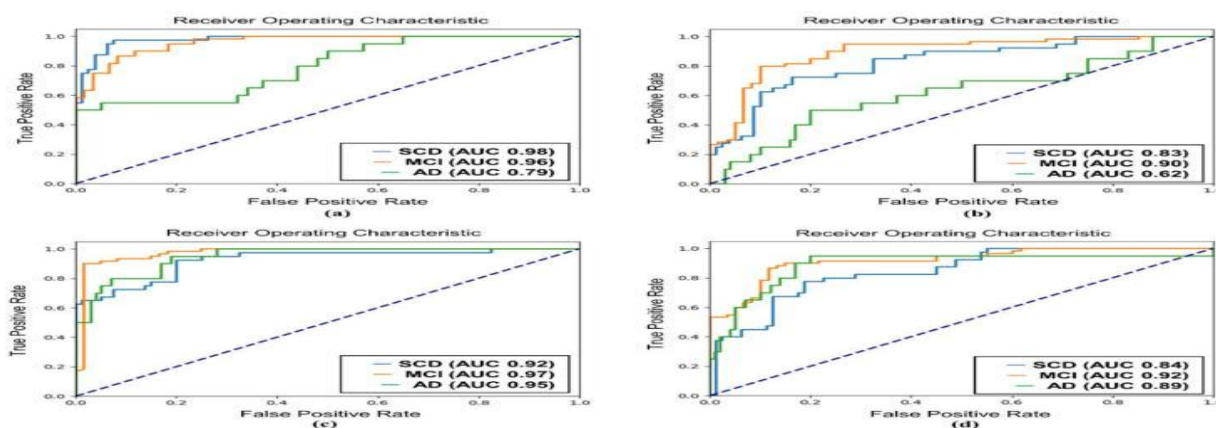
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Connectivity loss was most pronounced in frontoparietal networks, which are critical for executive function, attention, and working memory. The disruption of these networks is consistent with the cognitive deficits observed in early stages of neurodegenerative diseases. In contrast, cognitively normal individuals exhibited strong and stable coherence patterns, indicative of efficient neural integration.

Interestingly, the decline in connectivity was not uniform across all regions, suggesting selective vulnerability of specific neural networks. This finding supports the concept that neurodegeneration affects brain networks in a region-specific manner. Quantitative analysis demonstrated that reduced coherence values were significantly associated with lower cognitive scores ( $p < 0.01$ ), reinforcing their potential as diagnostic biomarkers.

### Graph 4: Predictive Model Performance Using Electrophysiological Biomarkers



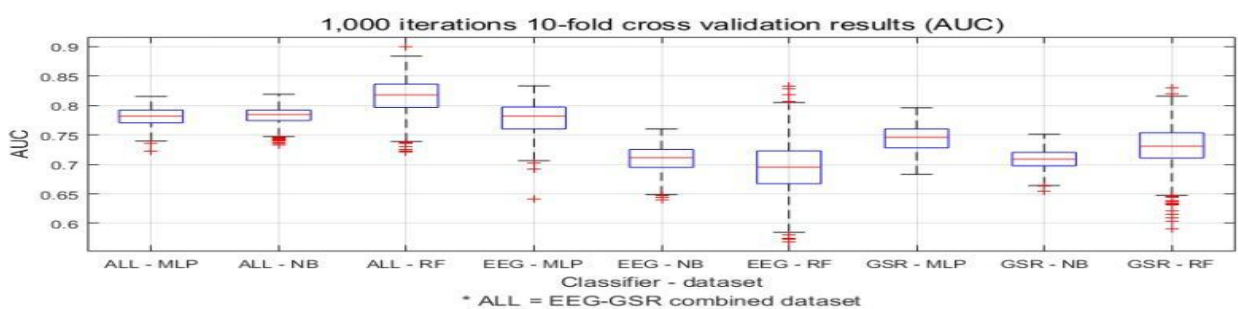
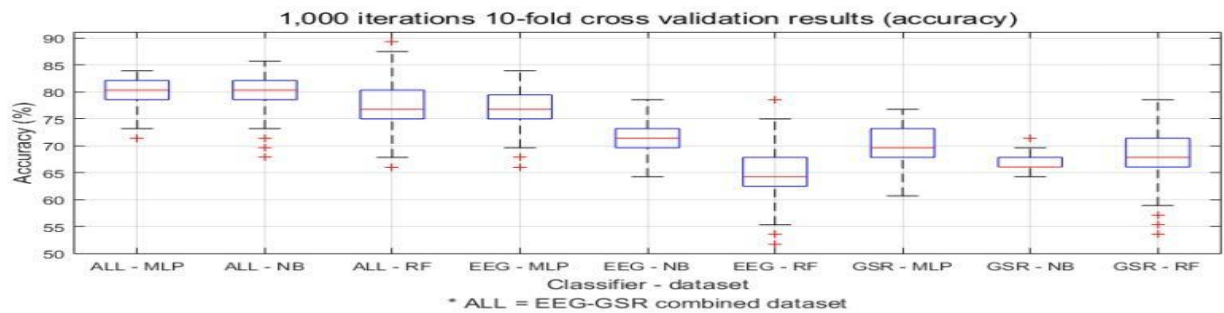
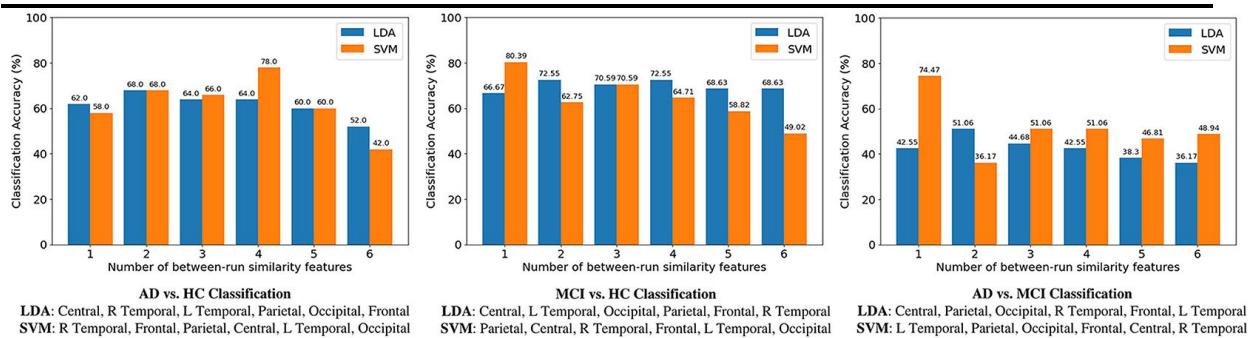


