

ELECTROENCEPHALOGRAPHY IN CHILDREN WITH AUTISM

by

Nikola N. Lucas

A Dissertation Submitted to the Faculty of

The Charles E. Schmidt College of Science

In Partial Fulfillment of the Requirements for the Degree of

Doctor of Philosophy

Florida Atlantic University

Boca Raton, Florida

December 2013

Copyright by Nikola N. Lucas 2013

ELECTROENCEPHALOGRAPHY IN CHILDREN WITH AUTISM

by

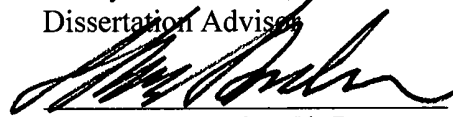
Nikola N. Lucas

This dissertation was prepared under the direction of the candidate's dissertation advisor, Dr. Nancy Aaron Jones, Department of Psychology, and has been approved by the members of her supervisory committee. It was submitted to the faculty of the Charles E. Schmidt College of Science and was accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

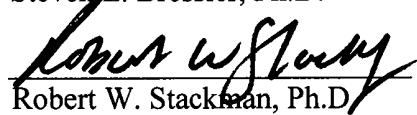
SUPERVISORY COMMITTEE:



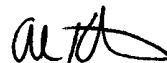
Nancy Aaron Jones, Ph.D.
Dissertation Advisor



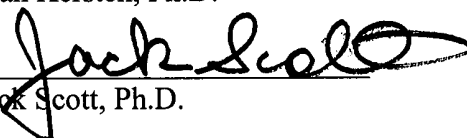
Steven L. Bressler, Ph.D.



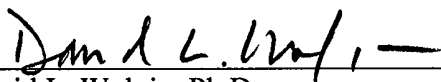
Robert W. Stackman, Ph.D.



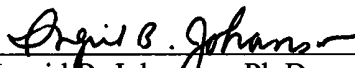
Alan Kersten, Ph.D.



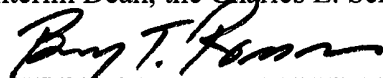
Jack Scott, Ph.D.



David L. Wolgin, Ph.D.
Chair, Department of Psychology



Ingrid B. Johanson, Ph.D.
Interim Dean, the Charles E. Schmidt College of Science



Barry T. Rosson, Ph.D.
Dean, Graduate College

7/8/13

Date

ABSTRACT

Author: Nikola N. Lucas
Title: Electroencephalography in Children with Autism
Institution: Florida Atlantic University
Dissertation Advisor: Dr. Nancy Aaron Jones
Degree: Doctor of Philosophy
Year: 2013

Autism is a neurodevelopmental disorder that is characterized by deficits involving social interaction, communication, and perception. Although there is much research that has examined functional neural connectivity in individuals with autism, few have conducted these studies in very young children while awake across EEG power and coherence measures. Anomalies in EEG coherence and power have been associated with deficits in executive function and mental activity. The present study examined neural activation and functional connectivity with an EEG, in children ages 3 -5, during an eyes-closed baseline period. Discrete Fourier Transform was performed on artifact-free segments of EEG data to produce power density values. In addition, coherence measurements were examined to assess functional connectivity in the alpha bandwidth during the baseline recording. Children with autism spectrum disorder (ASD) demonstrated reduced alpha coherence in fronto-temporal regions and between right temporal sites when compared to typically developing (TD) children. In addition, the

reduction in coherence was based on ASD severity, such that high-functioning children with ASD showed greater coherence than low-functioning children with ASD. Children with ASD also displayed reduced power in the alpha, beta, and theta frequency bandwidths in frontal, temporal, central, and occipital regions compared to TD children. Interestingly, delta power differentiated children based on developmental status such that high-functioning children with ASD demonstrated the greatest delta power, followed by TD children, and then low-functioning children with ASD. Finally, TD children demonstrated left anterior temporal EEG asymmetry in the alpha bandwidth, whereas children with high-functioning ASD exhibited left posterior temporal EEG asymmetry and right frontal EEG asymmetry. Thus, the results suggest that children with ASD exhibit atypical patterns of brain activity and functional connectivity compared to their typically developing counterparts.

ELECTROENCEPHALOGRAPHY IN CHILDREN WITH AUTISM

List of Tables	viii
List of Figures	ix
Introduction.....	1
Theories on the Etiology of ASD.....	2
Anatomical Differences	5
Electroencephalography and Brain Activity.....	10
Basal Neural Function in ASD	15
EEG Measures of Baseline Activity	15
Functional Magnetic Resonance Imaging.....	23
Face Processing.....	25
Observation of Emotional Facial Expression	39
Present Study and Hypotheses	47
Method	50
Participants.....	50
Procedure	52
EEG Recordings.....	54
EEG and Statistical Analyses.....	55
Results.....	59
Identification and Imitation of Facial Expressions	60
Power	60
Frontal Region	61

Temporal Region	63
Central Region	65
Occipital Region	67
Coherence	70
Frontal Region	70
Temporal Region	71
Frontal - Temporal Region.....	72
Occipital - Frontal Region	74
Asymmetry.....	75
Correlations.....	77
Discussion.....	79
EEG Power.....	80
Alpha Coherence and Correlations	82
EEG Asymmetry Patterns.....	85
General Discussion	86
Limitations	88
Conclusions and Recommendations	90
Appendix.....	93
References.....	125

TABLES

Table 1. Relative Power for TD and ASD Groups by Region.....	94
Table 2. Alpha 1 EEG Coherence for ASD and TD Groups by Region.....	95
Table 3. Alpha 2 EEG Coherence for ASD and TD Groups by Region.....	96
Table 4. Power Comparisons of ASD to TD Participants	97
Table 5. Coherence Comparisons of ASD to TD Participants.....	98

FIGURES

Figure 1. Electrode Placement	99
Figure 2. Correct Trials for Identification and Imitation	100
Figure 3. Effect of Development on Frontal Power.....	101
Figure 4. Effect of Development on Temporal Power.....	102
Figure 5. Effect of Development on Central Power	103
Figure 6. Effects of Development X Occipital on Alpha 1 Power	104
Figure 7. Effects of Development on Occipital on Alpha 2 Power	105
Figure 8. Effect of Development on Occipital Beta, Delta, & Theta Power	106
Figure 9. Development X Temporal Region on Alpha 1 Coherence.....	107
Figure 10. Development X Temporal Region on Alpha 2 Coherence.....	108
Figure 11. Development X Fronto-Temporal on Alpha 1 Coherence	109
Figure 12. Development X Fronto-Temporal on Alpha 2 Coherence	110
Figure 13. Development X Occipital-Frontal on Alpha 1 Coherence	111
Figure 14. Mean Difference for Alpha 1 and Alpha 2 Asymmetry in TD Group	112
Figure 15. Mean Difference for Occipital Asymmetry in TDEO Group.....	113
Figure 16. Mean Difference for Frontal Asymmetry in HFASD Group	114
Figure 17. Mean Difference for Temporal Asymmetry in ASD Group	115
Figure 18. Relationship between ASD Severity and T4-T6 Alpha 1	116
Figure 19. Relationship between ASD Severity and T4-T6 Alpha 2	117

Figure 20. Relationship between ASD Severity and T4-F4 Alpha 1.....	118
Figure 21. Relationship between ASD Severity and T4-F8 Alpha 1.....	119
Figure 22. Relationship between ASD Severity and T3-F7 Alpha 1.....	120
Figure 23. Relationship between ASD Severity and T3-F3 Alpha 2.....	121
Figure 24. Relationship between ASD Severity and T3-F7 Alpha 2.....	122
Figure 25. Relationship between ASD Severity and T4-F4 Alpha 2.....	123
Figure 26. Relationship between ASD Severity and T4-F8 Alpha 2.....	124

INTRODUCTION

With the increasing number of children diagnosed with autism and autism spectrum disorders, autism research is more important than ever. Autism spectrum disorders (ASD) include autism, Asperger's disorder, and pervasive developmental disorder, not otherwise specified (American Psychiatric Association, 1994). Autism is a neurodevelopmental disorder that is characterized by deficits involving social interaction, communication, perception, and often mental retardation. Prevalence estimates have dramatically increased over the last 50 years (Levy, Mandell, & Schultz, 2009) with the current prevalence estimated at one in 88 births, most of which are boys (Centers for Disease Control and Prevention, 2012). Intervention efforts are aimed at early identification and treatment via behavioral therapeutic techniques. In most cases, the disorder is diagnosed by three years of age. Although there is no cure for autism, early treatment seems to ameliorate deficits in social functioning and learning.

There are several theories regarding the origins of autism ranging from environmental factors to genetic abnormalities. Although the cause of the disorder is likely due to a number of interacting factors, it is not clear what specific brain regions are involved in the disordered perception and behavior observed in children with ASD. Part of the problem in pinning down specific regions of the brain responsible for the disordered behavior is that ASD is highly heterogeneous, with varying symptoms and disabilities exhibited. However, it is thought that with the increasing capabilities of

neuroimaging and neurorecording technology, questions regarding the relationship between autism and neuronal function may be answered. Are particular neural structures damaged or functionally differentiated in children with ASD compared to typically developing (TD) children? Or do children with ASD have faulty neural communication when processing information?

Theories on the Etiology of ASD

As autism and ASD include a number of varying symptoms, the causes are likely multifactorial. In terms of neural development, most theories are genetically-based and range from abnormalities of neural connectivity and organization to hypo-and-hyperactivity of various neuronal structures. These theories are not mutually exclusive and each may explain some facet of ASD.

Several theories of under-connectivity and/ or disordered neural connectivity have been proposed as an explanation for ASD symptomology over the last 10 years (Hughes, 2007; Just, Keller, Malave, Kana, & Varma, 2012; Kana, Libero, & Moore, 2011; Rippon, Brock, Brown, & Boucher, 2007; Wass, 2011). In their research of epileptiform activity, Hughes and Melyn (2005) found that non-epileptic children with ASD displayed a greater incidence of epileptiform discharges than their TD counterparts. This discharge activity is typically localized compared to seizures which are known to extend beyond their focal point (Hughes, 2007). Hence, as the epileptiform discharges did not spread they concluded that individuals with ASD may have impaired cortico-cortical connections keeping the discharge activity focused in a single area. Kana et al. (2011) proposed that there are decreases in long-range connections as well as increases in short-range

connections that developed as a means to compensate for the deficits in long-range connections in ASD. Research utilizing various techniques to examine structural and functional connectivity has yielded results consistent with disordered connectivity theories. In particular, reductions in functional connectivity have been found in regions associated with language, communication, and emotion, abilities characteristically affected in ASD (Cherkassy, Kana, Keller, & Just, 2006; Coben, Clarke, Hudspeth, & Barry, 2008; Just, Cherkassy, Keller, & Minshew, 2004; Kleinhans et al., 2008; Murias et al., 2007). The decrease in functional connectivity appears to be most prominent between medium and long distance cortico-cortical connections (Kana et al., 2011; Wass, 2011).

Research examining fiber tracts and myelination also indicate reduced structural connectivity in ASD (Boger-Megiddo et al, 2006; Vidal et al., 2006; Wolff et al., 2012; Zikopolous & Barbas, 2010). It has been reported that the number of long-range axons are reduced and short-range axons are increased in the frontal regions of ASD brains (Zikopoulos & Barbas, 2010). Furthermore, the fibers of the corpus callosum are smaller in individuals with ASD (Boger-Megiddo et al, 2006; Vidal et al., 2006).

Correspondingly, by two years of age, infants with ASD demonstrate a reduction in myelinated fibers in comparison to TD infants (Wolff et al., 2012). Thus, aberrant structural connections are found intrahemispherically in frontal regions as well as between hemispheres.

ASD has been associated with a number of diseases based on genetic disorders. In particular, autism has been linked with fragile X syndrome (Chelly & Mandel, 2001;

Kumar & Christian, 2009), epilepsy (Tuchman & Rapin, 2002; Hughes & Melyn, 2005), tuberous sclerosis, and cytogenetic abnormalities (Kumar & Christian, 2009). However, there is no specific causal link between these disorders and autism. Still, ASD has a strong genetic component in that the risk of having a second child diagnosed with ASD is 20 to 50 times higher than in the general population (O’Roak & State, 2008; Levy et al., 2009). Estimates of heritability suggest that approximately 90 percent of the variance in autism can be accounted for by genetic factors (Levy et al., 2009). In fact, at least 29 genes have been identified from whole-genome screens in multiplex families that contribute to ASD (Gepner & Féron, 2009; Sutcliffe, 2008). It is believed that the identified genes encode proteins that are involved in brain development and/ or neurotransmission (Muhle, Trentacoste, & Rapin, 2004). Indeed copy number variations (Gepner & Féron, 2009; Sebat et al., 2007) and mutations have been found that are associated with cortical organization, synaptic dysfunction, and neuro-modulation (Gepner & Féron, 2009).

Of the genes identified as possible candidates involved in the causation of autism, only a few have been identified as common variants, meaning they have been associated with autism in more than one study (Veenstra-Vanderweele, Christian, & Cook, 2004). Wang et al. (2009) identified an intergenic region between cadherin 9 and 10 as a common variant underlying autism. Cadherins are involved in the neuronal migration (Levy et al., 2009) and connectivity (Takeichi, 2007) associated with neural development. Along the same lines, mutations of the RELN gene and the resultant alterations in the protein Reelin have been implicated in ASD (Fatemi et al., 2005). The protein Reelin is involved in neuronal migration and cortical layering during

development (Fatemi et al., 2005) and thus it follows that alterations of this protein can result in abnormal brain development.

Synaptic dysfunction, such as abnormal synapse formation and faulty transmission across synapses, has also been suggested as a contributing factor in ASD (Gepner & Féron, 2009; Levy et al., 2009). Mutations in the neural cell adhesion and synaptic molecules neuroligin 4 (NLGN4X) and neuroligin 3 (NLGN3) have been found in those with ASD (Jamain et al., 2003; Tabuchi et al., 2007). These X-linked molecules appear to be associated with synaptic development of glutamate and GABA networks, which are impaired in some individuals with ASD (Hughes & Melyn, 2005). Several neuroligins (i.e., NLGN1, NLGN3, and NLGN4X/Y) are found post-synaptically at glutamatergic synapses and neuroligin 2 (NLGN2) is found at GABAergic synapses (Varoqueaux et al., 2006). Genes that encode neurexins have also been associated with ASD (Autism Genome Project Consortium, 2007). Neurexins are heavily involved in glutamatergic and GABAergic synaptogenesis and are localized at presynaptic terminals (Graf, Zhang, Jin, Linhoff, & Craig, 2004). They exert their influence over GABA and glutamate synapses through their connections with neuroligins (Graf et al., 2004). These synaptic abnormalities may contribute to dysfunctional neural communication in ASD.

Anatomical Differences

It has been reported that children with ASD often demonstrate typical development after birth and that the symptoms of ASD do not emerge until around the first year of life (Zwaigenbaum et al., 2005; Ozonoff et al., 2010). Thus, changes in brain structure after the first postnatal year may engender the symptoms characteristic of ASD.

Several laboratories have examined anatomical differences in the brains of children with autism compared to TD children using magnetic resonance imaging (MRI) to evaluate head circumference and white matter tract development.

As children with ASD have been noted to have larger heads than their typically developing counterparts, Hazlett et al. (2012) examined data from the Infant Brain Imaging Study (IBIS), which is a longitudinal study investigating children at risk for ASD utilizing MRI. Children at risk for ASD were identified based on having a sibling with ASD, which would increase the genetic possibility of developing autism. High and low risk infants were followed from 6 to 24-months of age at which point they underwent diagnostic assessment for ASD. Throughout the study, neuroimaging and behavioral data were collected from 98 high risk infants and 36 low-risk infants at ages 6, 12, and 24 months. However, for this report (Hazlett et al., 2012), only the scans for the 6-month data were discussed.

Neuroimaging data were collected with 3-T Siemens Tim Trio MRI scanner using a head coil with 12 channels. The imaging scans, performed while the infants were sleeping, were assessed and rated separately by two neuroradiologists who were blind to the study. Measurements of brain volume were obtained for the cerebrum, cerebellum, lateral ventricles, and for the total brain, defined as gray and white matter combined, and finally for total CSF. In addition, head circumference was measured using the HeadCirc tool, which is an image processing instrument.

No differences were found between the low and high risk 6 month old infants in terms of head circumference, total brain volume, total tissue, CSF, cerebral cortex and

cerebellum volume, or in the lateral ventricles. It is likely that differences between children who develop ASD and those who don't manifest toward the end of the first postnatal year. The authors suggest that the increase in brain volume observed in children with ASD may be due to processes that occur prior to the first year of life. Furthermore, it is thought that early intervention may affect the development of ASD symptomology in high risk children.

Another study from the same lab also utilized the IBIS MRI data to explore differences in white matter tract development in infants with ASD versus TD infants. Wolff et al. (2012) examined axonal development in infants from 6 to 24-months of age using diffusion tensor MRI. Again, children were assessed for ASD at 2 years of age using the Autism Diagnostic Observation Schedule (ADOS). At 2 years, the sample consisted of 28 children with ASD and 64 TD children.

Brain images were obtained using 3-T Siemens TIM Trio MRI scanner at 6, 12, and 24-months of age. Data were collected while the infants were sleeping. Seed label maps were constructed for white matter tracts previously reported to be associated with ASD. The fiber tracts of interest included the corpus callosum, fornix, inferior longitudinal fasciculus, anterior thalamic radiation and the internal capsule. Fractional anisotropy, which is a measure of microstructural fiber integrity, was used to analyze each of the fiber tracts of interest.

As expected, increases in fractional anisotropy were observed in both the ASD infants and the TD infants from 6 to 24 months. However, the rate with which these changes occurred differed such that TD children showed greater change over time in the

fornix and inferior longitudinal fasciculus and uncinate than infants with ASD. In addition, growth trajectories for the internal capsule and left thalamic radiation showed a steeper incline for TD infants than ASD infants.

At 6 months of age, the majority of the tracts examined showed higher fractional anisotropy values for ASD infants than TD infants. This was observed in the left fornix, left longitudinal fasciculus and left uncinate, the body of the corpus callosum, and the right posterior limb of the internal capsule. In contrast, at 12 and 24 months of age, fractional anisotropy values were greater in left anterior thalamic radiation of TD infants than in infants with ASD. By 24-months, the TD infants also demonstrated greater fractional anisotropy values in the left anterior limb of the internal capsule than ASD infants. Thus, infants who developed ASD initially showed greater fractional anisotropy, which seemed to level off to values similar to those of the TD infants by 12 months of age. However, by 24 months, TD infants surpassed the ASD infants in terms of white matter tract developmental trajectories. The authors maintain that infants with ASD exhibit abnormal networks of neuronal connectivity that affect regions throughout the brain, as opposed to a single area. It is noted that the processes of pruning and myelination may produce the aberrant white matter tract development observed in infants with ASD.

Post-mortem studies have also investigated axonal structure in the brains of individuals with autism to provide insight regarding neural connectivity patterns. Zikopoulos and Barbas (2010) examined myelinated axons located beneath 3 prefrontal lobe regions in the post-mortem brains of adults with ASD. More specifically, axonal

density and thickness of myelin sheaths was assessed in the areas of the anterior cingulate cortex, the orbitofrontal cortex, and the lateral prefrontal cortex. These regions were selected for investigation because they are involved with processes that are impacted in those with ASD, such as executive function and emotion (Courchesne & Pierce, 2005, as cited in Zikopoulos & Barbas, 2010).

Tissues samples were obtained from the brains of 5 adults with ASD and 4 typically developed controls of the same age from the Harvard Brain Tissue Resource Center in collaboration with the Autism Tissue Program. Samples were collected from both shallow and deep locations in the regions of interest. Tissue was post-fixed with a paraformaldehyde solution and cut into 50 micron (μm) coronal sections using a vibratome. Tissue then underwent immunohistochemistry to label for oligodendrocytes and neurons and to exclude cells from locations outside of the regions of interest. Tissue was also Nissl stained to examine cytoarchitecture. Computerized light microscopy was used to determine the number of neurons and volume of each section. To analyze the number of myelinated axons, sections were examined using confocal microscopy. Finally, electron microscopy was used to establish axonal density and to measure the thickness of axons and myelin sheaths.

