

# Investigating Neural Connectivity in Autism Spectrum Disorder: A Multimodal Neuroimaging Approach

## Abstract

Autism spectrum disorder (ASD) is a complex neurodevelopmental condition characterized by persistent difficulties in social communication and interaction, as well as restricted, repetitive patterns of behavior, interests, or activities (American Psychiatric Association, 2013). Understanding the underlying neural mechanisms of ASD is critical for improving diagnosis, developing targeted interventions, and elucidating the etiology of this heterogeneous disorder. This paper presents a multimodal neuroimaging approach that integrates high-density electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) to comprehensively investigate abnormal patterns of neural connectivity in individuals with ASD.

## Introduction

Autism spectrum disorder (ASD) is a lifelong neurological condition that affects an individual's ability to communicate, interact socially, and engage in restricted, repetitive behaviors (American Psychiatric Association, 2013). While the diagnostic criteria for ASD are based on behavioral observations, there is growing evidence that the disorder is underpinned by atypical patterns of brain connectivity and function (Geschwind & Levitt, 2007; Vissers et al., 2012). Elucidating the neural mechanisms associated with the core symptoms of ASD is crucial for improving early identification, informing targeted interventions, and shedding light on the etiology of this heterogeneous disorder.

Neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and electroencephalography (EEG), have emerged as valuable tools for investigating the neural basis of ASD. fMRI provides high spatial resolution in mapping brain regions involved in social cognition and information processing, while EEG offers superior temporal resolution in capturing the dynamic patterns of neural activity (Logothetis, 2008; Michel & Murray, 2012). By integrating these complementary neuroimaging modalities, researchers can gain a more

comprehensive understanding of the spatiotemporal characteristics of brain connectivity in individuals with ASD.

The present study aims to investigate the neural connectivity patterns associated with ASD using a multimodal neuroimaging approach. Specifically, we will combine high-density EEG and fMRI data to create a detailed spatiotemporal map of brain connectivity in individuals with ASD and typically developing (TD) controls. Through the application of advanced data analysis techniques, including machine learning and deep learning algorithms, we will identify connectivity patterns and potential biomarkers that may distinguish individuals with ASD from their TD counterparts.

## Methodology

**Participants** The study will include 40 individuals with a clinical diagnosis of ASD and 40 age-, sex-, and IQ-matched TD controls. All participants will undergo comprehensive clinical and neuropsychological assessments to ensure they meet the inclusion criteria for the respective groups.

## Data Acquisition

Participants will undergo simultaneous EEG and fMRI data acquisition during a series of task-based and resting-state paradigms designed to probe social cognitive processes, such as facial emotion recognition, theory of mind, and joint attention

## EEG Data Acquisition and Analysis

High-density EEG data (128 or 256 channels) will be recorded using a specialized MRI-compatible system. The EEG data will be carefully preprocessed to remove artifacts, including those related to the strong magnetic field and gradient switches of the MRI scanner (Hochstetter et al., 2004). Source localization techniques, such as the multiple discrete equivalent current dipole (mECD) approach, will be used to transform the surface potentials into source-level activity, allowing for improved spatial resolution and separation of neural sources (Scherg et al., 2002; Michel & He, 2019).

## fMRI Data Acquisition and Analysis Functional

MRI data will be acquired using a 3T scanner, with a standard echo-planar imaging (EPI) sequence. Preprocessing steps will include slice timing correction, motion correction, spatial normalization, and spatial smoothing. Task-related fMRI analysis will involve the use of general linear models to identify brain regions showing differential activation patterns between the ASD and TD groups during the social cognitive tasks (Friston et al., 2014).

## Data Fusion and Connectivity Analysis

The source-level EEG data and fMRI activation patterns will be integrated using advanced data fusion techniques. This will allow for the identification of spatiotemporal patterns of neural connectivity that characterize the social brain network in ASD (Hoechstetter et al., 2004; Friston et al., 2014). Metrics of functional connectivity, such as phase synchronization and Granger causality, will be computed to quantify the strength and directionality of information flow between key nodes in the social brain network (Buzsáki et al., 2012; Gotts et al., 2012).

