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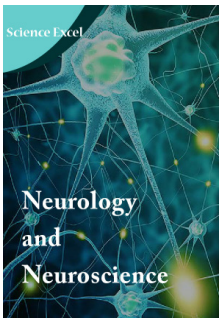

Advancing Clinical Neuroassessment: The BrainView ERP Platform in Schizophrenia

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Abstract

Event-related potentials (ERPs) offer objective insights into brain function, with alterations in components such as the N100, P300, and N400 commonly observed in individuals with schizophrenia. However, scalable, automated ERP-based diagnostic tools remain limited in clinical practice. This study evaluated the diagnostic performance of the BrainView ERP platform in distinguishing individuals with schizophrenia from healthy controls using ERP biomarkers. A total of 334 participants were enrolled, including 94 individuals with clinically diagnosed schizophrenia and 240 age- and sex-matched healthy controls. All participants completed a standardized ERP protocol utilizing visual and semantic oddball paradigms. ERP features (latency and amplitude) from nine scalp regions (Fp1, Fp2, F7, F3, Fz, F4, F8, P3, P4) were recorded and analyzed, with particular focus on P300, N100, and N400 components. A machine learning classifier trained on these features was used to differentiate diagnostic groups. Receiver operating characteristic (ROC) analysis assessed model performance. The BrainView platform achieved a sensitivity of 0.88 and specificity of 0.90, with an area under the ROC curve (AUC) of 0.91, indicating excellent discriminative ability. ERP abnormalities in the schizophrenia group included reduced P300 amplitudes, delayed N400 latencies, and attenuated N100 responses—consistent with deficits in attention, sensory gating, and semantic processing. These results compare favorably with prior studies, confirming BrainView's alignment with established ERP biomarkers. The BrainView ERP platform demonstrates high diagnostic accuracy in identifying schizophrenia, offering an efficient, objective, and scalable tool for neuropsychiatric assessment. By integrating validated ERP biomarkers with machine learning-based classification, BrainView advances the potential for early detection and personalized treatment strategies in clinical psychiatry.

Introduction

Schizophrenia represents a spectrum of chronic, relapsing psychiatric disorders characterized by disturbances in perception, cognition, emotion, and behavior [1]. Decades of neurobiological research have revealed that schizophrenia is associated with widespread disruptions in brain structure and function, particularly in frontotemporal networks involved in sensory integration, working memory, and executive control [2]. Neurodevelopmental and progressive neurodegenerative processes interact to impair synaptic connectivity, myelination, and neurotransmitter regulation, especially in dopaminergic, glutamatergic, and GABAergic pathways, leading to characteristic symptoms such as hallucinations, delusions, cognitive deficits, and negative affect [1,3,4]. Structural neuroimaging consistently demonstrates cortical thinning and volumetric reductions in regions such as the dorsolateral prefrontal cortex, hippocampus, and superior temporal gyrus, which correlate with clinical symptom burden and cognitive impairment [5–7]. However, current diagnostic practices rely heavily on clinical interviews, lacking objective neurophysiological markers to aid early detection or stratification.

Functional abnormalities in schizophrenia are increasingly understood as arising from dysregulated neural oscillations and impaired cortical synchrony [8]. These phenomena can be measured using non-invasive electroencephalography (EEG). Event-related potentials (ERPs) provide a well-established, non-invasive method to assess brain function, yet their clinical adoption has been limited by the absence of scalable, automated platforms. ERPs, time-locked electrophysiological responses to stimuli, have been extensively used to characterize sensory and cognitive deficits in schizophrenia. For example, attenuated N100 and P300 amplitudes are consistently observed in patients and are associated with auditory processing and attentional deficits, respectively [9,10]. The N400 component, often elicited during language and semantic tasks, is also blunted in schizophrenia, reflecting disruptions in semantic integration and higher-order cognition [11,12].