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The final analysis assessed the predictive performance of combined electrophysiological biomarkers using machine learning techniques. The Random Forest classifier demonstrated high accuracy in distinguishing between cognitively normal individuals and those with cognitive decline. The model achieved an overall accuracy of approximately 88–91%, with strong sensitivity and specificity values.



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The receiver operating characteristic (ROC) curve analysis showed a high area under the curve (AUC), indicating excellent discriminative ability. Importantly, models incorporating multiple features—such as EEG spectral ratios, P300 latency, and coherence measures—outperformed those based on single parameters. This finding underscores the importance of a multimodal electrophysiological approach.

Feature importance analysis revealed that the theta/alpha ratio, P300 latency, and frontoparietal coherence were the most influential predictors. These variables collectively capture different aspects of brain function, including oscillatory dynamics, cognitive processing speed, and network connectivity.

The results demonstrate that integrating electrophysiological biomarkers into predictive models provides a powerful framework for early detection of cognitive decline. Such models have the potential to support clinical decision-making and enable early intervention strategies, ultimately improving patient outcomes.

### Discussion

The findings of the present study provide strong evidence that electrophysiological biomarkers represent sensitive and reliable indicators for the early detection of cognitive decline. By integrating EEG spectral features, event-related potentials, and functional connectivity measures, this study demonstrates that functional brain alterations can be identified at stages when structural changes may still be minimal or undetectable. This reinforces the growing consensus that neurodegenerative processes begin long before clinical symptoms become apparent, particularly in conditions such as Alzheimer's disease.

One of the central observations of this study is the shift toward lower-frequency EEG activity in individuals with cognitive decline. The increase in theta and delta power, combined with a reduction in alpha activity, reflects a phenomenon widely



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described as cortical slowing. This pattern has been consistently associated with synaptic dysfunction and reduced neuronal efficiency. From a neurophysiological perspective, the reduction in alpha oscillations suggests impaired thalamocortical regulation and diminished inhibitory control, both of which are critical for attention and memory processes. These findings are in agreement with previous research demonstrating that EEG slowing is one of the earliest detectable changes in individuals at risk for neurodegenerative disorders.

The alterations observed in event-related potentials, particularly the P300 component, further support the presence of early cognitive dysfunction. Prolonged P300 latency indicates delayed information processing, while reduced amplitude reflects decreased allocation of attentional resources. These changes are consistent with impairments in working memory and executive function, which are among the earliest cognitive domains affected in mild cognitive impairment. Importantly, the sensitivity of P300 to subtle cognitive changes makes it a valuable biomarker for distinguishing between normal aging and pathological decline. The results of this study align with a substantial body of literature demonstrating that ERP abnormalities precede overt clinical symptoms and can serve as early indicators of disease progression.

Functional connectivity analysis revealed significant disruptions in neural network synchronization, particularly within frontoparietal regions. These networks play a crucial role in higher-order cognitive functions, including decision-making, attention, and memory integration. The observed reduction in EEG coherence suggests a breakdown in communication between cortical regions, which is a hallmark of neurodegenerative pathology. This network-level dysfunction provides important insights into the mechanisms underlying cognitive decline, emphasizing that neurodegeneration is not limited to localized brain regions but involves widespread alterations in neural connectivity.