## Machine Learning and Biomarker Identification

The multimodal neuroimaging data will be subjected to machine learning and deep learning algorithms to identify patterns of neural connectivity that may serve as potential biomarkers for ASD. Feature extraction techniques will be used to identify the most discriminative connectivity measures, which will then be used to train classification models for distinguishing individuals with ASD from TD controls (Sato & Uono, 2019).

## Expected Outcomes

This multimodal neuroimaging study is expected to provide a comprehensive spatiotemporal map of brain connectivity in individuals with ASD, shedding light on the neural mechanisms underlying the core symptoms of the disorder. By integrating high-density EEG and fMRI data, we anticipate identifying specific patterns of neural connectivity that are altered in ASD, particularly within the social brain network.

The application of machine learning algorithms to the multimodal neuroimaging data may lead to the identification of potential biomarkers that could improve early diagnosis and guide the development of targeted interventions for individuals with ASD. Furthermore, the insights gained from this study may contribute to a better understanding of the etiology of ASD and inform future research on the neural underpinnings of this complex neurodevelopmental disorder.

## Conclusion

The proposed multimodal neuroimaging approach, combining high-density EEG and fMRI, offers a powerful tool for investigating the neural connectivity patterns associated with autism spectrum disorder. By leveraging the complementary strengths of these neuroimaging techniques, this study aims to create a comprehensive spatiotemporal map of brain connectivity in individuals with ASD, potentially identifying novel biomarkers that could enhance early diagnosis and inform personalized treatment strategies. The findings of this research will contribute to our evolving understanding of the neural mechanisms underlying the core symptoms of ASD and pave the way for more targeted and effective interventions for individuals on the autism spectrum.

## References

- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.
- Buzsáki, G., Anastassiou, C. A., & Koch, C. (2012). The origin of extracellular fields and currents—EEG, ECoG, LFP and spikes. *Nature Reviews Neuroscience*, 13(6), 407-420.
- Friston, K. J., Kahan, J., Razi, A., Stephan, K. E., & Sporns, O. (2014). On nodes and connections in resting-state fMRI. *NeuroImage*, 59(3), 2211-2223.
- Geschwind, D. H., & Levitt, P. (2007). Autism spectrum disorders: developmental disconnection syndromes. *Current Opinion in Neurobiology*, 17(1), 103-111.
- Gotts, S. J., Simmons, W. K., Milbury, L. A., Wallace, G. L., Cox, R. W., & Martin, A. (2012). Fractionation of social brain circuits in autism spectrum disorders. *Brain*, 135(9), 2711-2725.

- Hoehstetter, K., Bornfleth, H., Weckesser, D., Ille, N., Berg, P., & Scherg, M. (2004). BESA source coherence: A new method to study cortical oscillatory coupling. *Brain Topography*, 16(4), 233-238.
- Logothetis, N. K. (2008). What we can do and what we cannot do with fMRI. *Nature*, 453(7197), 869-878.
- Michel, C. M., & He, B. (2019). EEG source localization. *Handbook of Clinical Neurology*, 160, 85-101.
- Michel, C. M., & Murray, M. M. (2012). Towards the utilization of EEG as a brain imaging tool. *NeuroImage*, 61(2), 371-385.
- Sato, W., & Uono, S. (2019). The atypical social brain network in autism: Advances in research on the mirror neuron system. *Review Journal of Autism and Developmental Disorders*, 6(3), 187-199.
- Scherg, M., Ille, N., Bornfleth, H., & Berg, P. (2002). Advanced tools for digital EEG review: Virtual source montages, whole-head mapping, correlation, and phase analysis. *Journal of Clinical Neurophysiology*, 19(2), 91-112.
- Vissers, M. E., Cohen, M. X., & Geurts, H. M. (2012). Brain connectivity and high functioning autism: a promising path of research that needs refined models, methodological convergence, and stronger behavioral links. *Neuroscience & Biobehavioral Reviews*, 36(1), 604-625.