

# The Role of Electroencephalography (EEG) in the Diagnosis and Subtyping of Autism Spectrum Disorder: A Review

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**Abstract.** Autism Spectrum Disorder (ASD) is thought to be linked with atypical neural connections. Currently, neural connectivity is a theoretically structured construct that is not easily measurable. Research in network science and time-series analysis indicates that the configuration of neural networks serves as an indicator of neural activity, which may be assessed using electroencephalography (EEG). EEG offers various analysis techniques to potentially identify brain irregularities. This review aims to assess the efficacy of two EEG signal analysis approaches in diagnosing and categorizing ASD. Literature review categorized studies into functional connectivity analysis and spectral power analysis based on predominant EEG analysis methods. Most researches reported significant distinctions between ASD individuals and non-autistic individuals. While, the diverse outcomes preclude definitive conclusions, and presently, no single method emerges as a reliable diagnostic tool. Due to limited research, these methods cannot adequately delineate ASD subtypes. While confirming EEG abnormalities in ASD, current findings fall short of diagnostic utility. Future investigations with larger cohorts and robust methodologies may enhance the sensitivity and consistency of ASD characteristics, fostering the development of novel diagnostic modalities.

## 1. Introduction

Autism Spectrum Disorder (ASD), commonly referred to as autism, is a prevalent early neurodevelopmental disorder. Affected children exhibit common clinical behaviors known as ‘core symptoms of autism’: a significant preference for repetitive behaviors and a near-universal lack of social interest. Although many of these children show differences from typically developing children within the first six months of life, a definitive diagnosis is generally recognized to be made at or after the age of two. ASD has a high degree of familial heritability within the population; for example, if one of a pair of identical twins has autism, it is highly likely that the other will exhibit symptoms of autism as well. However, over 50% of affected children do not exhibit significant pathogenic genetic variations in their genomes. In addition to the core symptoms mentioned above, affected individuals vary in severity, leading to the classification of ASD as a spectrum disorder. Autism patients may experience emotional abnormalities, ADHD, anxiety disorders, depression, and intellectual disabilities as comorbid conditions. Some patients may have lower intellectual abilities along with language impairments, while others may have intellectual and language skills significantly above average. Therefore, some experts suggest defining and exploring the clinical manifestations of this population from the perspective of neurological diversity. So far, there are no recognized

effective biological diagnostic markers for diagnosing childhood autism, and clinicians primarily rely on behavioral assessments and diagnoses. The subtypes of ASD include, but are not limited to, the following: Classic autism, also known as typical autism, is the most common and typical form of autism spectrum disorder. It is characterized by difficulties in social interaction and communication, repetitive behaviors and interests, and impaired language development. Asperger’s syndrome, previously considered a subtype of autism spectrum disorder, is characterized by difficulties in social interaction, repetitive behaviors and interests, but typically with normal language and intellectual development. Childhood disintegrative disorder, which is somewhat similar to classic autism but may show some improvement in symptoms over time. Atypical autism refers to individuals with autism spectrum disorder who do not meet the criteria for classic autism or other subtypes, and may present with a variety of different manifestations. Pervasive developmental disorder not otherwise specified (PDD-NOS) refers to individuals who have some autistic features but do not meet the full criteria for a diagnosis of autism. It is important to note that autism spectrum disorder is a broad spectrum, and individuals may exhibit a wide range of symptoms, leading to various subtypes.

Analyzing dynamic system characteristics of the brain from electroencephalography (EEG) time series offers insights into atypical neural connections linked to

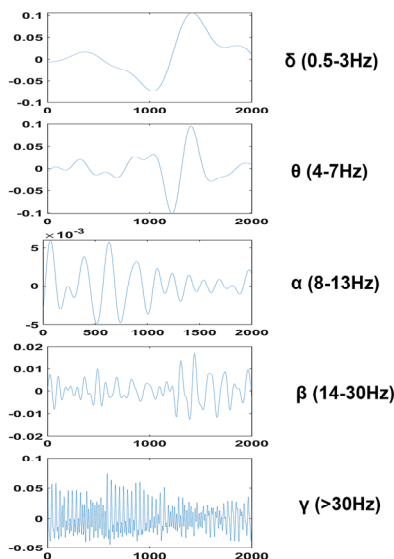
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ASD [1]. This research approach involves analyzing time-series data obtained from EEG recordings, which capture the electrical activity of the brain at different time points. The aim of this method is to identify abnormal activity patterns in the brains of ASD patients, particularly examining whether there are anomalies in the connectivity between different brain regions. This contributes to revealing the relationship between ASD and neural connectivity, thereby providing a deeper understanding of the pathological mechanisms underlying ASD.