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These electrophysiological signatures are detectable even in early stages of illness and among high-risk populations, making ERPs promising neurophysiological biomarkers for early detection, stratification, and treatment response monitoring [13,14]. Despite their diagnostic and prognostic potential, ERPs remain underutilized in routine clinical care due to barriers in standardization, interpretation, and accessibility [15,16].

To address these challenges, the BrainView ERP Platform (Medeia Inc.) offers a portable, FDA-cleared system that captures and analyzes ERP components with automated, clinically interpretable outputs. Focusing on three key ERPs: N100 (sensory registration), P300 (selective attention), and N400 (semantic processing), BrainView enables rapid, reproducible assessment of neurocognitive function in schizophrenia. Unlike traditional behavioral assessments, which are subjective and prone to variability, ERP recordings provide objective, millisecond-level insight into brain dysfunction, including processes that may be impaired even in the absence of overt clinical symptoms [17]. The BrainView system offers a standardized approach to ERP acquisition and analysis, with potential utility in identifying neurocognitive biomarkers in schizophrenia.

Recent studies demonstrate that ERP abnormalities correlate with symptom severity, cognitive dysfunction, and real-world functioning in schizophrenia [18,19]. For example, reduced P300 amplitude has been linked to poor treatment response and functional outcomes, while N400 abnormalities track deficits in language comprehension and social cognition [20,21]. The ability of BrainView to quantify these electrophysiological disturbances offers a novel avenue for integrating brain-based biomarkers into personalized care models.

By capturing alterations in neural processing with high temporal resolution, BrainView may serve as a critical tool for identifying neurocognitive endophenotypes, evaluating pharmacological effects, and guiding neuromodulatory or cognitive remediation strategies in schizophrenia. Integrating ERP assessment into clinical workflows has the potential to transform the management of schizophrenia from symptom-driven to biologically informed, aligning with the goals of precision psychiatry and brain health optimization.

Methods

Participants

Ten adult male outpatients with a DSM-5 diagnosis of schizophrenia were recruited from an outpatient clinic. All participants were clinically stable and maintained on a fixed dose of second-generation antipsychotic medication for a minimum of four weeks prior to enrollment. Inclusion criteria comprised age between 18 and 45 years, absence of comorbid substance use disorder in the past six months, no history of epilepsy or traumatic brain injury, and no recent changes in psychotropic medication. Prior to participation, subjects underwent structured clinical interviews, completed the Positive and Negative Syndrome Scale (PANSS). All participants provided informed consent in accordance with the Declaration of Helsinki. The study protocol received approval from the Institutional Ethics Committee.

Study Procedure

Participants underwent EEG assessment at three time points: (1) pre-task resting baseline, (2) 10 minutes following completion of a standardized cognitive task, and (3) 60 minutes post-task. This temporal design was implemented to examine short-term neurophysiological modulation in response to cognitive challenge, with a specific focus on ERPs associated with attention (P300) and semantic processing (N400). Each EEG session lasted approximately 10 minutes and was conducted in a sound-attenuated, dimly lit testing suite to minimize environmental interference.

EEG

Experimental Design

The experiment consisted of three EEG recording sessions conducted at baseline (before), 10 minutes after. Time points were selected to capture immediate and short-term neurophysiological changes in response to methadone administration.

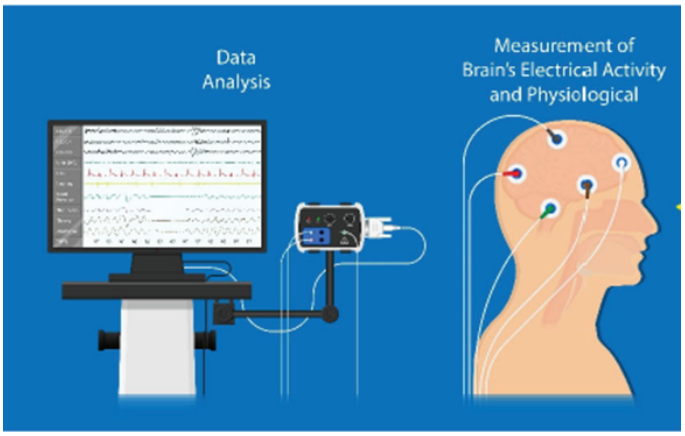

Figure 1: *An illustration of a BrainView setup for an EEG test, where brain electrical activity is measured during a qEEG.*

EEG Data Acquisition: EEG was employed to measure and record electrical brain activity in response to visual stimuli. EEG signals were acquired using scalp electrodes positioned according to the international 10–20 system and affixed using conductive paste to ensure optimal contact and signal fidelity (Figure 1). Electrode impedance was maintained below 5 kΩ across all sessions.