The axon density underlying prefrontal regions was shown to be comparable in the ASD and TD brains examined. However, a decrease in long-range, thick axons and an increase in short to medium range, thinner axons were identified in the anterior cingulate and orbitofrontal cortices of autistic brains. As the prefrontal areas were not enlarged in the adult, autistic sample, the authors assert that the previously reported

overgrowth of this region in autistic children is likely temporary. Nevertheless, the discrepancy in the number and thickness of the axons observed in the autistic brains may provide some explanation for the deficits characteristic of individuals with autism. The authors suggest that disruption of prefrontal networks, via connections of the orbitofrontal cortex with the amygdala and the connections of the anterior cingulate cortex with the lateral prefrontal cortex, would affect emotional and attentional processes.

Electroencephalography and Brain Activity

The idea that brain regions that are activated at or near the same time are involved in the processing and/ or execution of a specific task is the basis for research using several forms of neuroimaging and recording technology. The electroencephalogram (EEG) has been used as a tool for examining the brain since 1924 (Berger, 1924; as cited in Pizzagalli, 2007). The EEG is a dynamic measure of the electrical activity present at the scalp. The electrical activity recorded from a given region on the scalp represents the fluctuation of the underlying field potentials for that region across time. Its specific properties (i.e. amplitude and frequency) depend, among other things, on the temporal synchrony and spatial location of its underlying generators. As cortical pyramidal neurons reside near the scalp and have the characteristics necessary to generate potentials including parallel alignment and synchronized activity, they are thought to be the primary generators of the EEG (Elul, 1972; Speckmann & Elger, 1982). Thus, the electrical activity recorded by the EEG reflects the extracellular potentials of nearby cortical pyramidal neurons, whose activity may be modulated by a wide range of cortical and subcortical inputs (Kandel, Schwartz & Jessel, 2000). Rhythmic oscillations have been

observed consistently across several frequency bandwidths in different regions of the brain. The primary frequency bandwidths examined include delta (1 – 3 Hz), theta (4 – 7 Hz), alpha (8 – 12 Hz) and beta (13 – 30 Hz). However, gamma (greater than 30 Hz) (Engel & Fries (2010) seems to be gaining more interest among EEG researchers. Using EEG, bandwidths of different frequencies have been associated with development, states of consciousness, and various cognitive activities.

The major frequency bandwidths are often divided into two groups with delta, theta, and alpha associated with global processing with the aim of integrating signals from different cortical regions across the brain (Knyazev, 2012). In contrast, beta and gamma oscillations are more localized and are believed to be involved in more specific cognitive functions (Knyazev, 2012). However, as each bandwidth has been associated with multiple functions, they cannot be associated with a single activity or process (Başar, Başar-Eroglu, Karakaş, & Schürmann, 2001; Engel & Fries, 2010). That said, some consistency between frequency bandwidths and human behavior has been observed.

Research with humans has shown that slow wave oscillations such as delta and theta are prevalent in early stages of development (Scher, 2008; Vladimirova, 1991) and are known to decrease with age (Gasser, Verleger, Bächer, & Sroka, 1988). Delta is increased in infants and in young children when compared to adults (Lüchinger, Michels, Martin, & Brandeis, 2011; Michels et al., 2013). In adults, increased delta oscillations have been associated with slow wave sleep (Engel & Fries, 2010; Knyazev, 2012), and motivation, especially in relation to award systems (Knyazev, 2007). Furthermore, increased delta activity is associated with several forms of brain pathology including

brain lesions (Gloor, Ball, & Schaul, 1977), hypoxia (Ginsburg, Pasternak, & Gurvitch, 1977), and developmental disorders (Barry, Clarke, & Johnstone, 2003). Similarly, oscillations in the theta frequency band have also been associated with developmental disorders. Increases in both delta and theta oscillations have been observed in those with attention deficit hyperactivity disorder (ADHD) (Barry et al., 2003), fetal alcohol syndrome (FAS) (Mattson et al., 1992) and Down syndrome (Babiloni et al., 2010; Kaneko, Phillips, Riley, & Ehlers, 1996). Theta activity has also been associated with selective attention (Başar-Eroglu, Başar, Demiralp, & Schürmann, 1992) and working memory, particularly for verbal tasks (Jenson & Tesche, 2002). In fact, studies of working memory have associated intracranial recordings of increased theta activity with tasks involving spatial skills in a human maze (Caplan, Madsen, Raghavachari, & Kahana, 2001) and during the Sternberg verbal working memory task, which requires one to remember lists of consonants (Raghavachari et al., 2001). Increased theta coherence has also been observed during memory retention of visuospatial information (Sarnthein, Petsche, Rappelsberger, Shaw, & von Stein, 1998).

In contrast to lower frequency bandwidths, higher frequency alpha and beta oscillatory activity increases with age (Barry, Clarke, Johnstone, & Brown, 2009; Gasser et al., 1988). Alpha activity appears to be most prominent over the occipital and parietal cortices and is prevalent in the adult brain (Lopes da Silva, 1991). Attenuation of alpha activity reflects brain activity beyond a resting state (Shagass, 1972; as stated in Vuga, Fox, Cohn, Kovacs, & George, 2008). The posterior alpha rhythm is believed to occur in response to attention and expectancy (Klimesch, Doppelmayr, Russegger, Pachinger, & Schwaiger, 1998). Moreover, alpha oscillations have been associated with emotion and

approach- avoidance behavior as well as visual attention (Gasser, Bacher, & Steinberg, 1985; Jones, Field, Davalos, & Pickens, 1997; Jones, Field, Fox, Davalos, & Gomez, 2001; Vuga et al., 2006; Vuga et al., 2008). Additionally, frontal alpha asymmetry measures are most associated with emotion and are highly stable over time (Dawson, 1994; Jones et al., 1997; Vuga et al., 2008).

Research suggests that beta band activity is indicative of the maintenance of the “status quo” and of top-down processing involving perceptual information (Engel & Fries, 2010). Thus, beta activity is increased during times when one’s behavior is not expected to change in the immediate future. This idea has been supported by studies of motor control. Beta activity localized over sensorimotor cortices is increased during muscle contractions, such as in tasks that require inhibition of behavior (Klostermann et al., 2007). Intracranial EEG has found an increase in beta activity over both inferior frontal gyrus and primary motor areas during an inhibitory Go/ No Go task demonstrating top-down processing during the stop response (Swann et al., 2009). In addition to motor areas, others have reported motor related beta activity over parietal-temporo-occipital cortex (De France & Sheer, 1988 as cited in Lopes da Silva, 1991). In relation to cognitive processes, increases in beta band activity over occipital and parietal areas have been found during a visual top down processing task in response to the presentation of face stimuli (Okazaki, Kaneko, Yumoto, & Arima, 2008). Hence, beta oscillatory activity seems to be related to motor activity as well as to the top down processing of sensory information. Indeed, studies presenting novel stimuli requiring bottom-up processing have shown attenuation of beta activity and an increase in gamma activity (Engel & Fries, 2010; Engel, Fries, & Singer, 2001). Therefore, gamma activity has been

associated with tasks requiring bottom-up cognitive processing (Engel, Fries, & Singer, 2001). In particular, gamma has been associated with information processing for sensory perception and higher cognitive activities such as verbal memory encoding (Fell et al., 2006).

In terms of human growth, the spectral properties of EEG are dynamic and undergo substantial changes over the course of development. While each frequency bandwidth is associated with certain cognitive abilities, there is not a single property that each is related to. This is especially true for children as brain development and organization is incomplete.

EEG coherence provides a measurement of the functional interactions among neural systems operating in separate frequency bands and may produce information about network formation and functional integration (Srinivasan, Winter, Ding, & Nunez, 2007). These measures are often correlated with cognitive and behavioral activities (Nunez et al., 1997). Thus, coherence in EEG represents the functional coupling of activity among brain regions involved in particular tasks. EEG coherence measures specifically describe the correlation between any pair of signals, as a function of frequency, based on the consistency of relative amplitude and phase (Murias, Webb, Greenson, & Dawson, 2007; Srinivasan et al., 2007). Coherence is represented by a squared correlation coefficient. It varies with the spatial locations of electrodes on the scalp and spectral frequency (Srinivasan, Nunez, & Silberstein, 1998). A high coherence value indicates synchronized neural oscillations (based on phase) between two EEG signals, whereas low

coherence values suggest functional independence of the EEG signals (Murias et al., 2007).

Basal Neural Function in ASD

The idea of disordered functional connectivity in the brains of individuals with autism has been gaining support based on the results of studies that use neuroimaging and recording techniques. Rhythmic oscillations that occur together are believed to represent functional connectivity, which is the process the brain uses to integrate information that has been processed in noncontiguous regions (Lopes da Silva, 1991). Thus, the nature of coherence provides a suitable method for examining functional connectivity between neocortical regions.

EEG measures of baseline activity. Murias and colleagues (2007) examined the functional cortical connectivity of 18 high-functioning, adult males with ASD and 18 TD adults using EEG coherence measures. Participants ranged in age from 18 to 38 years old. ASD diagnoses were established using diagnostic interviews and clinical judgments based on criteria presented in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV). Participants' EEGs were obtained while each was sitting down and with eyes closed in the resting state. The spontaneous EEG was recorded from 124 electrodes using a Geodesic Sensor Net. After recordings were collected, the coherence spectra of electrode pairs that were separated by at least 3 cm were analyzed. This separation was used to ensure that the activity of different populations of neurons was examined. In addition, relative power values were examined for frequencies of 2 to 30

Hertz (Hz). Relative power was acquired by calculating the fraction of power at each 1 Hz band and then dividing by the sum total of power across 2 – 30 Hz.

The EEG coherence measures were significantly different between the ASD and TD adults during the resting state at both 3 – 6 Hz and 8 – 10 Hz frequencies. The ASD group demonstrated greater coherences across the 3 – 6 Hz band than the TD group in 10.3% of electrode pairs. In contrast, the TD group showed greater coherence values across the 8 – 10 Hz band than the ASD group in 22.7% of electrode pairs. The relative power values also differentiated the ASD participants from the TD participants. Relative power was elevated in 32% of frontal and prefrontal recording sites in the ASD group across the 3 – 6 Hz band. Participants with ASD also showed a reduction in power across the 9-10 Hz band at 48% of frontal/ prefrontal and occipital/ parietal regions. Finally, elevated relative power was observed across the 13 – 17 Hz band at 9% of recording sites in the occipital and parietal areas in ASD adults.

Murias and colleagues (2007) maintain that the observed coherence and power differences observed between the ASD and control participants reflect distinct patterns of functional over-and under-connectivity at specific spatial and temporal scales. In particular, it is concluded that the alpha range differences indicate that the frontal lobe of ASD adults has weak functional connections with the rest of the cortex. In contrast, the authors suggest that the theta range (3 – 6 Hz) results suggest local cortical over-connectivity, particularly in the left frontal and temporal cortices. Thus, it is suggested that the long range functional connections within the brains of adults with ASD are not well developed, whereas shorter, local functional connections are rather extensive.

Similar to the study by Murias et al. (2007), Coben and colleagues (2008) examined power and coherence differences between 20 children with autism and 20 TD children who were 6 to 11 years of age. Children were seated on a reclining chair during EEG recordings, which were completed in one session. Recordings were collected from 19 electrode sites that were placed using the International 10-20 System during an eyes closed baseline.

A minimum of 75 seconds of artifact-free EEG data was used for analysis. Power indices were calculated for four frequency bands including delta (1.5 – 3.5 Hz), theta (3.5 – 7.5 Hz), alpha (7.5 – 12.5 Hz), and beta (12.5 – 25 Hz). The power values in these bands were then compared across the left frontal (Fp1, F3, and F7), midline frontal (F2), right frontal (Fp2, F4, and F8), left central (T3 and C3), midline central (Cz), right central (T4 and C4), left posterior (T5, P3, and O1), midline posterior (Pz), and right posterior (T6, P4, and O2) regions. Coherence indices were calculated for eight intrahemispheric and interhemispheric electrode pairs for a total of 16 electrode pairs.

The results revealed significant absolute (actual voltage in microvolts squared) and relative power differences between the autistic group and the TD control group. Participants with autism demonstrated reductions in absolute power in the delta band, particularly in the left frontal and posterior regions. They also showed significant reductions at central regions. Relative theta power was shown to be greater in the autistic group than the control group in frontal and posterior regions than at central regions. In addition, the right hemisphere showed more elevated power in the posterior region than in the frontal region in autistic participants. Reductions in beta power were also found in

the autistic participants, particularly in the right hemisphere when compared to controls. Significant differences in absolute or relative alpha power were not observed between groups.

In terms of coherence, autistic participants showed reduced delta and theta intrahemispheric coherence over short to medium distances and long inter-electrode distances. They also displayed lower delta and theta interhemispheric coherences in frontal and temporal regions and reduced alpha band coherences in the temporal regions. Finally, interhemispheric coherences were reduced in central/parietal/occipital regions in delta, theta, and beta frequency bands in the autistic group as compared to the control group.

It was concluded that the elevated theta over the right posterior area is indicative of abnormal functioning in children with autism. It was further noted that excess theta activity has been associated with problems regarding executive functioning and mental activity. The reduction in delta band power over the frontal lobe is thought by the authors to reflect problems with functional integration in this region.

The coherence measures also reflect patterns of under-connectivity in autistic participants based on lower coherence values for both short to medium and long inter-electrode distances. These findings were comparable interhemispherically and intrahemispherically, supporting the idea that neural organization and connectivity is abnormal in individuals with autism.

Cantor, Thatcher, Hrybyk, and Kaye (1986) used EEG to differentiate between autistic children, developmentally delayed children, and TD children. Eleven autistic

children, who ranged in age from 4 to 12 years, were compared to 88 age-matched TD children, 18 age-matched developmentally delayed children, and 13 mentally age-matched, TD toddlers, aged 16 months to 5 years.

During data collection, children were fitted with a 19-lead electrode cap, with electrodes placed according to the 10 – 20 system, referenced to linked earlobes. EEG recordings were acquired during an eyes open resting condition. Measures were collected for relative and total power, coherence, and amplitude asymmetry for the delta (1.5 – 3.5 Hz), theta (4 – 7.5 Hz), alpha (8 – 12 Hz), and beta (13 – 30 Hz) frequency bands.

Children with autism were shown to have greater power in the delta frequency band and less power in the alpha band in the fronto-temporal regions bilaterally and left temporal region than the age- matched developmentally delayed and age-matched TD children. However, TD children had greater power in the occipital regions than children with ASD and toddlers. Finally, toddlers were shown to have greater power in the left central, midline central, and left fronto-temporal regions than children with autism.

In terms of EEG asymmetry, the children with autism showed asymmetry patterns similar to the toddlers and showed less asymmetry than the age-matched TD and developmentally delayed children. When amplitude asymmetries were observed in the autistic children, they were present in the posterior-temporal, central, and occipital regions and showed predominance in the left hemisphere over the right. This is in contrast to the age-matched groups that showed the predominance of activity in the right hemisphere. In addition, autistic children and toddlers exhibited larger amplitudes in the

left anterior temporal region than the TD children. Autistic children also showed greater amplitudes in the right posterior regions than the age-matched, TD children and toddlers. Overall, a gradient of asymmetry was demonstrated between the children, such that the greatest asymmetries were observed in the age-matched TD children, followed by the developmentally delayed children, then the toddlers, and then the autistic children.

Coherence values were greater between and within hemispheres in both toddlers and children with autism when compared to the typically developed and developmentally delayed children. The children with autism demonstrated greater coherence between hemispheres in the beta frequency band than the three comparison groups and greater coherence in the alpha band than the age-matched, typically developed children. Although toddlers showed more coherence in the frontal regions in the delta band than autistic and developmentally delayed children, autistic children also had greater coherence in the left frontal region than the developmentally delayed children. In addition, the autistic group had greater coherence in left parieto-central regions than toddlers. In the right hemisphere, autistic children exhibited greater coherence in the parieto-occipital and central-parietal regions than the age-matched groups. They also showed greater coherence in the right parieto-central region than the toddlers.

There were several similarities in the EEGs of toddlers and autistic children including more slow-wave activity, less alpha activity, less amplitude asymmetry, and greater coherence than the other children examined. As such, Cantor et al. (1986) maintain that the similar EEG spectral profiles of autistic children and toddlers suggest a maturational delay in the brain development of the autistic children. However, the

toddlers still maintained greater percent alpha and lower percent delta than the children with autism. It was also noted that the high coherence demonstrated by the autistic children reflects a high amount of redundancy in cortical connections and consequently little functional differentiation.

Finally, a recent study conducted by Duffy and Als (2012) compared the EEG coherence patterns of children with ASD to TD children, ranging from 2 to 12 years of age. The researchers aimed to determine whether coherence measurements could be used to differentiate ASD from TD children. Participant data was obtained from a database of EEG recordings that had been collected previously by Duffy with the purpose of screening patients for epilepsy and/ or anomalies involving the processing of sensory information. Four hundred sixty three patients were selected for the ASD group based on diagnosis using DSM-IV or ADOS guidelines. The control group consisted of 571 patients who were designated as full functioning and healthy.

EEG recordings were collected using gold-cup electrodes during an eyes open, alert state by EEG technicians who were blind to the group designation of the participants. Data was collected for 8 to 20 minutes per patient. Epochs of artifact-free data were analyzed for 24 channels. Of these channels, 19 were placed according to the International 10-20 system and 5 were placed according to a 10-10 measurement system. The 10-10 subset of electrodes was used to record data from frontal temporal regions (FT9 & FT10), temporal-parietal regions (TP9 & TP10), and the midline occipital area (Oz).

Each coherence measurement was used as a variable for factor analysis. A total of 40 factors were identified, using discriminant function analysis, which successfully distinguished children with ASD from TD children. In addition, as the age of the participants ranged from 2 to 12 years, children were divided into 3 groups for separate statistical analyses, 1) 2 to 4 years, 2) 4 to 6 years, and 3) 6 to 12 years of age. Within the 2 to 4-year age range, the TD control group was classified accurately 92.9% of the time and the ASD group was correctly classified 99.5% of the time. In the 4 to 6-year range, both children with ASD and TD children were correctly differentiated with 100% accuracy. In the 6 to 12-year age group, TD children were classified with 98.7% accuracy whereas children with ASD were identified with 96% accuracy. Of the 40 factors, 33 were shown to be the best predictors of developmental status. Of these, 16 factors involved electrodes in the frontal lobe, 14 factors were associated with central region electrodes, 24 factors involved the temporal lobe, 16 factors involved the parietal lobe, and 16 factors showed occipital lobe involvement.

Overall, EEG coherence was reduced in 70% of the factor loadings in the children with ASD when compared to the TD children. Factor 15 was the most frequently identified and corresponds to coherence measurements between anterior and posterior temporal lobe regions in the left hemisphere and between anterior temporal and frontal regions of the left hemisphere. A reduction in EEG coherence was observed for factor 15 in the ASD group when compared to the TD control group. In contrast, children with ASD showed greater coherence in 30% of the factors when compared to the TD group. Unlike the Murias et al. (2007) study with adults, regions of increased coherence were shown between long distance electrode pairs throughout the brain. In addition, the

spectral patterns were shown to be wide (10 Hz) and stable across the coherence factor loadings. Surprisingly, no consistent pattern of hemispheric asymmetry or regional involvement was shown.

The authors concluded that the disparate patterns of the coherence factor loadings successfully differentiated between children with ASD and TD children. They further suggest that these patterns may represent a first step in the development of a neurophysiological marker for ASD. Finally, the authors maintain that the reduction in coherence observed in the factor 15 loading may signify abnormal activity in the arcuate fasciculus contributing to the language deficits reported in children with ASD.

