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Review Article

# Electroencephalogram Coherence Patterns in Autism: An Updated Review

**Sophie Schwartz BS [a], Riley Kessler BA [b], Thomas Gaughan BS [b], Ashura W. Buckley MD [b,*]**

[a] *Graduate Program for Neuroscience, Boston University, Boston, Massachusetts*
[b] *Pediatrics and Developmental Neuroscience Branch, National Institute of Mental Health, National Institutes of Health, Bethesda, Maryland*

ABSTRACT

Electrophysiologic studies suggest that autism spectrum disorder is characterized by aberrant anatomic and functional neural circuitry. During normal brain development, pruning and synaptogenesis facilitate ongoing changes in both short- and long-range neural wiring. In developmental disorders such as autism, this process may be perturbed and lead to abnormal neural connectivity. Careful analysis of electrophysiologic connectivity patterns using EEG coherence may provide a way to probe the resulting differences in neurological function between people with and without autism. There is general consensus that electroencephalogram coherence patterns differ between individuals with and without autism spectrum disorders; however, the exact nature of the differences and their clinical significance remain unclear. Here we review recent literature comparing electroencephalogram coherence patterns between patients with autism spectrum disorders or at high risk for autism and their non-autistic or low-risk for autism peers.

***Keywords:*** autism, EEG, coherence, synchrony, electroencephalography

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## Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by clinically recognized deficits in social communication and repetitive and restricted behaviors and interests.[1] Although the behavioral symptoms of ASD are fairly well defined, researchers have yet to determine the underlying neural contributors of the disorder. Electrophysiologic studies pinpoint aberrant functional neural circuitry as a key underlying feature in this disorder.[2] Pruning, synaptogenesis, and myelination are key processes that facilitate ongoing changes in neural wiring during typical brain development.[3] Theoretically, disruptions in one or more of these processes leads to an array of atypical neural networks that then manifest as a very recognizable and stereotypic behavioral phenotype.[3-5]

There is evidence that synaptic dysfunction in ASD occurs both at the local level of single axons and at the global level of neural networks.[6,7] Careful analysis of electrophysiologic patterns across the brain using electroencephalogram (EEG) coherence is one way to noninvasively evaluate this synaptic dysfunction. EEG coherence characterizes the consistency and magnitude of a relationship between simultaneously recorded and spatially separated oscillatory nodes. When two signals in the same frequency are active with a consistent phase relationship over time, they are considered coherent and we assume there is a high degree of coordinated activity between the underlying brain regions producing those two signals.[2,8,9] It is assumed that the two signals do not originate from the same generator when their phases are

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* Communications should be addressed to: Dr. Buckley; Pediatrics and Developmental Neuroscience Branch; National Institute of Mental Health; National Institutes of Health; 10 Center Drive; MSC 1255; Bethesda, MD 20892-1255.
*E-mail address:* Shu.Buckley@nih.gov

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coupled but not identical.[10] EEG coherence is currently one of the only proxies for network organization in the human brain. Its principal limitation is that the connectivity of deep brain structures must be inferred given the surface location and timing of activity measured at the scalp.[8] Nonetheless, although somewhat lacking in spatial resolution, EEG coherence is excellent at providing temporally precise information on global network processing.

Given the strengths of EEG coherence, its quantification in diverse samples of ASD provides a promising path toward discovering a proximal biomarker that potentially could reflect differences in behavioral function, not only between people with and without the disorder, but also between subtypes of the disorder with different underlying etiologies. Over the past ten years, there have been several studies using EEG to compare coherence patterns between individuals with ASD and nonautistic, age-matched peers, as well as between infants at high and low risk for developing ASD. Although these studies generally agree that coherence patterns are different in those with, or at risk for, ASD, there remains considerable debate about the details and their significance.