The spectrum of ASD also encompasses varying degrees of impairment within every symptom category among individuals [2, 3]. These subtypes are not exhaustive but are among the most frequently discussed in research literature, particularly those chosen for the paper. The significance of neural connectivity disruptions, such as those seen in ASD, lies in the potential for EEG analysis to uncover neural network irregularities associated with the functional and behavioral manifestations of the disorder [4, 5]. Reliable and relatively inexpensive EEG measurements offer valuable biomarkers for early risk assessment and disease progression monitoring. This review aims to assess the effectiveness of EEG in detecting such abnormalities for ASD diagnosis and subtype delineation.

Scalp electroencephalography sensors capture the collective potentials of millions of neurons. Traditionally, they are categorized into five 'classic' frequency bands:  $\delta$  (0.5-3Hz),  $\theta$  (4-7Hz),  $\alpha$  (8-13Hz),  $\beta$  (14-30Hz), and  $\gamma$  (>30Hz), though definitions may differ (see figure 1). These frequency bands reflect diverse brain states, each associated with distinct functional, physiological, and cortical mapping characteristics. Nonetheless, recent EEG analysis approaches, like multiscale entropy, assess 'scale' instead of the conventional frequency bands.



**Figure 1.** Example of EEG bands.

Correlation analysis is used to assess the connectivity properties between power in different frequency bands and brain regions. Methods for EEG analysis, including spectral analysis, functional connectivity analysis, and

the more recent information dynamics analysis, have been utilized to identify quantitative characteristics linked to changes in ASD behavior [6, 7, 8, 9]. These computed values from diverse analysis techniques can be collectively termed as EEG signal features.

The concrete questions proposed in the paper are as follows:

(1) Can the analysis of EEG detect ASD patients, and can the enhancement or reduction of alpha-band connectivity between different brain regions serve as a diagnostic criterion for ASD patients?

(2) Can the characteristics of different frequency bands in EEG distinguish subtypes of ASD patients?

## 2. Methods

### 2.1. Retrieve literature

Literature retrieval was performed across three peer-reviewed databases: PubMed, Embase, and PsycInfo. Keyword searches were conducted to locate studies most relevant to this review. The search terms employed included 'ASD', 'Asperger's syndrome', 'autism', 'EEG', 'spectral analysis', and 'functional connectivity'. Each database search encompassed the three key terms representing the disorder and its subtypes, as well as terms describing methodologies. Furthermore, the selection criteria for the studies under review encompassed the following aspects:

(1) Studies conducted in humans, whether children or adults;

(2) Comparisons between ASD and healthy control groups, and comparisons between ASD patients with others subtypes;

(3) Study outcomes included EEG features of ASD, rather than comorbidities;

(4) Studies utilized EEG and analyzed signals using spectral analysis and functional connectivity measurement methods.

Examination of the literature selection for data extraction revealed two types of EEG signal analysis used for detecting ASD, spectral analysis, functional connectivity and coherence analysis.

### 2.2. Data analysis

In autism diagnosis, functional connectivity analysis and spectral power analysis can provide information about brain function and structure [10]. Functional connectivity analysis helps us understand whether the connectivity patterns within the brain and between different brain regions of autism patients are abnormal, revealing characteristics of their nervous system. Spectral power analysis helps detect abnormal activity or functional anomalies within specific frequency ranges in the brains of autism patients. Therefore, these two analytical methods are crucial for understanding the neurobiological basis of autism and assisting in diagnosis.

Functional connectivity refers to the analysis of the temporal and spatial relationships between different

brain regions by recording brain electrical activity to understand their coordination and interaction during specific tasks or states. Specifically, functional connectivity analysis aims to reveal the synchronicity and degree of mutual influence between various brain regions within the brain [11, 12]. Methods for analyzing functional connectivity in EEG include, but are not limited to, the following: coherence analysis, phase synchronization analysis, complex network analysis, Granger causality analysis and small-world network analysis. Using these methods can provide insights into the interactions and information transmission mechanisms between various brain regions, revealing the working mechanisms of the brain under different cognitive and emotional states.

Spectral analysis is one of the most commonly used quantitative methods for analyzing and interpreting EEG signals. It divides the continuous frequency range into predefined frequency bands and evaluates the distribution of signal energy within these bands, typically including  $\delta$ ,  $\theta$ ,  $\alpha$ ,  $\beta$ , and  $\gamma$  frequency bands. The spectral power of each frequency band can be computed at various sensor locations. Sometimes, the power across individual frequency bands is summed to obtain a single power value for the entire scalp region. The study evaluated intergroup differences between individuals with ASD and healthy individuals control groups. Results are presented in terms of relative power (the ratio of band power to total power in the band).

The utility analysis of each method includes its general description, critical evaluation of statistical significance to differentiate between ASD individuals and non-autistic individuals, or among different subtypes of autism spectrum disorder. Additionally, it involves the examination of the strengths and limitations of the techniques in the literature, along with a summary of conclusions and discussions on the future prospects of utilizing the method as a tool for autism detection and improvement.