Functional magnetic resonance imaging. Using functional magnetic resonance imaging (fMRI), Dinstein and colleagues (2011) examined neural activity in children with autism. The researchers collected data from children, between 1 to 3.5 years of age, while they were sleeping. Twenty-nine children with autism and 13 children with language delay were compared to 30 typically developing children in terms of neural regions involved in language processing. Autism was diagnosed using the ADOS by a clinical psychologist. In addition, the Mullen scale was used to assess expressive language in the toddlers, with lower scores (under 40) indicating language deficits. Interestingly, the language scores attained by the ASD and the language delay group were similar, but only the ASD group demonstrated the social and communicative deficits characteristic of autism.

The researchers obtained both functional and structural MRI scans using a 1.5T Signa scanner. The functional and anatomical images were matched and then converted

to Talairach coordinates. Six regions of interest (ROIs) were selected for analysis. ROIs consisted of the lateral occipital area, anterior intraparietal sulcus, motor and somatosensory cortex, superior temporal gyrus (STG; also known as Wernicke's area), inferior frontal gyrus (IFG; also known as Broca's area), and the lateral prefrontal cortex. While fMRI was obtained, sleeping participants were exposed to four types of auditory stimuli. Blocks of stimulation included words and pseudo words, sentences, tones, and environmental sounds. Blocks of stimuli were presented for 20 to 35 seconds and were alternated with quiet blocks without auditory stimuli for the same amount of time. Responses to the auditory stimuli that were thought to be evoked responses were regressed out of the data prior to analysis. This was completed to focus analyses on the spontaneous fluctuation in the data as opposed to the elicited stimulus response.

The fMRI scans collected demonstrated strong correlations for each ROI and the homologous region in the contralateral hemisphere for all children, except the STG and the IFG. Children with autism showed significantly weaker correlations in STG and IFG when compared to the language delay and TD children. In fact, children were able to be differentiated based on correlation strength in the STG and IFG. Children with weak correlations in either region were categorized as autistic, whereas children with stronger correlations in both the STG and IFG were from the TD control group. Thus, children with autism demonstrated reduced interhemispheric activity between the temporal and frontal regions involved in the comprehension and production of language. In addition, for children in the autism group, a significant positive correlation was found between expressive language scores and cortical activation strength in the IFG. Furthermore, a significant negative relationship was observed between strength of activation in IFG and

autism severity, as assessed with the ADOS. Hence, as autism severity increased, the cortical activation strength in IFG decreased. As such, the authors proposed that reduced interhemispheric activity in language areas may be an important feature of ASD in young children.

Taken together, individuals with ASD have demonstrated elevated frontal theta coherence and power and reduced alpha coherence and power at frontal, parietal, and occipital sites. In addition, increased delta power has been observed in individuals with ASD when compared to TD controls. Elevated delta and theta have been reported in those with brain pathology (Babiloni et al., 2010; Kaneko et al., 1996) and learning disorders (Barry et al., 2003). Alpha power is expected to be increased in TD adults when the eyes are closed (Berger, 1933, as cited in Barry et al., 2009) and hence decreased alpha activity is uncharacteristic and may indicate anomalous brain function. However, in children, alpha activity is less prevalent than in adults and increases with age. Finally, studies of beta indicate decreases in right hemisphere beta activity in those with ASD. Research with fMRI has revealed reduced interhemispheric activity in participants with autism, particularly between temporal and frontal regions associated with language (Dinstein et al., 2011). Therefore, reduced patterns of neural activity observed with fMRI and atypical patterns of EEG spectral activity may be characteristic of autism and indicative of ASD.

Face Processing

Of particular interest to those investigating ASD is the impaired ability to understand the emotions of others. Comprehending the emotions of others is imperative

to successful communication. One of the primary means of interpreting one's mood is by observing the expressions on another's face. However, in order to correctly understand the expressions on a person's face, it is important to be able to perceive facial characteristics. There is an increasing body of evidence that suggests that individuals with ASD struggle with normal face processing, which would also interfere with perception of facial expression.

Wallace, Coleman, and Bailey (2008) examined face and object processing in adults with ASD. They were specifically interested in the ability to use configural and feature processing strategies in face discrimination tasks. Configural processing refers to perceptual strategies to process faces based on holistic information and second-order information such as the spatial configuration between facial features. Participants consisted of 26 adults with ASD and 26 age-matched, TD individuals as a comparison group. The groups were also matched based on handedness and vocabulary, which was assessed with Raven's Progressive Matrices – Standard Edition and the British Picture Vocabulary Scale.

The Benton Test of Facial Recognition was used as a standardized measure of face processing. During the behavioral task, participants were told they would view pictures of faces or cars presented in pairs in sequence. Their task was to determine if the pairs of images were the same or different. The face image stimuli consisted of ninety images of male and female faces from an internet library. All faces displayed a neutral facial expression and were taken in a frontal pose. None of the images displayed faces with facial hair. A discrimination task was used whereby a red fixation cross was

presented in the center of a computer screen for 350 milliseconds (ms). To test holistic processing, the face or car images were then shown for 40, 70, or 100 ms. A pattern mask followed the presentation of each target image for 350 ms. There were 120 trials and an inter-trial interval of 1,500 ms was used to provide a break during the half-way point.

In the test of second-order processing, the stimuli consisted of 20 images of both male and female faces that were equally represented. In this task, instead of images of cars, images of houses were presented. During each trial, a red fixation cross was presented in the center of the computer screen for 350 ms. The target image was then presented for 3 seconds. Following the target image, a pattern mask was shown for 350 ms. The test stimulus was then presented for 1,000 ms. Participants were asked to determine whether the 2 sequentially presented images of faces or houses were the same or different by pressing a button on a keyboard. On the trials in which the test stimulus was different from the target stimulus, the image was slightly changed based on either configural or feature properties. There were 80 trials with an inter-trial interval of 1,500 ms and a break provided at the half-way point.

It was shown that the TD control group scored significantly better than the ASD group on the Benton Test of Facial Recognition. On tests of holistic processing, all participants processed faces more accurately than cars and performance improved with longer stimulus exposure durations. However, the TD group had more accurate facial identification when processing faces than the ASD group. On tests of second-order processing, all participants were better able to discriminate between faces than houses.

Participants were also better able to identify alterations of feature properties than configural properties for both houses and faces. Again, the TD group performed more accurately on the face processing task than the ASD group. However, there was no difference between the participant groups in accuracy when judging the changes made to house stimuli.

It was concluded that the poor performance demonstrated by the participants with ASD reflects a comprehensive cognitive deficit in face processing ability. It was noted that unlike other studies that found superior object processing in individuals with ASD when compared to TD controls, that finding was not substantiated in this study. Instead, the authors' results support the idea that the poorer face processing performance observed in participants with ASD is due to either lack of use or impairment of holistic-processing methods.

A similar study used a different approach to investigate face processing and the strategies utilized during face recognition tasks in participants with ASD. Wolf et al. (2008) administered the identity component of the Let's Face It! Skills Battery to 85 children and adolescents with ASD who ranged in age from 8 to 14 years. Confirmation of ASD diagnosis was accomplished using the Autism Diagnostic Interview – Revised (ADI-R) and the Autism Diagnostic Observation Schedule – General (ADOS-G), which was administered by a clinician. A TD, age and intelligent quotient (IQ) matched control group, was recruited for comparison.

Participants were administered a number of neuropsychological and behavioral tests within the Let's Face It! Skills Battery over a period of two days. The Let's Face It!

Skills Battery consists of 10 assessments that examine facial identity, facial emotion, and object processing. Only the 5 assessments that make up the facial identity component and the two objects processing assessments were used. These assessments included: 1) Matching Identity Across Expression, 2) Matching Identity Across Masked Features, 3) Featural and Configural Face Dimensions, 4) Parts/ Whole Identity, 5) Immediate Memory for Faces, 6) Featural and Configural House Dimensions, and 7) Immediate Memory for Cars. Accuracy, in terms of the number of items correct, was measured in each identity test.

The findings indicated that the TD participants performed at a higher rate of accuracy on the Matching Identity Across Expression Test than the participants with ASD. The Matching Identity Across Masked Features Test examined the ability to match facial identity to a probe face that had particular features blocked. Probe faces could have either the eyes or mouth regions masked. The TD group performed better than the ASD group when identifying faces with no mask. However, no differences were found between groups when the faces had either the eyes or mouth masked. The Featural and Configural Face Dimensions task required the ability to differentiate faces based on either featural (individual facial features) or configural (holistic) information. Again, this assessment focused on the eye and mouth region of each face stimulus. All participants differentiated featural information more accurately than configural information. However, TD participants performed better when discriminating configural eye information than configural mouth information, whereas there was no difference between the discrimination of these regions for the participants with ASD. In addition, the TD control group performed better on eye items than the ASD group, though there was no

difference between groups on the items that focused on the mouth. On the Parts/ Whole-Identity Test, participants had to discriminate faces based on either an entire face or part of the face. Here the TD group performed with superior accuracy on eye items, but not mouth items, during the configural portion of the test compared to the ASD group. Although the difference between eye and mouth items was greater for the control group, both groups showed higher accuracy on eye items than mouth items. Further findings showed that all participants identified “whole” items with better accuracy than “part” items, especially when presented with mouth items. Finally, when considering “part” items, trials involving eye discrimination were performed with greater accuracy than were mouth items for both groups of participants. On the Immediate Memory for Faces Test, which examined short-term memory for faces, the TD group out-performed the ASD group.

In the assessments of object discrimination, participants needed to discriminate between houses that were the same or different. On the House Dimensions Test, participants demonstrated greater accuracy for configural information than featural information across groups. However, individuals with ASD were better able to discriminate between houses than the TD individuals, regardless of stimulus type (i.e., configural or featural information). Furthermore, the Immediate Memory for Cars Test did not reveal any differences between groups for the short-term memory of car images. This task was used as a control for the Immediate Memory for Faces Test. Finally, a negative correlation was found between the eye items of the Featural and Configural Face Dimensions Test and the ADOS socialization and communication + socialization scores.

Individuals with higher ADOS scores, indicating greater ASD severity, had poorer accuracy in tasks requiring discrimination based on the eye region.

Many assessments were conducted in this study. Based on the Immediate Memory for Faces Test and Matching Identity Across Masked Features Test, the authors concluded that individuals with ASD showed impairment in recognizing the identity of faces when orientation, expression, or feature information was changed. Although participants with ASD were able to differentiate faces based on mouth information, they showed difficulty when required to make decisions based on the eye region. Similar findings were shown for the Parts/ Whole Identity Test, such that the ASD group demonstrated deficits in face recognition when presented with the eye region in both the “part” and “whole” face conditions, but were not impaired in face recognition based on mouth information. Thus, the authors conclude that instead of a global impairment in face perception, individuals with ASD demonstrate a selective deficit that is limited to the eye region. Individuals with ASD do not typically make eye contact and instead attend to the mouth region (Wolf et al., 2008).

Other researchers have found few behavioral differences in face processing, but have found neural differences in the processing of faces. Pierce, Müller, Ambrose, Allen, and Courchesne (2001) revealed structural differences between adults with autism and a TD control group in regions known to be involved in the processing of face stimuli. The researchers examined 7 male adults, aged 21 – 41 years, with autism and 8 age-matched controls using fMRI during a face perception task.

Prior to fMRI, the researchers measured the volumes of the fusiform gyrus, the inferior temporal gyrus, the middle temporal gyrus, and the amygdala using 3D reconstructed datasets that were used by anatomists to trace regions based on landmarks determined by human brain atlases. These were traced on high-resolution anatomical images for each participant. During measurements of changes in blood oxygen level using fMRI, participants were asked to view images of male and female faces as well as circle and square shapes. The task required participants to press a button to identify female faces and circle stimuli. Stimuli were presented for 1.5 seconds with an inter-stimulus interval of 450 ms. Over the course of the 4 minute, 5 second fMRI scan, 120 non-repeating stimuli were presented to participants. The four regions of interest examined were the same as those used for the structural analysis of regions based on volume.

No behavioral differences were found with respect to the face perception task. Participants with autism performed as well as the control participants in terms of accuracy and response time for both the face and shape identification tasks. However, there were several brain regions that differed between the participant groups in terms of structural volumes and activation patterns. The volume of the amygdala was found to be 15% smaller, on average, bilaterally in the participants with autism than in the TD group. Although not statistically significant, the researchers also observed a trend whereby the fusiform gyrus was 8% smaller on average in the autistic participants than in the TD group.

Regional blood flow indicative of activation showed that the participants with autism demonstrated less activation bilaterally in the fusiform gyrus and in the left amygdala when compared to the TD group. In contrast, the TD participants showed strong activation to face stimuli in the fusiform gyri and amygdala. They also showed greater activity to face stimuli in the right fusiform gyrus than the autistic group. Differences in activity between groups were not observed in the right amygdala, the inferior temporal gyrus, or the middle temporal gyrus. However, additional regions of activation were observed in the TD group that were not seen in the autistic group. The inferior occipital gyrus and superior temporal sulcus responded more strongly to faces than shapes in the control group. Furthermore, all of the TD participants showed the greatest activation for faces in the lateral fusiform gyrus, also known as the fusiform face area, whereas the autistic participants demonstrated various regions of activity including the frontal lobe, fusiform face area, occipital lobe, anterior fusiform gyrus, and cerebellum.

The authors conclude that as the behavioral performance between groups for the face perception task was comparable, the fusiform face area is not entirely responsible for the ability to accurately perceive faces. The participants with autism displayed patterns of activation that included regions not typically associated with face perception, but were still able to complete the task effectively. Regardless, the authors maintain that the data suggest that the brains of autistic patients are organized differently from TD individuals and that this organization may not be optimal for perceiving all types of stimuli. It is likely that the impairment in face perception observed in autistic individuals is due to inefficient networks that encompass additional areas beyond the fusiform face area and

amygdala, such as fronto-parietal networks involved in top-down processing (Pierce et al., 2001).

A study by Kleinhans and colleagues (2008) used correlation to examine activation between the fusiform face area, the amygdala, and the inferior frontal gyrus, regions known to be involved in face processing. The researchers utilized fMRI during the attentive viewing of neutral faces and houses in individuals with ASD and a TD control group. Nineteen, high-functioning adults with ASD were compared to a group of 21 TD individuals.

Structural and functional MRI scans were obtained during the presentation of neutral faces and houses. Stimuli were presented for 3 seconds each in 8 blocks of 36 seconds with no interstimulus interval. Fixation blocks were also interleaved throughout the presentation of stimuli. Participants were asked to press a button to indicate when identical stimuli were presented in succession.

The right fusiform face area was focused on because more participants showed activation in this area than the left fusiform face area. Correlations were then examined between the right fusiform face area and six regions of interest, which included the right and left amygdala, right and left temporal lobe, and right and left inferior frontal gyrus. In addition, fMRI activity was correlated with severity of social impairment, which was determined using ADOS and ADI-R social scores.

All participants performed with high rates of accuracy during the behavioral task that required the observation of faces and houses. Likewise, there were no significant differences in fusiform gyrus activation to faces or houses between the participants with

ASD and the TD group. Both participant groups exhibited great amounts of activity in the fusiform face area to faces and in the medial fusiform gyrus to houses. Participants with ASD showed significant activity in the right amygdala and in the right anterior and posterior middle temporal gyrus. In contrast, the TD group displayed clusters of activation in the posterior cingulate, cuneus, superior colliculus, and thalamus. Activity was also observed bilaterally in the amygdala, which extended to the right anterior middle temporal gyrus in the TD individuals. Furthermore, the TD group showed higher correlations between activity in the right fusiform face area and left amygdala, bilateral posterior cingulate, and left cuneus than the ASD group. The participants with ASD exhibited reduced activation in the right fusiform face area and the thalamus. Finally, both groups demonstrated significantly correlated activity between the right and left fusiform face area.

The level of social impairment was found to be negatively correlated with the strength of activity in regions involved in social perception. Those with more severe impairments exhibited less activity between the right fusiform face area and left amygdala. In addition, a positive correlation was found between the degree of social impairment and activation between the right fusiform face area and right inferior frontal gyrus. Thus, as the severity of impairment increased, activation in these two regions also increased.

The findings by Kleinhans and colleagues (2008) show that at the level of the fusiform gyrus, individuals with ASD demonstrate normal activation in response to faces. As such, the deficits in face processing observed in autism are likely due to other

abnormalities. In particular, the ASD group showed a more limited network of face-specific activation compared to the TD group (Kleinhans et al., 2008). The authors propose that the face processing deficits in ASD may be the result of poor integration of brain regions in the “extended social brain network.” Therefore, the social difficulties experienced by those with ASD may result from aberrant neural connections that involve the limbic system. However, it is noted that global networks may not be universal in ASD. It is thought that several factors contribute to the deficits observed, such as clinical severity, early experiential factors, cognitive abilities, and task demands (Kleinhans et al., 2008).

A more recent study by Kleinhans et al. (2010) proposed that the social deficits, such as orienting and attention, observed in individuals with ASD may be associated with neural anomalies in the subcortical face processing system, which includes the amygdala, superior colliculi, and pulvinar. Kleinhans and associates (2010) examined the functioning of the subcortical face processing system in adults with ASD and TD controls using a rapid face detection task during fMRI and structural MRI. Thirty-one adults with ASD and 25 TD adults participated in the study. All participants were relatively high-functioning with full scale IQ (FSIQ) and verbal IQ (VIQ) scores greater than 80.

Behavioral pretests were administered before collecting the fMRI data, whereby participants viewed face stimuli, obtained from the Mac Brain Face Stimulus Set, to determine the fastest presentation rate that could be validly used. Participants were presented with faces or houses followed by a masked scrambled image. After each image-mask presentation, participants were asked to indicate whether a house or face was

displayed by pressing a button. After each response, a fixation cross was shown followed by the next image-mask pair.

During the fMRI trials, 78 images of fearful faces and 98 house images were presented over a period of 4 minutes and 30 seconds. As in the pretest, fearful face stimuli were obtained from the Mac Brain Face Stimulus Set. A block random design was used to present the different stimuli, which consisted of fearful faces masked by a scrambled image, houses masked by a scrambled image, pairs of scrambled images, and a blank screen. Each house or face image was presented for 23 milliseconds (ms), and then backwards masked with their own scrambled image, which was shown for 65 – 150 ms.

During the behavioral pretest, the participants with ASD performed worse than the TD group at the presentation rate of 11.7 ms. However, no differences in performance were found between groups at a presentation rate of 23.4 ms, which was the rate used during the fMRI scans. There were no between group differences in the number of errors made during the presentation of faces. In addition, both participant groups performed more poorly when identifying house stimuli compared to face stimuli.

Significant activation was detected in the fusiform gyrus bilaterally in both participant groups when presented with the fearful face stimuli. Nonetheless, similar to the Kleinhans et al. (2008) study, additional regions of activation were identified in the TD group that were not shown in the ASD group. The TD participants displayed activation in the right amygdala, right pulvinar, and bilaterally in the superior colliculus. In addition, greater activation was observed in the TD group bilaterally in the fusiform

gyrus, the left amygdala, right pulvinar, and bilateral superior colliculi than in the ASD group.

Kleinhans et al. (2010) suggest that the diminished activation of the fusiform gyrus demonstrated by participants with ASD might be associated with the reduced activation of the amygdala. Even though the participant groups showed discrepant patterns of activation, both groups were equally able to identify the face and house stimuli. This indicates that the stimuli were not processed in the same manner. Furthermore, the fusiform gyrus is known to be involved in the identification of faces, whereas the pulvinar, superior colliculi, and amygdala are involved in both identifying faces and in emotional processing (Johnson, 2005, as cited in Kleinhans et al. 2010). This is consistent with the idea that though individuals with ASD are able to identify faces accurately, they struggle with understanding emotional facial expressions.