Here, we critically reviewed recent research on EEG coherence in ASD, focusing on studies that could be considered moderately powered, with sample sizes of at least twenty. To constrain the number of compiled studies, we limited our review to task-based studies from the past five years and resting-state and sleep-based studies from the past ten years. The scope of the review was functional coherence as defined by linear and nonlinear methods of spectral coherence (most commonly computed through magnitude-squared coherence (MSC), which considers both magnitude of the spectral power and phase relationship as a frequency-domain correlation between signals) and phase lag coherence (which only considers the correlation of the two signals' phases and does not consider the magnitude). We did not address literature that investigated effective connectivity (e.g., entropy, graph theory, or granger causality).[6] Because chronological maturation has significant effects on EEG morphology and coherence in typical development, we segmented research based on the developmental stage of their subject cohorts.[11-14] In addition, this review followed the convention of organizing neural connectivity into separate frequency bands: delta (0.3 to 4 Hz), theta (4 to 7 Hz), alpha (8 to 12 Hz), beta (13 to 25 Hz), and gamma (25 to 60 Hz). Prior research has provided partial evidence for associations between these various frequency bands and corresponding cognitive tasks.[15-18] Organizing coherence based on frequency band allowed us to make occasional inferences about the effectiveness of signal transmission during these cognitive processes. Finally, we attempted to simplify the disparities in what different research groups call "long-" and "short-" range connections by considering the location and distance of the channel electrodes used in the computation of coherence. To draw parallels between studies, we used the following guidelines: (1) long-range connections referred to frontal to posterior parietal or occipital channel pairs and left temporal to right temporal channel pairs, (2) short-range connections referred to adjacent channel pairs in a 10-20 system, and (3) medium-range connections referred to any other channel pair connection.

The purpose of this review was to highlight the degree to which findings of perturbed long- and short-range, intra- and inter-hemispheric connections in ASD vary based on chronological age, behavioral phenotype, and methodologic differences in EEG recording.

## Early development: infants at risk, toddlers, and preschoolers

### *Infants: eliciting functional patterns of coherence*

The primary objective of studying EEG coherence in infants who are considered at high risk for developing ASD is to identify early ASD-specific biomarkers, electrophysiologic endophenotypes, and developmental trajectories of neural integration and coordination during the most critical stage of postnatal brain development.[19,20] Infants are most often considered at high risk for ASD when they have an older sibling diagnosed with ASD, as the prevalence of receiving an ASD diagnosis when a sibling carries the diagnosis rises from approximately 1% in the general population to around 19%.[21] Because EEG is noninvasive, is somewhat tolerant to motion, and does not require an active response from the subject, it is an ideal tool to be used for the evaluation of neural connectivity in very young individuals.

Three publications from the past five years have measured EEG coherence patterns in infants (Table 1). The largest study reviewed in this early developmental stage included 46 low-risk (low-risk control, or LRC) and 49 high-risk (high-risk for ASD, or HRA) infant subjects.[17] The study's primary focus was on left–right hemispheric lateralization of event-rated gamma-band MSC coherence between intrahemispheric frontal-posterior pairs during a face processing task.[17] The authors chose to look at gamma activity because it is thought to represent neural integration between local, specialized networks and therefore may be pertinent to the neural integration of facial features during face processing.[17] In addition, based on prior research, the authors suspected that the neurotypical response to viewing faces would be to recruit from the right hemisphere more so than the left.[17,22] The study showed that at 12 months, HRA infants had significantly increased left-lateralized intrahemispheric coherence when viewing faces compared with LRC infants.[17] Furthermore, through a retrospective analysis of a subsample of 36 infants who were clinically assessed for ASD at 18, 24, and 36 months, the study revealed that HRA infants later diagnosed with ASD (HRA+) had displayed the greatest leftward lateralization at 12 months of age, whereas HRA infants who were not later diagnosed with ASD (HRA−) had exhibited an intermediate level of lateralization between their HRA+ counterparts and LRC infants.[17] From these results, the authors hypothesized that aberrant, left-lateralized gamma coherence patterns during facial processing at a very early age may precede the atypical behavioral manifestations of facial processing and encoding that are more apparent by 18 to 36 months when children are diagnosed with ASD.[17,23]

In a smaller group of infants, these same researchers had previously conducted a similar study in which they investigated intrahemispheric event-related gamma-band linear coherence, but this time between anterior and posterior scalp regions while subjects heard speech sounds.[24] During