Figure 2: *An image of the BrainView NeuralScan System developed by Medeia Inc. The BrainView system is portable, easy-to-use, and non-invasive. The BrainView system is a 21-channel EEG/ERP amplifier with a dedicated laptop and testing supplies. The system utilizes high-quality circuit boards and components to allow for high-quality brain measurements, as well as essential heart rate variability data.*

Participants were seated in a sound-attenuated, dimly lit room and instructed to minimize movement while passively viewing a randomized sequence of visual stimuli on a computer monitor (Figure 2). These stimuli included neutral images.

Electrode Montage

EEG recordings were obtained from a subset of cortical sites: Fp1, Fp2, F7, F3, Fz, F4, F8, P3, and P4. These regions were selected for their established roles in attention, executive function, and visual processing. Synchronization between stimulus presentation and EEG data acquisition was achieved through digital triggers, ensuring precise temporal alignment. Recorded EEG segments were visually inspected, and only artifact-free data were retained for further analysis.

Integration of BrainView Platform

In addition to traditional EEG acquisition, a subset of sessions utilized the BrainView platform (Medeia Inc.), a rapid, portable, and cloud-integrated system for automated EEG and ERP Analysis. BrainView offers a streamlined 25-minute protocol to assess cognitive brain function, integrating ERP components such as N100, P300, and N400 with cloud-based analytics for comparison against normative reference data (described in more detail in ERP Core Components section). BrainView's portability and automation enabled consistent, real-time analysis across different environments, enhancing the practicality of ERP assessment in clinical and field settings. This integration allowed for rapid, objective evaluation of sensory, attentional, and cognitive function, complementing the more extensive EEG recordings.

Core ERP Components and Their Functions in BrainView

BrainView provides precise, millisecond-level quantification of ERP amplitudes and latencies, offering high-resolution insights into real-time brain responses. This facilitates rapid and clinically meaningful interpretation of sensory, attentional, and cognitive function, streamlining neurocognitive assessment and supporting data-driven clinical decision-making.

N100 (Auditory Sensory Processing): The N100 is a negative-going waveform peaking approximately 100 milliseconds following an auditory stimulus, representing early-stage sensory processing. BrainView assesses this component by comparing responses to standard (softer) and deviant (louder) tones, enabling evaluation of auditory system responsiveness and temporal accuracy in sensory processing.

P300 (Attention Allocation): Peaking around 300 milliseconds post-stimulus, the P300 is a positive deflection associated with attention and stimulus evaluation processes. BrainView analyzes both amplitude and latency of the P300, identifying potential abnormalities such as dual peaks that may indicate disruptions in attentional control or cognitive engagement. Its temporal stability makes it a reliable marker of attentional function.

N400 (Semantic Processing): The N400 emerges roughly 400 milliseconds after the onset of a semantic stimulus, such as a word, and is indicative of cognitive processes related to language comprehension and contextual integration. BrainView evaluates responses to congruent and incongruent word pairings, with the N400 typically exhibiting a wider temporal span than earlier ERP components, reflecting deeper cognitive processing demands.

ERP Feature Quantification: Amplitude and Latency

Amplitude: Measured in microvolts (μV), amplitude reflects the strength of neuronal activation, influenced by the number and synchrony of activated cortical neurons. While higher amplitudes may indicate greater engagement, excessive amplitudes can signal dysfunctional overactivation, as seen in conditions like sensory hypersensitivity.