Overall, these findings indicate that individuals with ASD are impaired in face processing abilities. In comparison to TD adults, adults with ASD performed poorly on tests of facial recognition. Studies with children and adolescents found that those with ASD struggled with tasks that required the matching of faces when the expression changed and when identifying faces based solely on the eye region compared to TD children. In addition, children with ASD demonstrated poorer memory recall for faces than TD children. In studies of fMRI, children with autism exhibited different patterns of activation during face perception tasks compared to TD children. Activation was observed in regions not typically associated with face processing, such as the cerebellum. Similarly, adults with ASD displayed less activation in the right fusiform area and left

amygdala in comparison to TD adults. These results have also been correlated with the degree of social impairment. In particular, increases in social impairment are accompanied by decreases in activation in the fusiform face area and amygdala during face processing.

Observation of Emotional Facial Expression

Extending previous work, Kleinhans et al., (2011) examined the neural foundation of emotional face processing in adults with ASD. Thirty-one, high-functioning adults with ASD and 25 age and IQ-matched TD adults participated in the study. All participants were right handed as determined by self-report.

Prior to the fMRI task, all participants completed the Social Avoidance and Distress Scale to assess anxiety. During the fMRI task, participants were presented with images of emotional faces and geometric shapes. The pictures of faces consisted of 24 men and women depicting anger or fear whereas shape images consisted of various round objects. Stimuli were presented in block format and each stimulus interval contained 6 images. Stimulus blocks were presented for 4.5 seconds with a 500 ms interstimulus interval. Interleaved within the stimulus blocks were instructional blocks that directed participants to match the shape stimuli or the emotional faces. During the instructional blocks, a target face was presented accompanied by 2 faces that one could choose from. To identify the matching face, participants were required to press a button that matched the identical face.

The fMRI scans were performed with a 1.5T Signa MR system. There were 9 brain regions of interest that were examined for activity during the face and object

matching tasks. The brain regions examined include the amygdala, lateral fusiform gyrus, inferior frontal gyrus, temporal lobe, and the occipital lobe. All regions were examined bilaterally.

In terms of performance on the face and object matching task, there were no differences between the TD adults and the individuals with ASD. Both groups of participants demonstrated significant activation to faces over shapes in the occipital lobe, bilateral fusiform gyrus, bilateral inferior frontal lobe, and right temporal lobe. However, the participants with ASD showed greater activation in the occipital lobe and less activation in the left inferior frontal lobe than the TD participants. Furthermore, a negative correlation was found between the Social Avoidance and Distress Scale and brain activity in the right fusiform face area in the participants with ASD. Participants with ASD who had higher anxiety scores showed reduced activation in the right fusiform face area. In addition, individuals with ASD that had higher anxiety scores also demonstrated increased amygdala and left temporal lobe activation to the emotional face stimuli.

The authors inferred that individuals with ASD who had greater social anxiety scores had increased sensitivity to emotional faces than those with lower anxiety scores and that this may make understanding and responding to emotional facial expressions more difficult, leading to greater avoidance behavior. The finding of reduced fusiform face area activation in association with higher anxiety levels led to the conclusion that anxiety in those with ASD may result in less experience with faces. It was also stated that instead, the anxiety may lead to gaze patterns that are consistent with avoidance

behavior as the temporal lobe has been implicated in eye and gaze processing (Kleinhans et al., 2011). The pattern of reduced activation during the face matching task in individuals with ASD indicates that higher order brain regions are not being employed to the same extent as in TD adults. Together with the increase of activity in the amygdala, the authors propose that the behavioral deficits observed in those with ASD may be due to a reduction in long distance cortico-cortical connections. It was further suggested that the frontal lobes may not be integrating information and providing feedback to sensory regions efficiently.

Consistent with research suggesting abnormal connectivity and functioning of particular brain regions in ASD is the idea that the human mirror neuron system, which is involved in both imitating as well and understanding the intention behind action (Bernier, Dawson, Webb, & Murias, 2007; Ramachandran & Oberman, 2006), is impaired in those with ASD. The human mirror neuron system is composed of three cortical regions: the pars opercularis, the inferior frontal gyrus, and the rostral portion of the inferior parietal lobe (Fecteau, Lepage, & Théoret, 2006). Interestingly, although they were not examining mirror neuron system activity, the study by Kleinhans and colleagues (2011) demonstrated reduced activity in the inferior frontal gyrus during the observation of emotional facial expression. The impaired mirror mechanism hypothesis, also known as the broken mirrors hypothesis, proposes that the behavioral issues observed in autism such as impaired language, communication, and the ability to understand others' intentions, is due to a faulty mirror neuron system (Rizzolatti & Fabbri-Destro, 2010). Mirror neurons seem to be involved in the ability to empathize with others and in the perception of others' intentions (Ramachandran & Oberman, 2006). Thus, mirror neuron

system impairment may contribute to the social difficulties individuals with ASD experience including the understanding of emotion in others.

Dapretto and colleagues (2005) examined brain activity in children with ASD during the imitation and observation of emotional facial expressions. Symptom severity was assessed using the ADOS-G and the ADI-R. Ten, high-functioning participants with ASD, aged 10 to 14 years, were compared to an age and IQ-matched TD group. Neural activity was recorded with fMRI during execution of the research tasks.

Participants were presented with 80 face images that expressed the emotions of anger, fear, happiness, sadness, or neutrality. Stimuli were presented to participants using high-resolution, magnet-compatible goggles. Face and null event stimuli were presented for 2 seconds each in a random sequence. Null events consisted of a blank screen with a fixation cross placed at eye level. Participants were tasked with either imitating the emotional expressions presented on the face stimuli or simply observing the face images. The children were also instructed to practice the task outside of the scanner to ensure that they could carry out the required actions. Two sets of 96 whole-volume images were obtained for each participant using a 3.0 Tesla head only scanner during the facial expression activities.

During the imitation task, the TD children showed activation in several regions bilaterally including the striate and extra-striate cortices (visual cortices), primary and pre-motor cortical areas, limbic structures such as the amygdala, insula, and ventral striatum, and in the cerebellum. Perhaps most interesting to this study is the finding of bilateral activation in the pars opercularis, located in the inferior frontal gyrus, and in the

pars triangularis. The strongest activation was found in the right hemisphere. Children with ASD also demonstrated activation in the visual cortices as well as the fusiform gyrus, primary and pre-motor areas for the face, and the amygdala. However, children with ASD did not show activity in the pars opercularis during the imitation of emotional facial expressions. The TD children demonstrated greater activity in the insular and peri-amygdaloid areas, the ventral striatum, and the thalamus than children with ASD. In contrast, the children with ASD showed greater activity in the left anterior parietal area and right visual association regions compared to the TD group. As in the imitation task, during the observation task, TD children showed greater activation in the right pars opercularis than the children with ASD.

To determine whether ASD severity was related to mirror neuron system activity during the facial expression tasks, the ADOS-G and ADI-R scores were examined in relation to neural activity. A negative correlation was found between ADOS-G and ADI-R scores and pars opercularis activity, such that higher scores, indicating greater ASD severity, were associated with less activity in the pars opercularis during imitation. In addition, ASD symptom severity was also negatively correlated with activation in the insula and amygdala. Again, greater severity was associated with less activation in these limbic regions. Although the fusiform gyrus has been implicated in face processing (Kleinhans et al., 2008; Pierce et al., 2001), no relationship was found between activity in the fusiform gyrus and activity in mirror neuron system regions during the imitation or observation tasks.

Although both groups of children were able to perform the imitation task, different patterns of neural activation were observed in TD children when compared to children with ASD. Thus, children with ASD appear to utilize a different neural network to accomplish the same task. Whereas TD children activated mirror neuron structures of the right hemisphere during the observation and imitation tasks, children with ASD employed regions involved in visual and motor attention. Therefore, the authors assert that mirror neuron system impairment may be responsible for the social difficulties observed in individuals with autism.

Recordings with EEG have also been found useful for examining mirror neuron system function based on mu wave suppression. The mu band has a frequency of 8 – 13 Hz and can be recorded with EEG by placing electrodes over the sensorimotor cortex (Bernier, Dawson, Webb, & Murias, 2007). It has been shown that the mu wave is blocked during both the imitation of a task and the observation of another person performing the same task (Ramachandran & Oberman, 2006). Thus, the mu rhythm is thought to reflect an execution/ observation matching system (Bernier et al., 2007).

Bernier and colleagues (2007) examined mu wave suppression during the observation and imitation of biological movement of the hands and face, in high-functioning adults with ASD. Fourteen adult males with ASD and 15 TD adults participated in the study. Participants were similar in terms of age, IQ, and handedness. Both behavioral and EEG assessments were used.

During the behavioral task, participants viewed a recorded model on a computer screen that displayed a variety of hand gestures including single and sequenced

movements, gestures requiring both hands, short meaningless hand movements, and hand movements that interacted with objects. Participants also viewed recordings of a model performing both single and sequenced facial expressions. After a trial depicting each gesture, the screen went blank and the participant was asked to imitate the observed behavior. An overall total score was calculated to reflect a “hand total” score and “face total” score.

EEG was recorded with a dense-array EEG system that recorded from a 128-channel Geodesic sensor net. Brain activity was recorded from all 128 channels while participants were presented with stimuli on a video monitor. The vertex was used as a reference and then later the data was re-referenced to an average reference. The initiation and termination of each stimulus presentation was listed with the EEG record for off-line separation of the data. Participants engaged in 4 conditions with 20 trials per condition each lasting 3 seconds. EEG was recorded during a resting state, observation of hand movement, execution of a task, and imitation of hand movements. The resting state consisted of having the participant sit quietly with his hands in his lap. During the observation condition, the participants also sat with hands in lap while observing an action being performed on the video monitor. In the execution condition, participants were verbally told to grip the object shown in the same manner as that displayed in the video. Finally, in the imitation condition, participants were required to imitate the experimenter gripping the object in the same way that was shown on the video tape.

For analysis, the EEG data were divided into segments that extended 2 seconds before and after each stimulus event marker. Fast Fourier Transform was carried out on

2- second segments of artifact free data to analyze power in the mu frequency band. Mu rhythm attenuation was analyzed using a log transformation of the power ratio during each condition and by using difference scores between the resting condition and task conditions.

On the behavioral imitation task, TD participants performed significantly better than individuals with ASD. Participants with ASD were impaired in their ability to accurately imitate the gestures and expressions displayed by the model in comparison to the TD group. In terms of mu attenuation, greater mu rhythm attenuation was demonstrated during the imitation condition than in the observation condition when compared against the resting state for the TD adults. Participants with ASD also showed less attenuation during the observe condition than in the execution and imitation conditions. They did not demonstrate any differences between the imitation and execution tasks. In direct group comparisons, there were no mu power ratio differences between the participant groups in the execution and imitation conditions. However, the participants with ASD did demonstrate a significantly lower mu wave power ratio during the observation task than the TD adults. To confirm that the observed attenuation of rhythmic activity was due to mu wave suppression and not posterior alpha activity, EEG activity from frontal and occipito-parietal leads were examined. No patterns of suppression were observed in the 8 – 13 Hz frequency band in these locations, which confirms that the mu wave attenuation was localized to the central electrodes (C3 & C4) and not due to alpha desynchronization. The posterior alpha rhythm is thought to occur over the occipital cortex in response to attention and expectancy (Klimesch, Doppelmayr, Russegger, Pachinger, & Schwaiger, 1998). Correlation analyses were used to examine

the relationship between mu attenuation and imitation skills. A positive correlation was found across groups for mu attenuation and imitation skills, such that greater mu wave attenuation was associated with better imitation skills and less attenuation was associated with poorer imitation skills. This finding was strongest for facial imitation skills.

The results from this study indicate that individuals with ASD demonstrate impaired imitation skills. In addition, the reduction in mu wave attenuation in adults with ASD suggests that the mirror neuron system may be disrupted in individuals with ASD. Thus, the authors provide evidence that the mirror neuron system of humans may be involved in imitation and that impairments in this network may contribute to some of the social deficits in autism.

Present Study and Hypotheses

In sum, the evidence indicates that during basal neural activity, adults and children with autism demonstrate reduced alpha power and coherence, particularly in frontal and temporal regions compared to their TD counterparts (Cantor et al., 1986; Coben et al., 2008; Duffy et al., 2012; Murias et al., 2007). Although the studies reviewed examined EEG in both eyes open and eyes closed resting states, all demonstrated reduced alpha in individuals with ASD. In addition, decreases in beta power have been observed in children predominantly in the right hemisphere (Coben et al., 2008). In contrast, the findings regarding theta and delta power and coherence have been inconsistent. While some have reported increases in theta power and coherence in those with ASD compared to TD groups (Murias et al., 2007), others have found decreases in theta coherence (Coben et al., 2008). Similarly, there have been reports of

both increases (Cantor et al., 1986) and decreases (Coben et al., 2008) in delta power in individuals with ASD.

Although there are several studies that have examined basal functional neural connectivity in individuals with autism, few have conducted these studies with both very young children during wakefulness and EEG power and coherence measures. Even fewer have conducted these studies using EEG with young children during facial observation tasks. Studies that have examined children combined data from toddlers, elementary school and junior high school age children, which may not adequately represent the spectral profiles of children in younger age groups. Combining age groups was likely performed to avoid the reduction in sample size that would result from separating groups based on age. In contrast, those with larger samples typically utilized EEG data from hospital databases that were collected for other reasons, such as the detection of brain pathology. As a result, there is a lack of control over data collection. Furthermore, research examining functional connectivity during facial expression observation has done so using fMRI technology. While fMRI has high structural resolution, it has lower temporal resolution than EEG and thus cannot make the same claims about functional connectivity. In contrast, EEG has lower structural resolution than fMRI, but higher temporal resolution permitting the examination of functional connectivity. Hence, the present study examines neural activation and functional connectivity with EEG, in children under age 5, during a relaxed baseline state and during a facial expression observation task. This task involves the visual presentation of faces demonstrating different emotions during EEG recording.

Based on the previously discussed literature, it is hypothesized that children with ASD will demonstrate reduced alpha and beta EEG power over the temporal cortex and in the frontal lobe regions in comparison to TD children. As slow-wave activity is associated with developmental disorders, it is expected that children with ASD will exhibit an increase in delta and theta power in all regions compared to TD children. In addition, it is expected that higher functioning children with ASD will have greater power ratios than lower functioning children with ASD. Furthermore, those with ASD will likely display reduced coherence between the right and left temporal lobes and between the temporal lobe and frontal lobe regions compared to TD children. In fact a gradient of functional connectivity, as represented by the coherence function, is expected such that TD children display the greatest coherence followed by high functioning children with autism, and finally low functioning children with autism. Finally, it is predicted that children with ASD (based on severity) will show less hemispheric asymmetry across the alpha bandwidth when compared to TD children. In terms of behavior, children with autism may demonstrate reduced ability to identify and/or imitate facial expressions when compared to TD children.

METHOD

Participants

Participants consisted of 6 children with ASD aged 3 to 5 years recruited from various schools and programs for children with ASD within Florida. Specifically, children were recruited from the Center for Autism and Related Disabilities (CARD) and Reaching Potentials in Boca Raton, the Hope Center for Autism in Stuart, the Renaissance Learning Center in West Palm Beach, Let's Communicate in Palm Beach Gardens, and the Center for Brain Training in Jupiter. Participants were recruited based on previous diagnosis of ASD based on DSM-IV guidelines that have been performed by a clinician prior to the start of the study. The Gilliam Autism Rating Scale: Second Edition (GARS-2) was used to confirm diagnosis and place children into low-functioning and high-functioning groups. The GARS – 2 is a norm-referenced, 42-item instrument used to estimate the severity of autism in children. It is based on the diagnostic guidelines of the DSM-IV-TR and the Autism Society of America and can be used to assess individuals from ages 3 to 22. The Autism Index of the GARS-2 has a mean of 100 with a standard deviation of 15. Thus, those who score above the mean demonstrate a substantial number of indicators for autism. An Autism Index of 100 corresponds to the 50th percentile, the mean score for individuals with autism. Individuals who score below the 16th percentile (Autism Index = 85) only classify as possibly having autism and those below the 2nd percentile (Autism Index = 70) are considered unlikely to have autism.

Hence one needs to score at or above the 16th percentile to be classified as autistic. Children who scored below the 50th percentile (Autism Index = 115), but above the 16th percentile, were classified as having high-functioning ASD, whereas those who scored above the 50th percentile were classified as having low-functioning ASD.

A group of 29 TD preschool children without ASD were recruited from the Karen Slattery Child Development Center in Boca Raton, Florida as a control group. Typically developing children were recruited based on negative screening for ASD. In addition, the M-CHAT and GARS-2 was administered to the parents and/ or teachers of all children involved in the study. The M-Chat is a short assessment of autism risk in children. Children were also screened for handedness as this can affect the structural laterality of the brain. Finally, written informed consent was obtained from parents before the start of the study and assent was obtained from the children who participated when appropriate. Parents received a \$10 gas card as reimbursement for travel to the laboratory and children were allowed to choose a small toy as incentive following participation. Children with psychiatric disorders and/ or who take medication were excluded. In addition, two children from the TD group were excluded because their scores on the GARS – 2 placed them in the range for ASD. The EEG data from an additional 8 TD children and 2 children with ASD were excluded because they either refused EEG (1 TD and 2 ASD children) or the EEG trace was of poor quality due to the presence of muscle and/ or heart rate activity (7 TD children). Thus, the final sample of EEG data consisted of 19 TD children (12 male, 7 female) and 4 children with ASD (all male). TD children were divided into two groups based on the ability to close their eyes during baseline EEG recording. As a result, there were 17 TD children with eyes closed and 2 children with

eyes open. Of the children with ASD, 2 were classified as high-functioning and 2 as low-functioning. The high-functioning children with ASD were able to close their eyes during EEG recording, but children in the low-functioning ASD group were not. Thus, EEGs of the low-functioning groups were recorded with eyes open. For the behavioral data, the sample consisted of 27 TD children (17 male, 10 female) and 6 children with ASD (all male) for the identification task. As 2 TD children (both female) refused to imitate the facial expressions, there were 24 TD children and 6 children with ASD for the imitation task.

Procedure

Prior to EEG sessions, children were provided with training and desensitization sessions to familiarize them with the experimenters, apparatus, and procedures as well as to acclimate the child to tactile stimulation of the scalp. Desensitization training was conducted when necessary in the same manner as that used by Dawson et al. (2002). The child was comfortably seated in a chair in the same manner in which the data were collected. One researcher provided the child with social and/ or edible reinforcement (i.e., Cheerios), while the other researcher touched the child's head with different objects over progressively longer periods of time. The trainings began by touching the child's head with a soft tape measure for 5 seconds. Succeeding trainings used a cotton wash cloth, a soft hat, and finally an EEG cap over increasing periods of time. Training was completed when the child could tolerate wearing the EEG cap for approximately 40 seconds.

During data collection, children were seated in a chair and fitted with a 14-lead EEG cap. All children were presented with a total of 80 pictures of faces displaying both fearful (40 pictures) and happy (40 pictures) expressions alternated with null event stimuli. The null event stimulus consisted of a blank screen with a red fixation cross in the center. Faces depicting emotional facial expressions were color images of male and female adults from a range of ethnicities obtained from the Mac Brain Face Stimulus Set (Nim Stim) (Tottenham et al., 2009). The Mac Brain Stimulus Set is a battery consisting of 646 facial expression images obtained from actors in New York University's Tisch drama program. Development of the MacBrain Face Stimulus Set was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development. Please contact Nim Tottenham at ntottenham@psych.ucla.edu for more information concerning the stimulus set. An equal number of male and female images were presented on a 9.7 inch, color iPad 2 monitor set approximately 45 cm in front of the child. The iPad 2 was selected because it is portable and does not have a keyboard, which could distract young children.

An initial baseline recording preceded the presentation of the face and null event stimuli. A baseline recording of 3 to 5 minutes was collected during quiet wakefulness. Children were instructed to close their eyes for the 3 minutes if they were able to. Otherwise, children alternated eyes closed and eyes open in 1-minute increments for 3 to 5 minutes. Face stimuli presented consisted of a set of fixed, randomly-chosen images. The task continued until the child observed all of the images in the trial or until the child became intolerant of the task. Following completion of the trial, children were asked to identify and imitate 4 happy and fearful faces from the Mac Brain Face Stimulus Set.