### 3. Results

The assessment of the chosen literature led to the presentation of two articles discussing EEG signal analysis methods employed in describing ASD.

Each study identified at least one statistically significant distinction in ASD across at least one frequency band connectivity when comparing ASD patients with non-autistic participants. Some studies employed coherence as a connectivity measure, while others calculated phase lag indices of time series and conducted clustering to ascertain levels of synchronization. EEG recordings were conducted under resting-state, with participants' eyes closed, sleeping, or while engaging in tasks related to object recognition, audio, or video.

While findings varied, certain patterns can be deduced. ASD commonly correlates with diminished connectivity in the  $\alpha$  band among the frontal lobe and other cerebral areas. This observation bolsters the hypothesis of connectivity deficits in ASD, a notion

backed by fMRI investigations. The most studies analyzed coherence in the alpha band, with some supporting the existence of connectivity deficits. Murias et al. found significant differences in alpha band connectivity, particularly reduced connectivity from frontal regions, using high-density EEG montage. Certain participants were under medication, which could have influenced the outcomes. Catalino et al. observed a general diminution in brain connectivity within the  $\alpha$  band among ASD patients engaged in recognition tasks. Recently, Carson et al. reproduced a decline in distant alpha band connectivity among younger subjects while viewing a video of a known or unknown individual preparing a tale. While, some studies showed opposite results. One longitudinal study found increased  $\alpha$  band connectivity between frontal and central regions in children at high possibility for ASD diagnosed at 14 and 38 months compared to low possibility children. Testing participants under relaxed, eyes-open conditions revealed decreased alpha connectivity within and between brain hemispheres. In another study, one examined children during sleep stages, finding increased coherence, particularly in the frontotemporal area, in ASD individuals compared to neurotypical participants. Additionally, theta oscillations were identified as the basis for locally dominant processes. Bartfeld et al. presented contradictory outcomes regarding the delta band, demonstrating reduced long-distance delta connectivity between frontal and occipital regions alongside heightened short-range delta connectivity in frontal areas. Coben also demonstrated reduced theta band coherence, while Boersma et al. detected a decline in connectivity. Coben and Lazarev investigated the beta band, where certain studies did not detect any notable differences. This complicates generalization due to variations in EEG recording conditions and discrepancies in the ages of study participants.

### 4. Conclusions

In summary, current EEG signal analysis methods still lack the sensitivity or specificity required to reliably identify ASD children for clinical utility. While, these analytical methods and the outcomes obtained thus far suggest significant function in characterizing the disorder and might serve as a valuable adjunct to existing techniques. Using EEG as a measure of the development of brain may finally turn into an index for children needing further evaluation [13]. Existing literature underscores the need for further investigation into the considerable importance of various electrophysiological characteristics and the substantial gaps that can be addressed. Considering that ASD is a childhood-diagnosed neurodevelopmental disorder, age considerations should inform experimental design. Moreover, longitudinal studies can enhance the significance of findings and elucidate the developmental phases of ASD. Embracing new, advanced analysis techniques alongside established ones is crucial for achieving the overarching objective: early identification

of burgeoning autism, potentially enabling early intervention and prevention strategies.

Current EEG research faces several limitations, including the lack of reliable diagnostic methods and the inability to fully differentiate subtypes of ASD. Firstly, EEG data interpretation is subject to subjective factors due to the absence of unified standards and reproducible analysis methods, leading to increased uncertainty in diagnostic outcomes. Additionally, existing studies often focus on specific brain regions or frequency ranges, overlooking the complexity and dynamic changes of the overall brain network [14]. This hinders our comprehensive understanding of ASD brain function and the differentiation between different subtypes.

To overcome these limitations, future research could proceed in several directions. Firstly, establishing stricter data standards and analysis procedures to ensure the consistency and reliability of EEG data is crucial. This involves implementing unified data collection methods, preprocessing steps, and analysis strategies to reduce subjective interference and result uncertainty. Secondly, developing more sophisticated data analysis techniques, including machine learning and artificial intelligence-based methods, can help identify biological markers and subtype characteristics of ASD more accurately. These techniques can uncover patterns and associations hidden within EEG data, facilitating more precise ASD diagnosis and subtype differentiation. Lastly, enhancing interdisciplinary collaboration and data sharing to facilitate cooperation and information exchange between different research teams can accelerate the progress of EEG research on ASD and promote clinical applications. Through these efforts, we can better utilize EEG technology to understand the neurobiological basis of ASD and provide more accurate and personalized methods for diagnosis and treatment.

## Acknowledgments

This article is supported by Key Research Laboratory of Chinese Medicine Psychology and Brain Science, PhD Research Startup Foundation of Jiangxi University of Chinese Medicine (2018BSRW001), 2020 Jiangxi University of Chinese Medicine Graduate Student "Ideological and Political Golden Course" and "Course Ideological and Political" Demonstration Course Construction Project (jxysz-029).

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