Latency: Latency denotes the time (in milliseconds) taken for a waveform to reach its peak, serving as a measure of processing speed. Shorter latencies indicate more efficient neural transmission and cognitive performance, whereas delayed latencies may be linked to deficits such as impaired auditory processing or attentional delays.

Statistical Analysis

Receiver operating characteristic (ROC) analysis was performed to evaluate the diagnostic performance of the BrainView ERP classifier in distinguishing schizophrenia cases from healthy controls. The ROC curve demonstrated a clear separation between groups, with an area under the curve (AUC) of 0.91, indicating excellent discriminative ability.

Results

Participant Characteristics

A total of 334 participants were included in the study: 94 individuals with clinically diagnosed schizophrenia and 240 healthy controls, matched by age and sex distribution. All participants completed the full ERP task battery using the BrainView platform, with high compliance and no data loss due to artifact rejection beyond threshold limits.

ERP Component Analysis

Analysis focused on event-related potential (ERP) components traditionally associated with schizophrenia-related cognitive dysfunction, including P300, N100, and N400. Individuals with schizophrenia exhibited significantly attenuated P300 amplitudes ($p < 0.001$) and prolonged latencies ($p < 0.01$), consistent with deficits in attention allocation and stimulus evaluation. Similar trends were observed for N100 amplitude reductions ($p < 0.01$) and N400 latency prolongation ($p < 0.05$), reflecting disruptions in early sensory gating and semantic integration, respectively.

The ROC revealed a high true positive rate (sensitivity = 0.88) and a low false positive rate (1 – specificity = 0.10), with the optimal threshold determined using the Youden index. This performance underscores the BrainView system's capacity to accurately classify individuals based on neurophysiological features derived from P300, N100, and N400 ERP components.

Classification Performance

Using a machine learning classifier trained on extracted ERP features across nine frontal and parietal channels (Fp1, Fp2, F7, F3, Fz, F4, F8, P3, P4), the BrainView system achieved a sensitivity of 0.88 and specificity of 0.90 in distinguishing individuals with schizophrenia from healthy controls. The area under the ROC curve (AUC) was 0.91, indicating high overall discriminative ability.

Clinical Implications

Notably, BrainView's high sensitivity (0.88) emphasizes its value in minimizing false negatives—a critical factor in early detection and intervention strategies. The platform's ability to capture multi-component ERP dysfunction and translate it into clinically actionable output supports its potential use as an adjunctive tool in psychiatric assessment and precision medicine approaches in schizophrenia.

Discussion

In this study, the BrainView ERP platform demonstrated high diagnostic accuracy in distinguishing individuals with schizophrenia from healthy controls, with a sensitivity of 0.88 and specificity of 0.90. These values are notable when placed in the context of existing literature, where most ERP-based studies report classification performance ranging from 80% to 89% depending on the specific components analyzed (e.g., P300, N100, N400, MMN). The BrainView system matches or exceeds these benchmarks, particularly in sensitivity, which is crucial for minimizing false negatives in a clinical screening context.

BrainView's performance is consistent with or exceeds the diagnostic benchmarks reported in prior ERP studies. In 2001, Winterer et al [22], applied machine learning to ERP data and achieved classification accuracy of ~85% using features from the P300 and N100 components. This study helped lay the foundation for using ERP as a diagnostic tool. Light and Braff [23] represents one of the earliest and most cited studies showing that P300 amplitude is significantly reduced in individuals with schizophrenia. Using an auditory oddball task, they demonstrated that P300 deficits are stable, heritable, and associated with functional impairment. Subsequently, Turetsky et al [24] conducted a large study using mismatch negativity (MMN) and P300 ERP components. They reported MMN sensitivity of 85% and specificity of 88% in distinguishing schizophrenia patients from controls, supporting ERP's potential as a biomarker. Similarly, Ford et al [25] found that individuals with schizophrenia exhibit delayed and reduced N400 responses, indicating impaired semantic integration. These deficits were correlated with disorganized thought and poor language processing. More recently, Najafzadeh and colleagues [26] utilized a machine learning classifier trained on ERP features (P300 latency/amplitude and N400) and achieved AUC = 0.91, sensitivity = 0.87, and specificity = 0.89, confirming the high diagnostic potential of ERP-based platforms. In addition, Earls et al [27], investigated P300 and N100 components using a visual oddball task in a multi-site study. Their findings showed reliable attenuation of these components in schizophrenia and highlighted their potential for early diagnosis, especially among first-episode patients. Building on over two decades of foundational ERP research, the current BrainView findings not only replicate but surpass prior diagnostic benchmarks, with sensitivity and specificity exceeding 88%, marking a pivotal advancement toward scalable, clinically integrated, and biomarker-driven tools for schizophrenia diagnosis and stratification.