Ability to perform these actions was coded by two researchers to obtain reliability. In addition, children were recorded with a video camera to examine eye gaze during the trial to ensure that children were looking at the face stimuli and to evaluate the imitation and identification behavior.

EEG Recordings

A stretch-lycra cap (Electro-Cap, Inc.) with electrodes positioned according to the international 10-20 system (Jasper, 1958) was positioned on the child's head (See Figure 1). Omni-prep gel and electrode gel was then inserted into the mid-frontal (F3, F4), lateral frontal (F7, F8), anterior temporal (T3, T4), posterior temporal (T5, T6), central (C3, C4), and occipital (O1, O2), sites and referenced to the vertex site (Cz). The vertex was used as it is the least disturbing site for use with infants and young children with special needs. Omni-prep gel was used to gently abrade the scalp and electrode gel was used to provide good conductance. All electrode impedances were less than 10K ohms or the site was re-abraded with the blunt end of a Q-tip until optimal impedances were obtained. The signal was passed through a Grass Model 12 Neurodata Acquisition System and amplified with 1 – 100 Hz bandpass filtering and low pass filtered with 60 Hz notch filter. The output from each amplifier was then directed to a Dell 325D PC fitted with an Analog Devices RTI-815 A/D board. The sampling rate was 512 samples per second. The data were streamed across a computer screen and saved to a hard drive using data acquisition software (Snapstream, v.3.21, HEM Data Corp., 1991).

EEG and Statistical Analyses

Unfortunately, the method of presenting visual stimuli was not reliable in terms of the length of time during which the delay between images occurred. Images were presented on an iPad 2 using the Slide Shark program. Slide Shark is the equivalent of PowerPoint for use on the iPad. Although each image was programmed to show for 3 seconds, the delay in between images could not be controlled and was inconsistent. As a result, the image and fixation cross conditions were not able to be accurately matched with the EEG data. As each image was only presented for 3 seconds, even a small discrepancy in time affects the ability to analyze the EEG data adequately. Therefore, the following analyses were performed on the baseline EEG data only.

Discrete Fourier Transform was performed on 3 to 5 minutes of artifact-free EEG data using a 1-second Hanning window with 50% overlap. The average number of artifact-free windows was 207 ($M = 207.42$, $SE = 12.90$). This procedure generates power values, in picowatt ohms (1 microvolt squared), for each frequency bandwidth at each channel. These analyses were executed using EEGEDIT software (James Long Company, Caroga Lake, New York). Relative power in delta, theta, alpha, and beta bandwidths was examined in the frontal (F3, F4, F7, & F8), temporal (T3, T4, T5, & T6), central (C3 & C4), and occipital (O1 & O2) brain regions. As the spectral properties of the EEG undergo modifications during the first years of life, a given behavior or physiological state is likely to exhibit different spectral properties at different stages of development. Hence, it has been suggested that EEG studies of infants and young children should not use adult frequency bands (Pivik, Broughton, Coppola, Davidson, Fox, & Nuwer, 1993). Although no finite consensus has been reached as to what the

adjusted parameters should be, a frequency band at and around 6 - 9 Hz for alpha appears to be the most popular choice, although some have suggested that a lower band of 4 - 6 Hz may be more suitable in early infancy (Marshall, Bar-Haim, & Fox., 2002). To address this issue, the present study examined two ranges for alpha, alpha 1 (5.5 – 9.5 Hz) and alpha 2 (7.5 – 12.5 Hz). As power values are not typically normally distributed, being positively skewed, natural log (ln) transformations were used for all statistical analyses of power.

Coherence measurements were examined between the frontal electrodes (F3-F4 & F7-F8), temporal lobe electrodes (T3-T4, T5-T6, T3-T5, & T4-T6), central region electrodes (C3-C4), as well as between the temporal and frontal regions (T3-F3, T4-F4, T3-F7, T4-F8, T5-F3, T6-F4, T5-F7, & T6-F8) and occipital and frontal regions (O1-F3 & O2-F4) to assess functional connectivity in the alpha bandwidth during the baseline recording. The alpha bandwidth was selected because it has been associated with emotion and visual attention (Gasser et al., 1985; Jones et al., 1997; Vuga et al., 2006; Vuga et al., 2008). The EEG coherence measurements between channels at alpha 1 and alpha 2 frequencies were obtained by using the Fourier coefficients and their complex conjugates and calculating the average cross spectrum. The value was then squared and normalized by the average residual power spectra of both channels to yield the coherence statistic.

As t-test analyses comparing TD children who closed their eyes (n = 9) to TD children who alternated eyes closed and open (n = 8) during EEG recording revealed no differences between groups on any of the dependent variable measures (all $p > .05$) they were combined into one group. However, TD children who kept their eyes open showed

a different pattern of EEG activity from the other TD children and were thus placed into a separate group for statistical analyses. Several mixed design analyses of variance (ANOVA) were performed with developmental status (between subjects) and several brain regions, including the frontal, temporal, central, and occipital regions (within subjects), as the independent variables and EEG coherence, power, and asymmetry as the dependent variables. Each independent variable has multiple levels (Developmental status: high-functioning ASD, low-functioning ASD, TD, and TD eyes open; Frontal Region: F3, F4, F7, and F8; Temporal Region: T3, T4, T5, and T6; Central Region: C3 and C4; Occipital Region: O1 and O2). Thus, mixed ANOVAs were performed to examine the effects of developmental status on regional (frontal, temporal, central, and, between frontal and temporal, and between occipital and frontal regions) EEG coherence. Mixed ANOVAs were also used to examine the effects of developmental status on EEG power across delta, theta, alpha, and beta bandwidths in frontal, temporal, central, and occipital brain regions. Tukey's HSD and planned comparisons were used to further compare the different developmental groups and regions with respect to EEG measurements. In addition, paired t-tests [$\ln(\text{right hemisphere}) - \ln(\text{left hemisphere})$] examined differences in alpha power asymmetry based on developmental status.

Behavioral data were examined with independent samples t-tests with developmental status (between groups) as the independent variable and the percentage of correct trials on the identification and imitation tasks as the dependent variables. For these analyses the independent variable has two levels (Developmental Status: TD and ASD). Measures of effect size were calculated for all analyses and are reported in terms of r and partial eta squared values. Finally, Pearson correlations were used to examine

the relationship between Developmental Status, as reflected by the GARS-2, and coherence measures.

RESULTS

Research on vulnerable/protected populations often results in small sample sizes because few individuals from those populations exist and fewer still volunteer to participate in research studies. This research was no exception. For analyses of EEG, only 2 children qualified for the high-functioning ASD group and 2 others qualified for the low-functioning ASD group. While the study does have 19 children in the control group, 17 children closed their eyes throughout EEG recording and 2 kept their eyes open during recording. Obviously the sample sizes are too small to use statistical significance as the sole criterion for evaluating the results. Thus, this manuscript also reports measures of effect size, measured by r and partial eta squared values, alongside traditional statistical significance tests to aid in the interpretation of the results. Measures of effect size are not constrained by the assumptions underlying parametric statistics, such as ANOVA, and can be used as an additional tool to evaluate analyses, especially when samples are small. While they are affected by variability within the measure of the dependent variable, they are not influenced by sample size (Cohen, 1994). As suggested by Cohen (1994) and Rosenthal and Rosnow (2008), the results from this study will be evaluated in terms of the patterns of effect sizes and their consistency with the hypotheses. Interpretation of effect size will use the conventions set by Cohen (1988) and Rosenthal (1996).

Identification and Imitation of Facial Expressions

As the assumption of equal variances was violated, the values reported are from the corrected model with equal variances not assumed. However, very large effect sizes were obtained for both analyses. TD children correctly identified facial expressions more frequently than children with ASD [$t(5.81) = 2.547, p = .045, r = .726$] (See Figure 2). On average TD children identified facial expressions with 70.19% accuracy (SE = 4.80), whereas children with ASD correctly identified facial expressions with 25% (SE = 17.07) accuracy. Similarly, TD children were able to imitate facial expressions more frequently than children with ASD ($[t(23) = 17.899, p < .001, r = .965]$). TD children correctly imitated facial expressions on 84.37% (SE = 4.71) of trials. In contrast, children with ASD were not able to imitate the facial expressions on any of the trials (M = 0, SE = 0) (See Figure 2).

Power

If the data are consistent with the hypothesis that children with ASD will demonstrate reduced alpha and beta power in temporal and frontal regions, then the TD children should have greater power values than children with ASD accompanied by effect sizes that are in the medium to large range. This was in fact what was found in the frontal, temporal, central, and occipital regions. In addition, if the hypothesis that children with ASD will exhibit increased delta and theta power is supported, then the TD children should have lower power values than children with ASD accompanied by medium to large effect sizes. While this was partially true in terms of delta power, the opposite was found for theta power in all regions examined.

Mixed repeated measures ANOVAs did not reveal patterns indicative of interactions between Developmental Status and Region on Power in any bandwidth for Frontal, Temporal, or Central areas. Correspondingly, there were no main effects of Frontal, Temporal, or Central Regions observed for any bandwidth. However, there were main effects for Developmental Status in all regions observed. Patterns indicating Developmental Status X Occipital Region interactions were also detected.

Frontal Region. A moderate main effect of Developmental Status on **Alpha 1** Power was discovered, [$F(3,19) = 3.580, p = .033, \eta^2 = .361$]. Tukey HSD comparisons showed that TD ($M = 23.856, SE = .281$) ($r = .772, p = .020$), TD eyes open ($M = 23.570, SE = .818$) ($r = .737, p = .163$), and the high-functioning ASD group ($M = 23.876, SE = .818$) ($r = .774, p = .101$) demonstrated greater alpha 1 power than children with low-functioning ASD ($M = 21.040, SE = .818$). No differences were observed between the TD groups or between either of the TD and high-functioning ASD groups. The same pattern was identified for alpha 2 power. A moderate main effect of Developmental Status on **Alpha 2** Power was found, [$F(3,19) = 4.432, p = .016, \eta^2 = .412$]. Tukey HSD comparisons revealed that TD ($M = 24.341, SE = .282$) ($r = .795, p = .011$) and TD eyes open ($M = 23.370, SE = .822$) ($r = .445, p = .306$) children exhibited greater power than children with low-functioning ASD ($M = 21.284, SE = .822$). Again, children with high-functioning ASD ($M = 24.461, SE = .822$) also showed greater power than those with low-functioning ASD ($r = .806, p = .058$). No differences were detected between the TD groups or between the TD groups and high-functioning ASD group.

There was a moderate main effect of Developmental Status on **Beta** Power, [F(3,19) = 4.355, $p = .017$, $\eta^2 = .407$]. Comparisons using Tukey's HSD showed that TD (M = 24.221, SE = .283) ($r = .797$, $p = .011$) and TD eyes open children (M = 23.542, SE = .825) ($r = .515$, $p = .201$) demonstrated greater power than children with low-functioning ASD (M = 21.132, SE = .825). Children with high-functioning ASD (M = 24.387, SE = .825) also displayed more power than children with low-functioning ASD ($r = .812$, $p = .052$). No differences between the TD and TD eyes open children were found. Similarly, no differences between the TD groups and high-functioning children with ASD were observed.

A large main effect of Developmental Status on **Delta** Power was shown, [F(3,19) = 18.727, $p < .001$, $\eta^2 = .747$]. Tukey's HSD test revealed that the high-functioning ASD group (M = 24.911, SE = .757) demonstrated greater power than the TD (M = 19.982, SE = .260) ($r = .917$, $p < .001$), TD eyes open (M = 19.227, SE = .757) ($r = .935$, $p < .001$), and low-functioning ASD (M = 17.248, SE = .757) ($r = .963$, $p < .001$) groups. In addition, the TD ($r = .787$, $p = .014$) and TD eyes open ($r = .460$, $p = .282$) children exhibited more power than the children with low-functioning ASD. There was no difference between the two TD groups.

Finally, the main effect of Developmental Status on **Theta** Power was strong, [F(3,19) = 10.410, $p < .001$, $\eta^2 = .622$]. Here, Tukey's HSD indicated that the TD children (M = 23.490, SE = .233) demonstrated greater power than the high-functioning ASD (M = 20.740, SE = .678) ($r = .820$, $p = .006$) and the low-functioning ASD (M = 20.313, SE = .678) ($r = .856$, $p = .001$) groups. The TD eyes open children (M = 23.153,

SE = .678) also displayed greater power than the high-functioning ($r = .782$, $p = .089$) and low-functioning ($r = .828$, $p = .037$) children with ASD. No differences were detected between the high-functioning and low-functioning ASD groups or between the TD groups (See Figure 3 for main effects of Developmental Status on Frontal Region Power in all bandwidths).

Temporal region. A moderate main effect of Developmental Status on **Alpha 1** Power was detected, [$F(3,19) = 3.278$, $p = .044$, $\eta^2 = .341$]. Tukey HSD comparisons showed that TD ($M = 23.513$, $SE = .316$) ($r = .756$, $p = .028$) and TD eyes open children ($M = 23.620$, $SE = .922$) ($r = .767$, $p = .112$) demonstrated greater alpha 1 power than low-functioning children with ASD ($M = 20.495$, $SE = .922$). High-functioning children with ASD ($M = 23.450$, $SE = .922$) also demonstrated greater power than low-functioning ASD children ($r = .749$, $p = .141$). Differences were not observed between TD, TD eyes open, and high-functioning children with ASD. In addition, there was no difference in alpha 1 power between hemispheres. For **Alpha 2** Power, a moderate main effect of Developmental Status was found, [$F(3,19) = 4.103$, $p = .021$, $\eta^2 = .393$]. Tukey's HSD test indicated that the TD group ($M = 23.946$, $SE = .303$) ($r = .793$, $p = .012$) and the TD eyes open group ($M = 23.474$, $SE = .882$) ($r = .744$, $p = .150$) showed more alpha 2 power than the low-functioning ASD group ($M = 20.688$, $SE = .862$). Again, the high-functioning ASD group ($M = 23.863$, $SE = .882$) also displayed more power than the low-functioning ASD group $r = .786$, $p = .085$). No differences between the TD, TD eyes open, and high-functioning ASD groups were found. Differences in alpha 2 power were not observed between hemispheres.

A moderate main effect of Developmental Status on Temporal **Beta** Power was shown, $[F(3,19) = 5.067, p = .010, \eta^2 = .444]$. Tukey's HSD comparisons revealed that both TD ($M = 24.200, SE = .305$) ($r = .821, p = .005$) and TD eyes open children ($M = 23.278, SE = .888$) ($r = .731, p = .174$) showed greater power than low-functioning ASD children ($M = 20.580, SE = .888$). High-functioning ASD children ($M = 23.789, SE = .888$) ($r = .787, p = .083$) also demonstrated greater power than low-functioning ASD children. Again, there were no significant differences between the TD, TD eyes open, and high-functioning ASD groups.

In terms of Temporal **Delta** Power, a strong main effect of Developmental Status was found, $[F(3,19) = 39.646, p < .001, \eta^2 = .862]$. Here, Tukey's HSD comparisons indicated that high-functioning ASD children ($M = 24.240, SE = .491$) demonstrated greater delta power than TD ($M = 20.298, SE = .168$) ($r = .943, p < .001$), TD eyes open ($M = 19.361, SE = .491$) ($r = .961, p < .001$), and low-functioning ASD ($M = 16.798, SE = .491$) ($r = .983, p < .001$) children. In addition, TD ($r = .929, p < .001$) and TD eyes open ($r = .879, p = .008$) children also demonstrated greater power than low-functioning ASD children. There was no difference between the two TD groups.

A pattern indicating a moderate effect of Developmental Status on Temporal **Theta** Power was identified, $[F(3,19) = 6.368, p = .004, \eta^2 = .501]$. Comparisons using Tukey's HSD indicated that the TD group ($M = 23.275, SE = .306$) showed greater power than both high-functioning ($M = 20.614, SE = .892$) ($r = .725, p = .049$) and low-functioning ($M = 19.927, SE = .892$) children with ASD ($r = .798, p = .010$). Likewise, the TD eyes open group ($M = 23.308, SE = .892$) also exhibited greater theta power than

the high-functioning ($r = .730$, $p = .177$) and low-functioning ($r = .801$, $p = .065$) children with ASD. No differences were found between the children in the TD groups or in the ASD groups (See Figure 4 for main effects of Developmental Status on Temporal Region Power in all bandwidths).

Central region. In terms of Alpha 1 Power, a moderate main effect of Developmental Status on **Alpha 1** Power was shown, [$F(3,19) = 5.071$, $p = .010$, $\eta^2 = .445$]. Tukey's HSD comparisons revealed that TD ($M = 24.827$, $SE = .343$) ($r = .823$, $p = .005$), TD eyes open ($M = 24.159$, $SE = .999$) ($r = .771$, $p = .105$), and high-functioning ASD ($M = 24.693$, $SE = .999$) ($r = .814$, $p = .050$) children demonstrated greater central region power than low-functioning ASD children ($M = 20.726$, $SE = .999$). Comparably, a moderate main effect of Developmental Status on **Alpha 2** Power was discovered, [$F(3,19) = 5.437$, $p = .007$, $\eta^2 = .462$]. As with alpha 1 central power, TD children ($M = 25.214$, $SE = .343$) ($r = .822$, $p = .005$) and TD eyes open children ($M = 23.636$, $SE = .999$) ($r = .449$, $p = .300$) displayed greater power than low-functioning ASD children ($M = 21.122$, $SE = .999$). Additionally, high-functioning ASD children ($M = 25.126$, $SE = .999$) showed greater alpha 2 power than low-functioning ASD children ($r = .817$, $p = .048$). There were no differences between the TD groups or between TD and high-functioning ASD children.

A moderate main effect of Developmental Status on Central Region **Beta** Power was found, [$F(3,19) = 4.973$, $p = .010$, $\eta^2 = .440$]. Tukey's HSD comparisons showed that the TD group ($M = 25.088$, $SE = .360$) ($r = .665$, $p = .006$) and the TD eyes open group ($M = 23.917$, $SE = 1.049$) ($r = .713$, $p = .210$) demonstrated greater beta power

than the low-functioning ASD group ($M = 20.897$, $SE = 1.049$). The high-functioning ASD group ($M = 25.067$, $SE = 1.049$) also displayed more beta power than the low-functioning ASD group ($r = .663$, $p = .050$). No differences were identified between either of the TD groups or between the two TD and high-functioning ASD groups.

The main effect of Developmental Status on Central **Delta** Power was large, [$F(3,19) = 18.154$, $p < .001$, $\eta^2 = .741$]. As with the frontal and temporal regions, the high-functioning ASD group ($M = 25.862$, $SE = .878$) exhibited greater delta power than the TD ($M = 20.683$, $SE = .289$) ($r = .897$), TD eyes open ($M = 19.648$, $SE = .787$) ($r = .928$), and low-functioning ASD ($M = 16.928$, $SE = .878$) ($r = .963$) groups (all $p < .001$). However, the TD ($r = .842$, $p = .003$) and TD eyes open ($r = .738$, $p = .161$) groups also demonstrated more delta power than the low-functioning ASD group. No differences were observed between the two TD groups.

For the analysis of Central **Theta** Power, a large main effect of Developmental Status was revealed, [$F(3,19) = 10.828$, $p < .001$, $\eta^2 = .631$]. Tukey's HSD test revealed that TD ($M = 24.572$, $SE = .323$) ($r = .652$, $p = .008$) and TD eyes open ($M = 23.949$, $SE = .942$) ($r = .751$, $p = .139$) children displayed more theta power than high-functioning children with ASD ($M = 20.915$, $SE = .942$) ($p = .001$). TD ($r = .869$, $p = .001$) and TD eyes open ($r = .837$, $p = .030$) children also demonstrated greater theta power than low-functioning children with ASD ($M = 19.871$, $SE = .942$). No significant differences were found between the low and high-functioning ASD groups or between the TD groups (See Figure 5 for main effects of Developmental Status on Central Region Power across bandwidths).