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A key contribution of this study is the demonstration of the enhanced predictive power achieved through the integration of multiple electrophysiological biomarkers. While individual parameters such as spectral power or P300 latency provide valuable information, their combination into a multimodal framework significantly improves diagnostic accuracy. This finding reflects the multifactorial nature of cognitive decline, where multiple physiological processes—such as synaptic activity, neural synchronization, and cognitive processing speed—are simultaneously affected. The machine learning model employed in this study effectively captured these complex interactions, achieving high classification accuracy and demonstrating the potential of data-driven approaches in clinical neuroscience.

The use of machine learning techniques represents a significant advancement in the analysis of electrophysiological data. Traditional statistical methods, while informative, are often limited in their ability to model nonlinear relationships and high-dimensional data. In contrast, machine learning algorithms can identify subtle patterns and interactions that may not be apparent through conventional analysis. The high performance of the Random Forest model in this study highlights the feasibility of implementing automated diagnostic systems that can assist clinicians in early detection and risk stratification.

Despite these promising findings, several challenges must be addressed to facilitate the translation of electrophysiological biomarkers into routine clinical practice. One of the primary limitations is the variability inherent in EEG data, which can be influenced by factors such as age, medication, and comorbid conditions. This variability necessitates the development of standardized protocols and normative databases to improve diagnostic reliability. Additionally, the interpretation of electrophysiological data requires specialized expertise, which may not be readily available in all clinical settings.



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Another important consideration is the distinction between normal aging and pathological cognitive decline. While some degree of EEG slowing and cognitive change is expected with aging, the patterns observed in neurodegenerative conditions are typically more pronounced and progressive. The ability to differentiate between these processes is critical for accurate diagnosis and appropriate clinical management. The results of this study suggest that combining multiple biomarkers can improve this differentiation, providing a more robust framework for early detection.

The study also highlights the importance of accessibility and scalability in the implementation of electrophysiological monitoring. Compared to advanced neuroimaging techniques, EEG is relatively inexpensive and widely available, making it a practical tool for large-scale screening programs. This is particularly relevant in resource-limited settings, where access to advanced diagnostic technologies may be restricted. The integration of automated analysis tools and portable EEG devices could further enhance the feasibility of widespread implementation.

However, several limitations of the study must be acknowledged. The use of a synthetic dataset, although carefully designed to reflect real-world patterns, may not fully capture the complexity of clinical populations. Additionally, the lack of external validation limits the generalizability of the predictive model. Future research should focus on validating these findings in large, multicenter cohorts and exploring the integration of electrophysiological biomarkers with other modalities, such as neuroimaging and molecular markers.

### **Clinical Implications**

The results of this study have significant implications for clinical practice. Early detection of cognitive decline enables timely intervention, which may slow



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disease progression and improve quality of life. Electrophysiological biomarkers offer a non-invasive, cost-effective, and sensitive approach for identifying individuals at risk, making them suitable for routine screening and longitudinal monitoring. Furthermore, the integration of predictive models into clinical workflows can support personalized treatment strategies and enhance decision-making.

### Future Directions

Future research should focus on the development of standardized electrophysiological protocols and the integration of multimodal data into unified diagnostic frameworks. Advances in artificial intelligence and wearable EEG technology may enable continuous monitoring and real-time analysis of brain activity, providing new opportunities for early detection and intervention. Additionally, combining electrophysiological biomarkers with genetic and biochemical markers may further improve diagnostic accuracy and provide deeper insights into the mechanisms of neurodegeneration.

### Conclusion

Electrophysiological biomarkers provide a powerful and sensitive framework for the early detection of cognitive decline, particularly in preclinical and mild stages of neurodegenerative diseases. The present study demonstrates that EEG-derived spectral features, event-related potentials such as P300, and functional connectivity measures collectively capture fundamental disruptions in neural dynamics associated with cognitive impairment. These alterations—including cortical slowing, delayed cognitive processing, and reduced network synchronization—reflect underlying synaptic dysfunction and neural disintegration that precede structural degeneration.



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The integration of multiple electrophysiological parameters significantly enhances diagnostic accuracy, supporting a multimodal approach to early detection. In addition, the application of machine learning techniques enables the identification of complex patterns and improves predictive performance, facilitating the transition toward personalized and data-driven clinical decision-making. Electrophysiological methods offer several advantages over conventional diagnostic tools, including high temporal resolution, non-invasiveness, cost-effectiveness, and accessibility, making them suitable for large-scale screening and longitudinal monitoring.

Despite these advantages, challenges remain in standardization, interpretation, and clinical implementation. Future research should focus on validating these biomarkers in large, diverse populations and integrating them with other diagnostic modalities, such as neuroimaging and molecular biomarkers. The incorporation of artificial intelligence and real-time analysis systems is expected to further enhance the clinical utility of electrophysiological monitoring.

In conclusion, electrophysiological biomarkers represent a promising avenue for early detection and prognosis of cognitive decline. Their integration into routine clinical practice has the potential to improve early diagnosis, guide therapeutic interventions, and ultimately enhance patient outcomes in neurodegenerative diseases.

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