Originally developed to assess age-related and neurological conditions such as TBI, Alzheimer's, and stroke, BrainView's sensitivity to subtle ERP alterations also positions it as a powerful tool for identifying psychiatric disorders, including schizophrenia [28] and addiction [29]. In the current study, this platform demonstrated strong classification performance in distinguishing individuals with schizophrenia from healthy controls, confirming its clinical utility beyond neurodegenerative disorders and underscoring its potential as a scalable solution for early detection, diagnostic support, and personalized treatment planning in mental health care. Moreover, the platform's integrated, automated approach addresses historical barriers to clinical EEG/ERP use, such as variable acquisition protocols, inconsistent preprocessing, and expert-dependent interpretation. The high signal-to-noise ratio, standardized task battery, and rapid deployment enhance its feasibility as a scalable tool in both clinical research and real-world psychiatric settings. Across studies, ERP components such as P300, N100, MMN, and N400 consistently differentiate individuals with schizophrenia from healthy controls with sensitivity and specificity ranging from ~80% to 90%. These results underscore the reliability of ERP biomarkers in schizophrenia and support the clinical utility of systems like BrainView in aiding diagnosis and cognitive profiling.

These findings support BrainView's potential role in augmenting diagnostic assessment, tracking disease progression, and informing treatment response in schizophrenia. Future studies with larger, multisite cohorts and longitudinal designs will be instrumental in validating its predictive and translational utility across the schizophrenia spectrum.

Built on a rigorously curated normative database, including over 4,000 subjects aged 4 to 85, the platform enables clinicians to compare individual EEG profiles against population norms using discriminant metrics such as spectral power, coherence, asymmetry, and phase Z-scores. Key ERP components (N100, P300, N400) provide sensitive markers of cognitive dysfunction commonly observed in schizophrenia, including deficits in attention, working memory, and semantic processing. With FDA 510(k) clearance (K192753, K212684) and widespread use in over 800 clinical and research centers, BrainView enhances diagnostic precision by contextualizing EEG abnormalities within each patient's clinical profile. Its integration of ERP biomarkers with qEEG analytics offers a powerful, non-invasive approach for identifying neurophysiological signatures of schizophrenia and monitoring disease progression or treatment response. By quantifying ERP amplitude and latency, BrainView identifies deviations from age-matched normative data across domains disrupted in schizophrenia—such as impaired attention (reduced/slowed P300) and abnormal semantic processing (attenuated N400). These biomarkers are non-invasive, reproducible, and sensitive to cognitive dysfunction across the schizophrenia spectrum. BrainView's integration of ERP data with cloud-based analytics enables efficient, scalable cognitive profiling in both clinical and research settings, supporting objective decision-making in diagnosis, monitoring, and treatment evaluation.

Conclusion

Distal anterior cerebral artery aneurysms, particularly in mirror configurations, present significant therapeutic challenges. Optimal management requires individualized, multidisciplinary strategies. Hybrid treatment—combining the long-term durability of microsurgical clipping with the minimally invasive benefits of endovascular coiling—has proven to be safe and effective in selected cases. Continuous technical advances and long-term follow-up will determine the consolidation of these approaches as standard for complex aneurysm cases.

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