Occipital region. A moderate main effect of Developmental Status on **Alpha 1** Power was shown, $[F(3,19) = 3.768, p = .028, \eta^2 = .373]$. However, a moderate Occipital Region X Developmental Status interaction was also detected, $[F(3,19) = 3.683, p = .030, \eta^2 = .368]$. Analysis of simple effects revealed that though there are differences between the developmental groups, this was only found in the right hemisphere, $[F(3,19) = 6.629, p = .003, \eta^2 = .715]$. Tukey's HSD showed that children with low-functioning ASD ($M = 20.087, SE = 1.099$) showed significantly less power in the right occipital region when compared to the children with high-functioning ASD ($M = 22.946, SE = .369$) ($r = .869, p = .011$), the TD children ($M = 22.379, SE = .189$) ($r = .816, p = .006$) and the TD eyes open children ($M = 23.387, SE = .048$) ($r = .897, p = .003$). Hence, though the low-functioning ASD group demonstrated less power than the TD, TD eyes open, and high-functioning ASD groups, this was only evident for the right occipital hemisphere (See Figure 6). No differences between groups were identified for the left occipital region. Analogous results were obtained regarding **Alpha 2** Power. A moderate main effect of Developmental Status on Alpha 2 Power was identified, $[F(3,19) = 3.593, p = .033, \eta^2 = .362]$. The effect of the Developmental Status X Occipital Region interaction was also moderate, $[F(3,19) = 4.716, p = .013, \eta^2 = .427]$. Analysis of the simple effects revealed that the differences between developmental groups was limited to the right occipital hemisphere, $[F(3,19) = 7.010, p = .002, \eta^2 = .724]$. Comparisons using Tukey's HSD found that children with low-functioning ASD ($M = 20.189, SE = 1.214$) demonstrated a significant reduction in alpha 2 power in the right occipital region when compared to children with high-functioning ASD ($M = 23.305, SE = .371$) ($r = .882, p = .007$), TD children ($M = 22.825, SE = .187$) ($r = .846, p = .002$), and TD eyes open children ($M =$

23.344, SE = .366) ($r = .885$, $p = .006$) (See Figure 7). Differences between the other developmental groups were not found.

A moderate main effect of Developmental Status on **Beta** Power was detected, [$F(3, 19) = 5.425$, $p = .007$, $\eta^2 = .461$]. Tukey HSD comparisons showed that beta power was reduced in the low-functioning ASD ($M = 20.917$, $SE = .706$) group compared to TD ($M = 23.904$, $SE = .242$) ($r = .831$, $p = .004$), TD eyes open ($M = 23.639$, $SE = .706$) ($r = .649$, $p = .059$), and the high-functioning ASD ($M = 23.231$, $SE = .706$) ($r = .757$, $p = .129$) groups. Differences were not observed between the other developmental groups.

A very strong main effect of Developmental Status on Occipital **Delta** Power was observed, [$F(3,19) = 31.316$, $p < .001$, $\eta^2 = .832$]. Tukey's HSD test revealed that the TD ($M = 20.414$, $SE = .183$) ($r = .921$, $p < .001$) children displayed less delta power than children with high-functioning ASD ($M = 23.983$, $SE = .553$), but more delta power than children with low-functioning ASD ($M = 16.790$, $SE = .533$) ($r = .923$, $p < .001$). The TD eyes open group ($M = 19.445$, $SE = .533$) showed the same pattern with reduced delta power compared to the high-functioning ASD group ($r = .948$, $p < .001$), but more delta power than the low-functioning ASD group ($r = .869$, $p = .011$). The high-functioning ASD group also demonstrated greater power than the low-functioning ASD group ($r = .978$, $p < .001$).

Lastly, there was strong main effect of Developmental Status on Occipital **Theta** Power, [$F(3,19) = 11.504$, $p < .001$, $\eta^2 = .645$]. Tukey HSD comparisons revealed that TD children ($M = 22.400$, $SE = .183$) displayed more occipital theta power than both high-functioning ($M = 20.110$, $SE = .533$) ($r = .835$, $p = .003$) and low-functioning ($M =$

20.032, SE = .533) ($r = .843$, $p = .002$) children with ASD. TD eyes open children ($M = 23.010$, SE = .533) also showed greater occipital theta power than children with high-functioning ($r = .887$, $p = .005$) and low-functioning ($r = .892$, $p = .004$) ASD (See Figure 8 for main effects of Developmental Status on Occipital Region Beta, Delta, and Theta Power). There was no difference between high-functioning and low-functioning children or TD and TD eyes open children in terms of occipital theta power.

Taken together, a similar pattern of effect sizes is observed for the main effect of Developmental Status in each region examined (i.e., Frontal, Temporal, Central, and Occipital). That is, the effects of Developmental Status on Alpha 1, Alpha 2, and Beta Power were consistently in the medium to medium high range ($r = .341$ to $r = .462$) in each region. Additionally, the interaction effects between Developmental Status and Occipital Region Alpha 1 and Alpha 2 Power were also in the medium range ($r = .368$ to $r = .427$). Furthermore, the simple effects and comparisons between groups had effect sizes in the very high range ($r = .715$ to $r = .978$). Patterns of strong effect sizes were found for the main effect of Developmental Status on Delta and Theta Power in each region. For the main effect of Developmental Status on Delta Power, effect sizes were consistently in the very high range ($r = .741$ to $r = .862$) and the comparisons between groups demonstrated even greater effects sizes ($r = .738$ to $r = .983$). Lastly, the effects of Developmental Status on Theta Power were also shown to be in the high range ($r = .501$ to $r = .645$). Comparisons between groups again exhibited a pattern of high to very high effect sizes ($r = .652$ to $r = .892$). Based on the patterns of effect size for analyses of Developmental Status and EEG Power, it appears that there are robust differences

between developmental groups, particularly for delta and theta power (See Table 1 for Power values for each developmental group by region).

Coherence

If the data are consistent with the hypothesis that children with ASD will demonstrate reduced alpha coherence within and between temporal and frontal regions, then the TD children should have greater coherence values in these regions than children with ASD accompanied by effect sizes that are in the medium to large range. Indeed, this is what was found in the temporal region and between frontal and temporal EEG sites. Patterns indicating interactions were not identified for developmental status and frontal and central regions, with respect to regional and inter-regional alpha 1 and alpha 2 coherence, regardless of the distance between electrodes. In addition, patterns consistent with main effects were not found for developmental status in frontal, temporal, or central regions or for the central region alone. However, consistent patterns were revealed in the frontal region, temporal region, between frontal and temporal regions and between the occipital and frontal regions. As the assumptions of sphericity were violated because of the small sample size, the Greenhouse-Geisser correction was used for the ANOVAs performed.

Frontal region. An interaction between Developmental Status and Frontal Region was not found. Nor was there an effect of Developmental Status on Alpha 1 and Alpha 2 power in the Frontal Region. However, a moderate main effect of Frontal Region on Alpha 1 coherence was observed [$F(1,19) = 8.403, p = .009, \eta^2 = .307$]. Interhemispheric functional connections with less distance between them (F3-F4) ($M =$

.538, SE = .047) showed greater coherence than longer distance connections (F7-F8) (M = .486, SE = .042) ($r = .428$, $p = .009$).

Temporal region. A main effect of Developmental Status was not observed, but there was a moderate pattern indicating a main effect of Temporal Region on Alpha 1 Coherence, [$F(1,19) = 16.795$, $p = .001$, $\eta^2 = .469$]. Pairwise comparison indicated that coherence between T3-T5 (M = .523, SE = .040) was stronger than that between T4-T6 (M = .381, SE = .034) ($r = .543$, $p = .001$). Thus, there was greater left intrahemispheric coherence observed in the temporal lobes. There was also a moderate pattern consistent with a Developmental Status X Temporal Region interaction on Alpha 1 Coherence, [$F(3,19) = 6.006$, $p = .005$, $\eta^2 = .487$]. Analyses of the simple effects showed that differences between developmental groups were restricted to the right hemisphere between T4-T6, [$F(3,19) = 4.645$, $p = .013$, $\eta^2 = .650$]. Comparisons using Tukey's HSD revealed that TD children (M = .596, SE = .029) ($r = .809$, $p = .008$) and TD eyes open children (M = .574, SE = .118) ($r = .790$, $p = .077$) displayed greater alpha 1 coherence in the right temporal region between T4-T6 than children with low-functioning ASD (M = .248, SE = .113). In addition, children with high-functioning ASD (M = .605, SE = .080) also demonstrated greater T4-T6 coherence than children with low-functioning ASD ($r = .815$, $p = .048$) (See Figure 9). Differences between TD, TD eyes open, and high-functioning ASD children were not apparent. There were no differences between overall interhemispheric temporal alpha 1 coherence or between anterior and posterior interhemispheric coherence.

Similar findings were revealed for analyses of alpha 2 coherence. Although there was not a main effect of Developmental Status, there was a moderate main effect of Temporal Region, $[F(1,19) = 11.703, p = .003, \eta^2 = .381]$. As with alpha 1 coherence, greater alpha 2 coherence was observed between T3-T5 ($M = .490, SE = .045$) than between T4-T6 ($M = .344, SE = .038$) ($r = .467, p < .003$). Hence, greater left intrahemispheric coherence was detected compared to right intrahemispheric coherence. In addition, a pattern indicative of a Developmental Status X Temporal Region interaction on Alpha 2 Coherence was revealed, $[F(3,19) = 5.015, p = .010, \eta^2 = .442]$. Analysis of the simple effects showed differences in coherence based on developmental status between T4-T6, but not between other temporal sites, $[F(3,19) = 5.197, p = .009, \eta^2 = .670]$. Again, Tukey's HSD revealed that the TD children ($M = .568, SE = .032$) ($r = .671, p = .005$), TD eyes open children ($M = .606, SE = .128$) ($r = .843, p = .024$) and the high-functioning ASD children ($M = .560, SE = .078$) ($r = .813, p = .049$) demonstrated greater T4-T6 coherence than low-functioning ASD children ($M = .185, SE = .028$) (See Figure 10). No differences were observed between overall interhemispheric temporal coherence or between anterior and posterior interhemispheric temporal sites.

Frontal - temporal. A moderate main effect of Developmental Status $[F(3,19) = 2.985, p = .057, \eta^2 = .320]$ and a very strong main effect of Frontal - Temporal Region $[F(1,19) = 55.940, p < .001, \eta^2 = .746]$ on Alpha 1 Coherence was observed. As expected, pairwise comparisons revealed greater coherence between anterior temporal and frontal regions ($M = .497, SE = .043$) compared to coherence between posterior temporal and frontal regions ($M = .282, SE = .030$) ($r = .861, p < .001$). Furthermore, a pattern suggesting an interaction between Developmental Status and Frontal - Temporal

Region on Alpha 1 Coherence was also found, $[F(3,19) = 3.736, p = .029, \eta^2 = .371]$. An examination of the simple effects revealed that differences between developmental groups were only identified for anterior temporal - frontal connections, $[F(3,19) = 3.997, p = .023, \eta^2 = .621]$. Tukey's HSD showed that TD ($M = .581, SE = .035$) ($r = .784, p = .014$), TD eyes open ($M = .607, SE = .050$) ($r = .805, p = .058$), and high-functioning children with ASD ($M = .565, SE = .061$) ($r = .769, p = .106$) demonstrated greater alpha 1 coherence between anterior temporal and frontal regions than children with low-functioning ASD ($M = .233, SE = .024$) (See Figure 11). No differences were identified between the right and left hemispheres for alpha 1 coherence.

Correspondingly, a moderate main effect of Developmental Status $[F(3,19) = 3.583, p = .034, \eta^2 = .358]$ and a moderate to high main effect of Frontal - Temporal Region on Alpha 2 Coherence was found, $[F(1,19) = 39.964, p < .001, \eta^2 = .678]$. Overall, coherence between anterior temporal – frontal sites ($M = .461, SE = .040$) was found to be greater than coherence between posterior temporal – frontal electrode sites ($M = .284, SE = .029$) ($r = .659, p = .001$). A pattern of interaction between Developmental Status and Frontal - Temporal Region on Alpha 2 coherence was also revealed, $[F(3,19) = 6.214, p = .004, \eta^2 = .495]$. Analysis of the simple effects showed that differences between developmental groups were only observed for functional connections between the anterior temporal and frontal lobes, $[F(3,19) = 5.555, p = .007, \eta^2 = .684]$. Tukey's HSD revealed that TD ($M = .528, SE = .033$) ($r = .817, p = .006$), TD eyes open ($M = .637, SE = .021$) ($r = .850, p = .008$), and high-functioning children with ASD ($M = .507, SE = .070$) ($r = .801, p = .068$) demonstrated greater intrahemispheric coherence between frontal and anterior temporal EEG sites than

children with low-functioning ASD ($M = .168$, $SE = .0007$) (See Figure 12). There were no differences between hemispheres in terms alpha 2 coherence.

Occipital - frontal. A moderate main effect of Developmental Status on Occipital –Frontal Region Alpha 1 Coherence was found, $[F(3,19) = 5.265, p = .008, \eta^2 = .454]$. However, an interaction between Developmental Status and Occipital – Frontal Region on Alpha 1 Coherence was also indicated, $[F(3,19) = 4.242, p = .019, \eta^2 = .401]$. Analyses of simple effects showed that the pattern of activity differed in the left $[F(3,19) = 2.987, p = .057, \eta^2 = .567]$ and right $[F(3,19) = 2.574, p = .084, \eta^2 = .536]$ hemispheres based on developmental group. Tukey’s HSD indicated that in the left hemisphere, the TD eyes open group ($M = .271, SE = .012$) demonstrated stronger occipital – frontal (O1-F3) alpha 1 coherence than the TD group ($M = .136, SE = .020$) ($r = .655, p = .144$) and the high-functioning ASD group ($M = .120, SE = .039$) ($r = .696, p = .266$). Similarly, the low-functioning ASD group ($M = .259, SE = .014$) showed higher coherence than the TD ($r = .622, p = .199$) and high-functioning ASD group ($r = .667, p = .329$). Thus, the children who kept their eyes open during EEG demonstrated greater occipital – frontal alpha 1 coherence than children who closed their eyes. There were no differences between the TD and high-functioning ASD groups or between the TD eyes open and low-functioning ASD groups. In contrast, in the right hemisphere, Tukey’s HSD showed that the TD eyes open group ($M = .335, SE = .056$) exhibited greater occipital – frontal (O2-F4) alpha 1 coherence than the TD ($M = .163, SE = .021$) ($r = .693, p = .072$), high-functioning ASD ($M = .129, SE = .068$) ($r = .755, p = .121$), and the low-functioning ASD ($M = .203, SE = .056$) ($r = .594, p = .454$) groups (See Figure 13). Differences in

patterns of activity were not observed between the occipital – frontal region for alpha 2 coherence.

In sum, the main effects of Developmental Status on Alpha 1 and Alpha 2 Coherence were consistently in the medium range ($r = .320$ to $r = .454$) between frontal - temporal and between occipital - frontal regions. Interaction effects between Developmental Status and Region were also in the medium to medium-high range ($r = .371$ to $r = .495$). Finally, the simple effects and comparisons between groups were consistently in the high to very high range ($r = .567$ to $r = .843$). These patterns of effect size would be expected if there is in fact a difference in EEG coherence based on developmental status (See Tables 2 & 3 for coherence values for developmental groups by region). Differences in coherence based on developmental status were further supported by the moderately sized Pearson correlations between the GARS-2 and coherence values in the temporal region ($r = -.528$ to $r = -.586$) as well as between frontal and temporal regions ($r = -.372$ to $r = -.623$). These correlations indicate that coherence values vary in relation to developmental status. In particular, lower GARS-2 values, reflecting typical development, are associated with greater coherence values, whereas higher GARS-2 values, suggestive of ASD, are related to lower coherence values.

Asymmetry

To support the hypothesis that children with ASD will display reduced EEG hemispheric asymmetry in comparison to TD children, children with ASD should demonstrate EEG asymmetry in fewer pairs of homologous electrode sites and reduced asymmetry power ratios when compared to TD children. This hypothesis was partially

supported in that children with low-functioning ASD did not exhibit patterns of asymmetry in comparison to the other developmental groups. Furthermore, different patterns of regional EEG asymmetry were observed between the ASD and TD groups.

Paired t-tests revealed that TD children demonstrated left alpha 1 asymmetry in EEG power between T4 and T3, [$t(16) = -1.963, p = .067, r = .440$]. The average alpha 1 power observed at T4 ($M = 23.387, SE = .171$) was less than that observed for T3 ($M = 23.715, SE = .219$). In addition, TD children showed left alpha 2 asymmetry between T4 and T3, [$t(16) = -1.930, p = .072, r = .434$]. Thus, there was greater power in the left hemisphere (T3) ($M = 24.163, SE = .215$) than the right (T4) ($M = 23.820, SE = .154$) in the anterior temporal region (See Figure 14). TD eyes open children demonstrated a different pattern of asymmetry than TD children. Right alpha 1 hemispheric asymmetry was displayed between O2 and O1, [$t(1) = 4.748, p = .132, r = .978$]. A greater amount of power was observed in the right hemisphere ($M = 23.387, SE = .048$) when compared to the left ($M = 23.243, SE = .018$). Right alpha 2 asymmetry was also observed between O2 and O1, [$t(1) = 3.944, p = .158, r = .969$]. More alpha 2 power was shown in the right occipital hemisphere ($M = 23.344, SE = .366$) compared to the left hemisphere ($M = 23.192, SE = .328$) (See Figure 15). High-functioning children with ASD demonstrated right hemispheric alpha 1 asymmetry between F8 and F7, [$t(1) = 6.973, p = .091, r = .989$]. Hence, more power was displayed in the right frontal region ($M = 23.740, SE = .598$) than the left ($M = 23.610, SE = .616$). Likewise, right alpha 2 asymmetry was also demonstrated between F8 and F7 [$t(1) = 18.308, p = .042, r = .997$]. Therefore, in the lateral frontal region, more power was displayed in the right ($M = 24.263, SE = .419$) hemisphere than the left ($M = 24.192, SE = .415$) (See Figure 16). Additionally, high-

functioning children with ASD demonstrated left asymmetry in alpha 1 power between T6 and T5 [$t(1) = -15.205, p = .035, r = .998$]. Hence, greater power was observed in the left posterior temporal region ($M = 23.381, SE = .509$) than in the right ($M = 23.173, SE = .523$) (See Figure 17). Children with low-functioning ASD did not demonstrate EEG asymmetry in the alpha 1 or alpha 2 bandwidth in any region.

The patterns of effect size for EEG Asymmetry were shown to be in the medium range for TD children ($r = .434$ to $r = .440$). However, patterns of effect size were stronger in the TD eyes open ($r = .969$ to $r = .978$) and high-functioning ASD ($r = .989$ to $r = .998$) groups. Thus, while the differences between homologous electrode sites may seem to be small, the effect sizes are robust, indicating a difference in EEG activity between hemispheres at these sites.

Correlations

A Pearson correlation examining the relationship between scores on the GARS-2 and T4-T6 alpha 1 coherence indicated a moderate negative correlation, ($r = -.528, p = .010$) (See Figure 18). Thus, as GARS-2 scores increased, indicating more severe symptoms of ASD, alpha 1 coherence between T4 and T6 decreased. As with alpha 1 coherence, a Pearson correlation indicated a negative correlation between GARS-2 scores and alpha 2 T4-T6 coherence, ($r = -.583, p = .003$) (See Figure 19). As GARS-2 scores increased, alpha 2 coherence between T4 and T6 decreased.

Pearson correlations examining the relationship between GARS-2 scores and anterior temporal - frontal coherence found moderate negative correlations between the GARS-2 and T4-F4 ($r = -.482, p = .020$), T3-F7 ($r = -.623, p = .002$), and T4-F8 ($r = -$

.430, $p = .040$) (See Figures 20 – 22). Thus, as GARS-2 scores increased, alpha 1 coherence between frontal and anterior temporal regions decreased. Like alpha 1 coherence, scores on the GARS-2 were negatively correlated with alpha 2 coherence between the anterior temporal and frontal regions. In particular, GARS-2 scores were negatively correlated with T3-F3 ($r = -.372$, $p = .081$), T4-F4 ($r = -.556$, $p = .006$), T3-F7 ($r = -.584$, $p = .003$), and T4-T8 ($r = -.426$, $p = .043$) (See Figures 23 – 26). Again, lower scores on GARS-2 indicating typical development were associated with greater coherence values, while higher GARS-2 scores indicative of ASD were related to lower coherence values between the frontal and anterior temporal regions.

Pearson correlations reflecting a relationship between developmental status, as measured by the GARS-2, and coherence between the occipital and frontal regions were not found. This is not surprising as there were differences in coherence between the two TD groups.

DISCUSSION

The present study examined the EEG spectral activity and functional connectivity of frontal, temporal, central, and occipital regions in children with ASD during quiet wakefulness. To better describe the distinctions between EEG activity in TD and ASD children, a discussion of EEG spectral activity and coherence in TD children is warranted. In 3 to 5 year old TD children, alpha power is represented by the 6 – 9 Hz frequency band, a shorter range than the adult alpha band (Marshall et al., 2002; Marshall et al., 2002). The presence of alpha power increases with age and the bandwidth expands (Barry et al., 2009). Young children also demonstrate more delta and theta activity than adults (Scher, 2008; Vladimirova, 1991). Thus, with development delta and theta activity decrease while alpha and beta activity increase (Gasser et al., 1988). These modifications in oscillatory activity continue throughout childhood and become more focused in particular brain regions. From 8 to 12 years of age, absolute and relative delta and theta power decrease and reductions in relative theta become more apparent in posterior regions during an eyes closed resting state (Barry & Clarke, 2009). In contrast, absolute and relative alpha power increases becoming more prominent in posterior regions while increases in beta activity are observed primarily at midline areas (Barry & Clarke, 2009). In terms of coherence, at 3 years of age, increases in long-distance functional connections are observed predominantly in sensory and frontal regions (Brown & Jernigan, 2012). Furthermore, increases in intrahemispheric, resting state alpha coherence continue to

occur between both short and long-range functional connections from 6 to 18 years of age (Gmehlin et al., 2011). Findings regarding EEG asymmetry in children have been mixed. Pickens, Field, and Nawrocki (2001), for example, reported a lack of hemispheric asymmetry in frontal and parietal regions in 3 to 6 year old children during an eyes open baseline period. However, Lushchekina, Podreznaya, Lushchekin, Novototskii-Vlasov, and Strelets (2013) found right hemisphere alpha asymmetry during an eyes closed resting state in children aged 5 to 7 years. This discrepancy may be due to the differences in data collection or due to differences in age.

EEG Power

In this study, relative power in the alpha and beta frequency bands differed as a function of developmental status. Consistent with Cantor et al. (1986), children in both TD groups and high-functioning ASD children demonstrated the greatest alpha power values and low-functioning children with ASD exhibited the lowest power values in frontal, temporal, central, and occipital regions (See Table 4). Furthermore, in the occipital region, the discrepancy in alpha power appears to result from the low-functioning ASD children exhibiting reduced power in the right occipital region only. Similarly, the TD groups and high-functioning ASD group exhibited more beta power compared to the low functioning ASD group. Beta-band activity has been associated with the maintenance of inhibitory motor control (De France & Sheer, 1988 as cited in Lopes da Silva, 1991; Klostermann et al., 2007). Correspondingly, TD and high-functioning children with ASD were more successful at staying still during EEG recording than low-functioning children with ASD, which may explain the difference in

beta power values. The high-functioning ASD group showed the highest delta power values across all regions examined when compared to both TD groups and the low-functioning ASD group. Unexpectedly, the TD groups also demonstrated greater delta power than the low-functioning ASD group. Thus, delta power differentiated the 3 participants groups based on developmental status. As there have been inconsistencies regarding delta power in individuals with ASD, the pattern of delta power exhibited by the 3 developmental groups is difficult to interpret. It is possible that studies reporting an increase in delta only examined high functioning children with ASD. However, as delta has been associated with motivational states (Knyazev, 2007) it is possible that the higher delta values in the TD and high-functioning ASD groups reflects greater motivation to perform the tasks required of them. Children were allowed to choose a small toy following participation as incentive and this may have been more attractive to the TD and high-functioning children than to the low-functioning children with ASD. Indeed, the low-functioning children with ASD did not seem interested in the toys offered. Finally, theta power was shown to be higher in the TD groups than in both groups of ASD children in all regions examined. This finding is in contrast to other studies (Coben et al., 2008; Murias et al., 2007) that found an increase in theta power in children with autism. Slow-wave oscillatory activity is more prevalent in children than adults and as such TD children would be expected to demonstrate theta activity. Therefore, the reduction of theta in the children with ASD may reflect atypical or slower development in these children. This discrepancy may also be the result of differences in data collection or sample characteristics as most studies have examined older participants.

Alpha Coherence

Overall, children with ASD, particularly those severely affected, demonstrated reduced regional alpha coherence compared to TD and high-functioning children with ASD. Consistent with recent studies of coherence (Duffy & Als, 2012; Murias et al., 2007), both TD, TD eyes open, and high-functioning children with ASD exhibited greater fronto-temporal alpha coherence than low-functioning ASD children, particularly between anterior temporal and frontal sites (See Table 5). This may indicate that there are weak functional connections between the anterior temporal and frontal regions in ASD. As hypothesized, TD, TD eyes open, and high-functioning ASD children also demonstrated greater alpha coherence within the temporal region than low-functioning children with ASD. However, this finding was also restricted to functional connections in the right temporal lobe. The temporal lobes have been implicated in many processes that are characteristically affected in ASD, such as face perception (Kleinmans et al., 2008; Pierce et al., 2001; Wallace et al., 2008; Wolf et al., 2008) and the emotional aspects of language (George et al., 1996). Correspondingly and consistent with studies that examined imitation (Bernier et al., 2007) and face processing (Wallace et al., 2008; Wolf et al., 2008), in this study, children with ASD exhibited deficits in the ability to identify and imitate different facial expression. Adults with ASD also exhibit impaired facial expression imitation skills (Bernier et al., 2007). Individuals with ASD characteristically avoid looking at the eye region when viewing faces, instead focusing on the lower mouth region (Wolf et al., 2008). Though this may impair one's ability to interpret facial expressions accurately, impairment in basal functional connectivity may also account for the social deficits observed in ASD. Similarly, the frontal lobes have

shown evidence of involvement in emotion, language, and executive function (De Fossé et al., 2004; Herbert et al., 2002; Just et al., 2007). Therefore, it follows that children with more severe symptoms of ASD may not be processing information as efficiently as TD children because of abnormal network connectivity in the temporal and between frontal and temporal regions, thus affecting functions governed by these regions.

In further support of the coherence findings, developmental functioning, assessed by the GARS-2, was negatively correlated with coherence in the temporal region and between the frontal and anterior temporal regions. Thus, lower GARS-2 scores reflecting typical development were associated with greater coherence values and thus more functional connectivity. In contrast, higher GARS-2 scores, indicative of ASD, were associated with smaller coherence values, indicating less functional connectivity between frontal and temporal regions and within the temporal lobe. In line with Tyszka, Kennedy, Paul, and Adolphs (2013), analogous patterns of functional connectivity were found between TD and high-functioning children with ASD in terms of alpha and beta band activity. Hence, individuals with high-functioning ASD may demonstrate a greater degree of neuronal development in terms of synaptic connectivity than those with low-functioning ASD, thus improving abilities often affected in ASD. Nonetheless, as ASD is a heterogeneous disorder, it is possible that differences between TD and high-functioning individuals with ASD may be reflected in the activity of frequency bandwidths not examined in this study.

The examination of coherence between the occipital and frontal regions revealed that children in the TD eyes open and low-functioning ASD groups exhibited greater

alpha 1 coherence than the TD and high-functioning children with ASD in the left hemisphere. Thus, children who had their eyes open during EEG recording showed more correlated alpha activity between electrode sites than children who closed their eyes. Though there was no difference in left hemisphere alpha coherence between the TD eyes open and the low-functioning ASD group, the TD eyes open group displayed more coherence than the TD, low-functioning ASD, and high-functioning ASD children in the right hemisphere. These findings were unexpected as studies of EEG power in adults and children over age 8 demonstrate alpha attenuation when the eyes are open (Barry et al., 2009; Başar, et al., 2001). In addition, distinctions in alpha activity between children under the age of 5 during eyes closed and eyes open conditions have not been reported. It is believed that modifications in alpha occur at a later age (Barry et al., 2009). In TD children, alpha coherence has been shown to increase with development (Mariosi et al., 1992). However, differences between groups were not indicated for the alpha 2 coherence measures, which correspond to the adult alpha band of 8 – 12 Hz. It is reasonable to expect different patterns of alpha activity over the occipital region when the eyes are open as reduced alpha activity has been associated with attention, particularly visual aspects of attention. However, it was surprising to observe an increase in alpha coherence as these children had their eyes open. It may be that the increase in 6 – 9 Hz alpha band coherence is reflecting an activity other than attention in these children or that their attentional abilities are not well developed at this point, thus resulting in increased alpha coherence when the eyes are open. On the other hand, as the children were not asked to do anything but relax during the baseline recording, perhaps the increase in alpha coherence is indicative of day dreaming or of the mind “wandering off.”

EEG Asymmetry Patterns

In contrast to Duffy and Als (2012), a disparity in hemispheric asymmetry patterns was shown between children with ASD and TD children in the alpha bandwidth. However, Duffy and Als (2012) did not distinguish between low and high functioning ASD participants or differentiate bandwidths based on the different age groups. Bandwidths have been shown to increase in width over the span of development, such that young children demonstrate the alpha band in the 6 – 9 Hz range, not the traditional 8 – 12 Hz range used with adults (Pivik et al., 1993). Thus, standard frequency ranges may not be appropriate for use with younger participants. In addition, Duffy and Als (2012) had a much larger sample with 463 participants with ASD and 571 TD participants, which could have concealed differences in asymmetry due to the lack of differentiation of ASD severity and frequency bandwidths. In the present study, TD children demonstrated alpha 1 and alpha 2 asymmetry in the anterior temporal region, with stronger power in the left hemisphere than the right. However, the TD eyes open children demonstrated right alpha 1 and 2 asymmetry in the occipital lobe only. This is likely related to the fact that their eyes were open. Alpha activity is largely dependent on visual attention as well as vigilance and emotional excitation in children (Gasser et al., 1985; Stroganova & Posikera, 1993, as cited in Stroganova et al., 2007). As in Cantor et al. (1986), high-functioning children with ASD displayed left alpha asymmetry in the posterior temporal region. In addition, high-functioning ASD children also exhibited right hemisphere alpha asymmetry in the lateral frontal regions. Right frontal asymmetry is related to withdrawal behaviors and negative affect (Sutton & Davidson, 1997; Davidson et al., 1990; Davidson & Fox, 1989). Children with ASD traditionally exhibit avoidance

behavior, preferring to spend time alone as opposed to socializing with others. It has also been reported that autistic children with language impairment show a reversal of asymmetry (greater activity in right hemisphere) in areas associated with language in the frontal lobe (De Fossé et al., 2004; Herbert et al., 2002). As Broca's area is located in the left hemisphere and is associated with speech production, the demonstration of greater right frontal activity in children with ASD may help to explain the characteristic deficits in speech communication. Finally, children with low- functioning ASD did not demonstrate any patterns of asymmetry. Asymmetry in TD children typically develops with age (Marshall et al., 2002), so it's possible that children with ASD are just slower to develop this pattern. Alternatively, as the high-functioning children with ASD demonstrated a different pattern of asymmetry than the TD children, it may be that atypical patterns of asymmetry develop in children with ASD, further affecting behavior that is processed by the frontal and temporal lobes.

General Discussion

In the context of classic brain development, the current findings lend support to the theory that individuals with autism have aberrant patterns of neural development and neural communication (Hughes, 2007; Just et al., 2004; Just et al., 2012; Rippon, et al., 2007; Wass, 2011). Synchronized rhythmic oscillations are believed to represent functional connectivity, the method by which different parts of the brain integrate information that has been processed in regions that are not necessarily structurally connected (Lopes da Silva, 1991). The results of this study suggest atypical functional connectivity and patterns of spectral activity in children with ASD. In line with the

findings by Murias et al. (2007) and the theory of cortical under-connectivity in ASD (Hughes, 2007; Rippon et al., 2007), children with low-functioning ASD demonstrated reduced functional connectivity in the right temporal lobe and between frontal and anterior temporal areas. The theory of cortical under-connectivity proposes that the social and cognitive impairments observed in ASD are due to reductions in regional and inter-regional neural communication because of fewer functional and/ or structural connections between brain regions. Cortical regions involved in the 3 defining impairments of ASD, communication, social interaction, and perception, are expected to display reductions and/ or aberrations in functional cortico-cortical connectivity (Hughes, 2007; Rippon et al., 2007). MRI studies have repeatedly found reductions in the size of the corpus callosum in ASD and reduced correlated activity between frontal regions and the fusiform face area of the temporal lobe (Hughes, 2007). Thus, the findings of reduced coherence in the temporal lobe and between anterior temporal and frontal areas in this study may suggest patterns of cortical underconnectivity in these regions. This idea is supported by the findings of Zikopoulos and Barbas (2010) who found a reduction in the number of thick axons in orbitofrontal and anterior cingulate cortices. In addition, research with fMRI has reported reduced correlated activity, particularly in the frontal lobe and temporal regions associated with face processing in ASD (Kleinhans et al., 2008; Kleinhans et al., 2010; Kleinhans et al., 2011) and it is likely that myelination plays an important role in the neural communication between these regions (Hughes, 2007). Indeed, reduced myelination has been reported throughout the brains of individuals with ASD (Wolff et al., 2012).

The human brain continues to develop extensively during infancy and childhood undergoing neuronal myelination, differentiation, and synaptogenesis (Kandel et al., 2000). These changes in cortical structure and synaptic function are consequently reflected in the properties of the EEG (Niedermeyer, 1982). Studies of genetics in autism (Gepner & Féron, 2009; Sutcliffe, 2008) have implicated mutations of several genes involved in neuronal organization and synaptic development, which would thus lead to abnormal patterns of structural and functional connectivity. As a result, there would be faulty communication between brain regions and problems with processing certain types of information. Nonetheless, due to the heterogeneity of ASD, the organization of neural networks may not be exactly the same in all individuals with ASD. It is likely that many factors contribute to the autism symptomology, such as clinical severity, experiences early in development, cognitive skills, and task requirements (Kleinhans et al., 2008).

Limitations

There are several limitations to this study. These include, but are not necessarily limited to, sample size, differences in the ability of children to keep their eyes closed, effort of the required task, and EEG artifact produced by movement. Although we expected a small sample of children with ASD, the number of children who would allow EEG data to be collected was smaller than anticipated. The resulting small sample of participants used in this study may not have been large enough to account for all sources of variance. The small sample size also makes it very difficult to generalize the results to the population and hence results can only be discussed in terms of the participants in this study. That said, even with the small sample, the effect sizes were robust and consistent.

Having a larger sample would have increased the power of this experiment, which may have revealed additional findings not observed and allowed more reliance on the inferential statistics used to examine the data. However, specific subgroups can also be hidden in very large samples like that of Duffy and Als (2012).

Another limitation of this study is that it is difficult to get young children to keep their eyes closed for a substantial length of time. For those who were unable to keep their eyes closed during the full baseline EEG recording, children were asked to alternate between eyes closed and eyes open for 1-minute at a time until the baseline data was collected. In adults, the alpha bandwidth attenuates during periods when the eyes are open (Başar, et al., 2001). As such, differences in alpha found between the low-functioning ASD group and the high-functioning ASD and TD groups may be the result of having an eyes open baseline in those children. That said, alpha coherence activity does not appear to attenuate during eyes open periods in children (Michels et al., 2013). However, reductions in alpha activity from eyes closed to eyes open conditions have been reported in children starting at 8 years of age (Barry et al., 2009). It is likely that alpha attenuation during awake, alert states is a characteristic that develops over time and may coincide with the development of attentional control.

While the data collected during the baseline is supposed to represent a relaxed, resting state, it is possible that this was not the case. Children were asked to keep their eyes closed and to stay still during data collection. However, the act of staying still during EEG recording may have required more effort for children with ASD than the TD children. In addition, while children were given time to acclimate to the lab environment,

children with ASD are more comfortable in familiar places. As a result, collecting data in the lab may have produced anxiety in these children. As such, the data for the low-functioning children with ASD may not actually reflect a relaxed, baseline state.

Lastly is the difficulty of eliminating artifact due to movement. Young children tend to have a difficult time sitting still, especially for prolonged periods of time. This problem is magnified when managing children for whom exaggerated movements, in the form of stimulatory behaviors (i.e., flapping arms, spinning, rocking back and forth, etc.), are characteristic. To offset this issue, baseline recordings were collected for an extended period of time so that when artifact was removed, there would still be sufficient data for analysis.

Conclusions and Recommendations

Research investigating brain function in very young children with ASD, especially while awake, has been limited and thus little is known regarding typical EEG brain activity in this population. Overall, the conclusions to be drawn from this study suggest that children with ASD exhibit different patterns of brain activity and functional connectivity compared to their typically developing counterparts. Autism and related spectrum disorders are marked by many social deficits that prevent successful interaction with others. It is possible that the reduced functional connectivity as well as the reduced power in the alpha and beta frequency bands observed in the children with ASD throughout the brain is responsible for the communicative and social difficulties that characterize ASD.

Although there are likely multiple factors that contribute to autism and ASD, the investigation of key features of the disorder and their associated biological components are important for the development of treatment options. The development of standardized methods of identification is imperative for early treatment. As of now, most children are diagnosed with ASD by 3 years of age. This is likely because many children with ASD do not present symptoms until they are between 2 to 3 years old. This may indicate that changes in neuronal structure of function occur at this time. Therefore, this study examined children between 3 to 5 years with the aim of characterizing EEG neural activity. To date, there are no biological or physiological screening methods to identify ASD. However, it may be possible to use baseline EEG coherence and power measures as a diagnostic tool to identify autism earlier in development. While this study does not purport to indicate that EEG can be used as a diagnostic tool at this time, it is a good first step in that direction as it describes the characteristics of baseline EEG spectral patterns and coherence in in young children with ASD. Baseline EEG measures may be more practical to obtain compared to behavior related EEG/ event related potential (ERP) as children under the age of 3 may not readily perform behaviors required for ERP research. In order to use EEG as a diagnostic instrument, there needs to be consistency in data collection methods so research can be adequately compared and replicated. Furthermore, larger samples of participants need to be examined who span the ASD spectrum in terms of symptomology. However, the inherent technical limitations of using EEG with children, such as movement artifact and tensing need to be managed in order to obtain EEG data from individuals with severe symptoms of ASD. Finally, EEG findings with autistic samples need to be compared not only to age matched TD controls, but also

against others with developmental delays to determine if EEG can differentiate ASD from other developmental disorders. Although fMRI may also prove valuable in the early detection of autism, EEG would provide a more economical means of doing so. In addition, the enclosed environment inherent in MRI equipment is often not tolerable for young children, especially as it also requires that the patient is immobilized. At present, few studies have examined very young children with ASD or low-functioning individuals with ASD. This is likely because of the difficulty obtaining data from individuals in this population. However, it is important that this hurdle does not prevent investigation with these individuals as information regarding this population is necessary to determine key physiological differences between low and high functioning ASD. Furthermore, examining differences in development from the age of diagnosis into adulthood will shed light on how those with ASD function over time. Finally, research with younger children with ASD will help to create better and earlier screening and treatment options.

APPENDIX

Table 1

Relative Power for TD and ASD Groups by Region

Region	HFASD (n = 2)		LFASD (n = 2)		TD (n = 17)		TDEO (n = 2)		p	r/ eta
Frontal	M	SE	M	SE	M	SE	M	SE		
Delta	24.911	.757	17.248	.757	19.982	.260	19.227	.757	< .001	.747
Theta	20.740	.678	20.313	.678	23.490	.233	23.153	.678	< .001	.622
Alpha 1	23.876	.818	21.040	.818	23.856	.281	23.570	.818	.033	.361
Alpha 2	24.461	.822	21.284	.822	24.341	.282	23.370	.822	.016	.412
Beta	24.387	.825	21.132	.825	24.221	.283	23.542	.825	.017	.407
Temporal										
Delta	24.240	.491	16.798	.491	20.298	.168	19.361	.491	< .001	.862
Theta	20.614	.892	19.927	.892	23.275	.306	23.308	.892	.004	.501
Alpha 1	23.450	.922	20.495	.922	23.513	.316	23.620	.922	.044	.341
Alpha 2	23.863	.882	20.688	.862	23.946	.303	23.474	.882	.021	.393
Beta	23.789	.888	20.580	.888	24.200	.305	23.278	.888	.010	.444
Central										
Delta	25.862	.848	16.928	.878	20.683	.289	19.648	.787	< .001	.741
Theta	20.915	.942	19.871	.942	24.572	.323	23.949	.942	< .001	.631
Alpha 1	24.693	.999	20.726	.999	24.827	.343	24.159	.999	.010	.445
Alpha 2	25.126	.999	21.122	.999	25.214	.343	23.636	.999	.007	.462
Beta	25.067	1.049	20.897	1.049	25.088	.360	23.917	1.049	.010	.440
Occipital										
Delta	23.983	.553	16.790	.433	20.414	.183	19.445	.533	< .001	.832
Theta	20.110	.533	20.032	.533	22.400	.183	23.010	.533	< .001	.645
Alpha 1 R	22.946	.369	20.087	1.099	22.379	.189	23.387	.048	.003	.715
Alpha 1 L	23.032	.468	21.242	2.274	22.445	.159	23.243	.018	.193	
Alpha 2 R	23.305	.371	20.189	1.214	22.825	.187	23.344	.366	.002	.724
Alpha 2 L	23.279	.400	21.502	2.376	22.890	.165	23.192	.328	.274	
Beta	23.231	.706	20.917	.706	23.904	.242	23.639	.706	.007	.461

Note. Relative power values for each developmental group [High-Functioning ASD (HFASD), Low-Functioning ASD (LFASD), Typically Developing (TD), TD eyes open (TDEO)] by region. For the Occipital Region, alpha 1 and alpha 2 power is presented for the left and right hemisphere to show the interaction between Developmental Status and Region. Differences between groups were only indicated for the right hemisphere. M = mean; SE = standard error.

Table 2

Alpha 1 EEG Coherence for ASD and TD Groups by Region

Region	HFASD (n=2)		LFASD (n=2)		TD (n=17)		TDEO (n=2)	
	M	SE	M	SE	M	SE	M	SE
Temporal								
<i>Right (T4-T6)</i>	.605	.080	.248	.113	.596	.029	.574	.118
<i>Left (T3-T5)</i>	.668	.032	.365	.046	.549	.041	.574	.091
Fronto-Temporal								
<i>AT - F</i>	.565	.061	.233	.024	.581	.035	.6079	.050
T3-F3	.484	.123	.267	.123	.496	.042	.584	.123
T4-F4	.535	.211	.178	.121	.543	.041	.564	.121
T3-F7	.592	.094	.306	.094	.677	.032	.637	.094
T4-F8	.650	.144	.181	.144	.611	.049	.647	.144
<i>PT - F</i>	.340	.067	.179	.018	.306	.023	.303	.071
T5-F3	.286	.076	.174	.076	.259	.026	.284	.076
T6-F4	.318	.073	.170	.073	.296	.025	.302	.073
T5-F7	.373	.088	.223	.088	.346	.030	.300	.088
T6-F8	.383	.095	.150	.095	.327	.033	.328	.095
Occipital - Frontal								
<i>Left (O1-F3)</i>	.120	.039	.259	.014	.136	.020	.271	.012
<i>Right (O2-F4)</i>	.129	.068	.203	.056	.163	.021	.335	.056

Note. Alpha 1 coherence values for each developmental group [High-Functioning ASD (HFASD), Low-Functioning ASD (LFASD), Typically Developing (TD), TD eyes open (TDEO)] by region. AT = anterior temporal; PT = posterior temporal; F = frontal; M = mean; SE = standard error.

Table 3

Alpha 2 Coherence for TD and ASD Groups by Region

Region	HFASD (n = 2)		LFASD (n = 2)		TD (n = 17)		TDEO (n = 2)	
	M	SE	M	SE	M	SE	M	SE
Temporal								
<i>Right (T4-T6)</i>	.560	.078	.185	.028	.568	.032	.606	.128
<i>Left (T3-T5)</i>	.569	.067	.288	.133	.531	.041	.614	.093
Fronto-Temporal								
<i>AT - F</i>	.507	.070	.168	.000	.528	.033	.637	.021
T3-F3	.448	.113	.166	.133	.432	.039	.624	.113
T4-F4	.478	.117	.051	.117	.492	.040	.585	.117
T3-F7	.538	.101	.270	.101	.623	.035	.688	.101
T4-F8	.567	.140	.189	.140	.567	.048	.655	.140
<i>PT - F</i>	.291	.059	.202	.033	.278	.022	.365	.106
T5-F3	.240	.075	.190	.075	.220	.026	.355	.075
T6-F4	.295	.064	.217	.064	.260	.022	.348	.064
T5-F7	.300	.087	.197	.087	.321	.030	.383	.087
T6-F8	.330	.088	.206	.088	.311	.030	.376	.088
Occipital - Frontal								
<i>Left (O1-F3)</i>	.126	.015	.178	.091	.117	.021	.347	.060
<i>Right (O2-F4)</i>	.137	.060	.107	.029	.132	.022	.419	.004

Note. Alpha 2 coherence values for each developmental group [High-Functioning ASD (HFASD), Low-Functioning ASD (LFASD), Typically Developing (TD), TD eyes open (TDEO)] by region. AT = anterior temporal; PT = posterior temporal; F = frontal; M = mean; SE = standard error.

Table 4

Power Comparisons of ASD to TD Participants

<i>Study</i>	<i>n</i> <i>(Age in years)</i>	<i>Delta</i> δ	<i>Theta</i> θ	<i>Alpha</i> α	<i>Beta</i> β	<i>Present Study</i>
Present Study						
HF ASD	2 (3 – 5)	Increased in all regions	Decreased in all regions	No difference	No difference	
LF ASD	2 (3 – 5)	Decreased in all regions	Decreased in all regions	Decreased in frontal, central & temporal regions and right occipital hemisphere	Decreased in all regions	
Cantor, Thatcher, & Hrybyk (1986)	11 (4 – 12)	Increased in bilateral fronto-temporal and left temporal regions	Not reported	Decreased in bilateral occipital regions	Not reported	Partially supports α & δ results. δ increased in HFASD and decreased in LFASD (new finding)
Coben, Clarke, Hudspeth, & Barry (2008)	20 (6 – 11)	Decreased particularly in left frontal regions, but also in posterior and central areas.	Increased particularly in frontal and right posterior regions	No difference	Decreased particularly in right hemisphere posterior regions	Partially supports δ and β results. In contrast, θ activity was increased (new finding)
Murias, Webb, Greenson, & Dawson (2007)	18 (18 – 37)	Not reported	Increased in Prefrontal and frontal areas	Decreased in prefrontal/ frontal and occipital/ parietal regions	Increased in occipital/ parietal regions	Supports α findings only.

Table 5

Coherence Comparison of ASD to TD Participants

<i>Study</i>	<i>n</i> <i>(Age in years)</i>	<i>Delta</i> δ	<i>Theta</i> θ	<i>Alpha</i> α	<i>Beta</i> β	<i>Present Study</i>
Present Study						
HF ASD	2 (3 – 5)					
LF ASD	2 (3 – 5)			Reduced in right temporal and anterior temporal - frontal regions. Increased in left occipital – frontal regions.		
Cantor, Thatcher, & Hrybyk (1986)	11 (4 – 12)			Increased in left frontal and right central-parietal and parieto-occipital areas	Increased inter-hemispheric coherence	Does not support
Coben, Clarke, Hudspeth, & Barry (2008)	20 (6 – 11)	Reduced b/w inter-hemispheric frontal, central, & parieto-occipital regions	Reduced frontal inter-hemispheric coherence	Reduced frontal inter- and intra-hemispheric SR, MR, & LR coherence	Reduced b/w inter-hemispheric central, & parieto-occipital regions	Supports SR α findings only
Murias, Webb, Greenson, & Dawson (2007)	18 (18 – 37)		Increased in frontal, temporal, & central regions	Reduced in all regions		Supports α results
Duffy & Als (2012)	463 (2 - 12)			Reduced b/w SR left anterior temporal and left frontal region and b/w left anterior and posterior temporal regions		Partially supports findings, but found differences in right temporal lobe & bilaterally in fronto-temporal areas

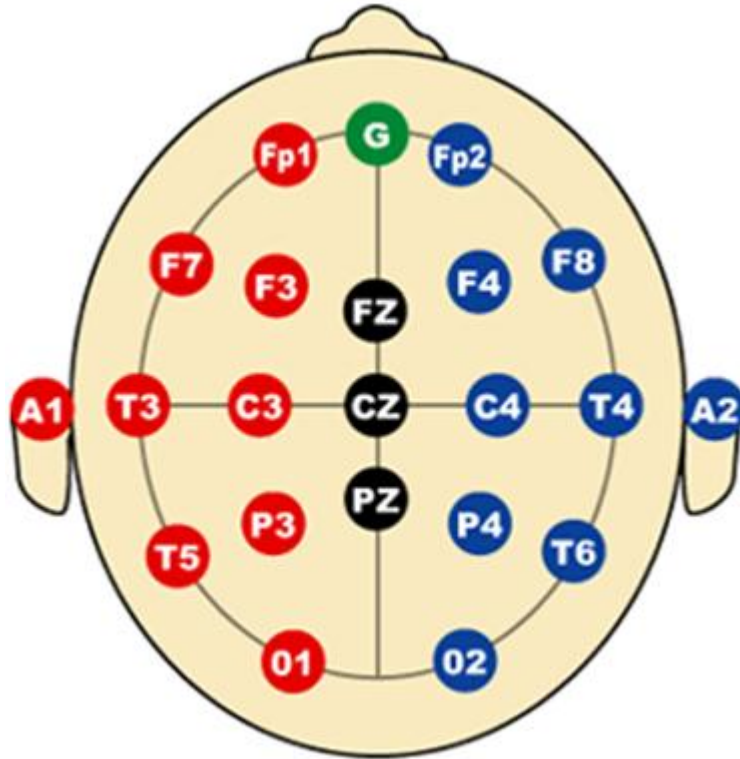


Figure 1. Image depicting electrode placement according to International 10-20 System. Electrodes were placed at mid-frontal (F3, F4), lateral frontal (F7, F8), anterior temporal (T3, T4), posterior temporal (T5, T6), central (C3, C4), and occipital (O1, O2), sites and referenced to the vertex site (Cz).

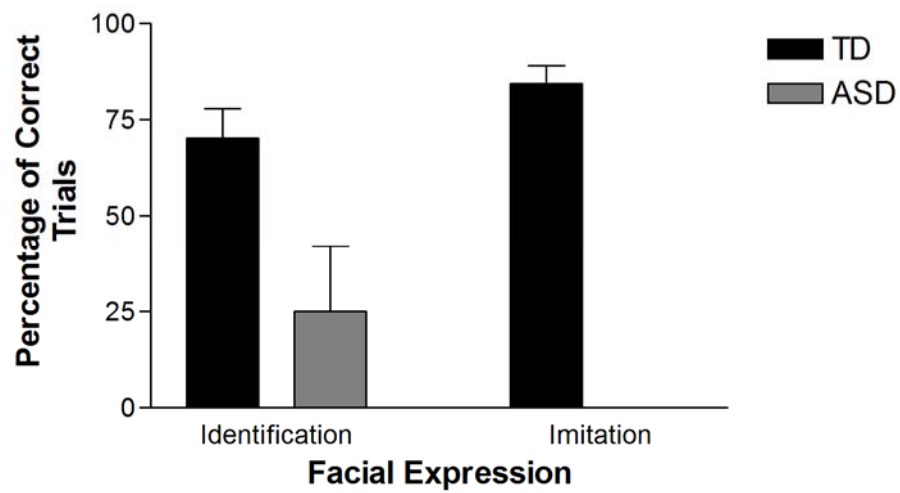


Figure 2. Mean percentage of correct trials for Identification and Imitation of facial expression. TD children performed the identification and imitation tasks with greater accuracy than children with ASD. Error bars reflect standard error of the mean.

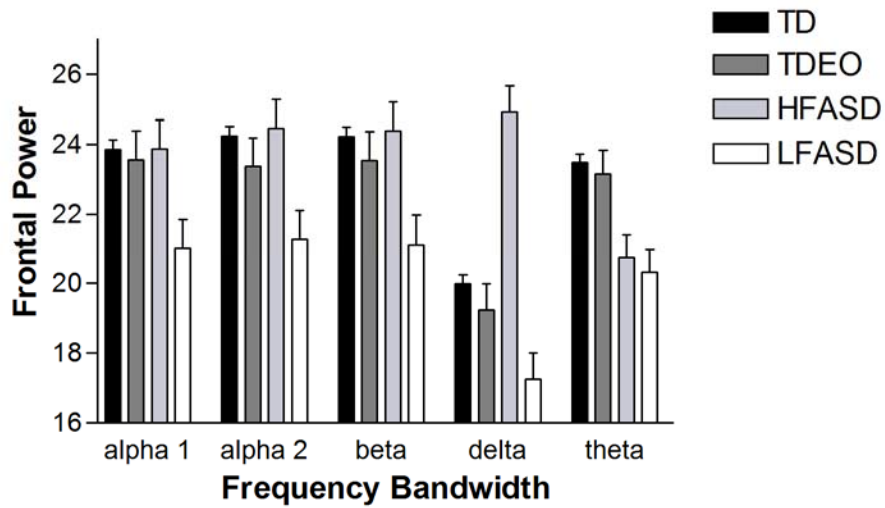


Figure 3. Main effect of Developmental Status (TD, TDEO, HFASD, LFASD) on Frontal Region Power (Means) across bandwidths. TD, TDEO, and HFASD groups exhibited greater power values than the LFASD group in the alpha 1, alpha 2, and beta bandwidths. The high-functioning ASD group demonstrated greater delta power than the TD, TDEO, and LFASD groups. The TD and TDEO groups also showed greater delta power than the low-functioning ASD group. The two TD groups demonstrated greater theta power than both ASD groups. Error bars reflect standard error of the mean.

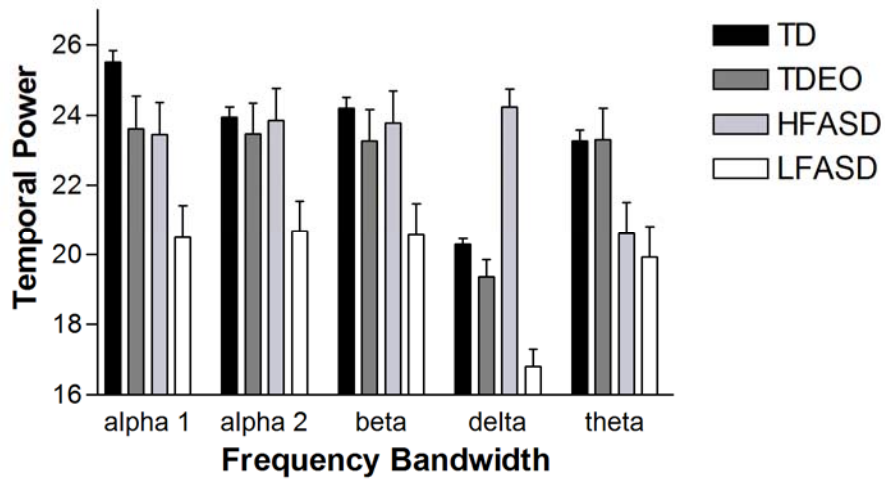


Figure 4. Main effect of Developmental Status (TD, TDEO, HFASD, LFASD) on Temporal Lobe Power (Means) across bandwidths. TD, TDEO, and HFASD groups exhibited greater power values than the LFASD group in the alpha 1, alpha 2, and beta bandwidths. The HFASD group demonstrated greater delta power than the TD and LFASD groups. The TD and TDEO groups also showed greater delta power than the LFASD group. The two TD groups demonstrated greater theta power than both ASD groups. Error bars reflect standard error of the mean.

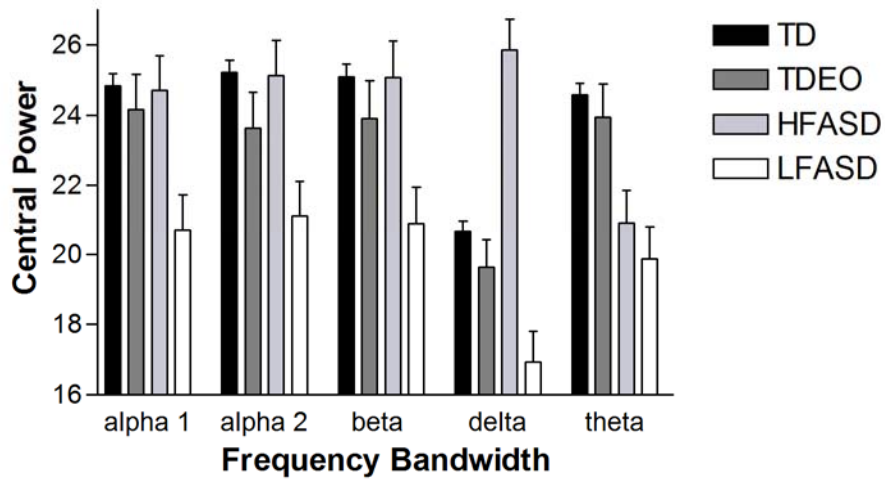


Figure 5. Main effect of Developmental Status (TD, TDEO, HFASD, LFASD) on Central Region Power (Means) across bandwidths. TD, TDEO, and HFASD groups exhibited greater power values than the LF ASD group in the alpha 1, alpha 2, and beta bandwidths. The HFASD group demonstrated greater delta power than the TD, TDEO, and LF ASD groups. Both TD groups also showed greater delta power than the LFASD group. The TD and TDEO groups demonstrated greater theta power than both ASD groups. Error bars reflect standard error of the mean.

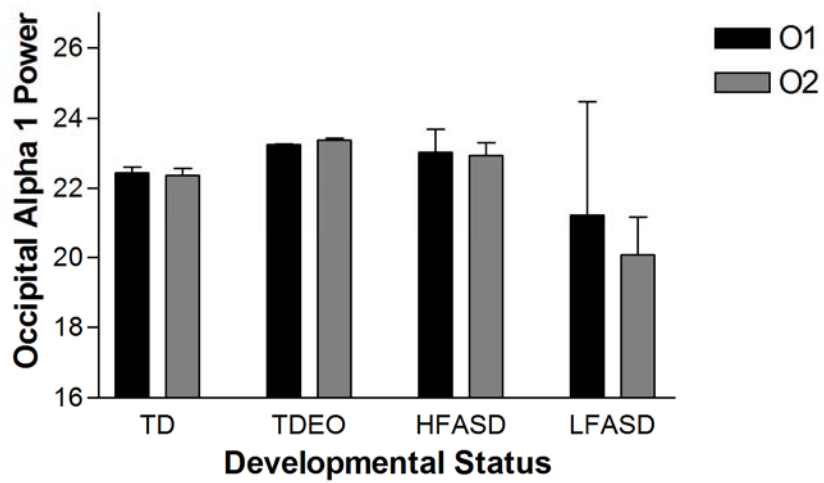


Figure 6. Simple effects of Developmental Status (TD, TDEO, HFASD, LFASD) X Occipital Region on Alpha 1 Power (Means). Although the TD, TDEO, and HFASD groups demonstrated greater power than the LFASD group, this was limited to the right occipital hemisphere. Error bars reflect standard error of the mean.

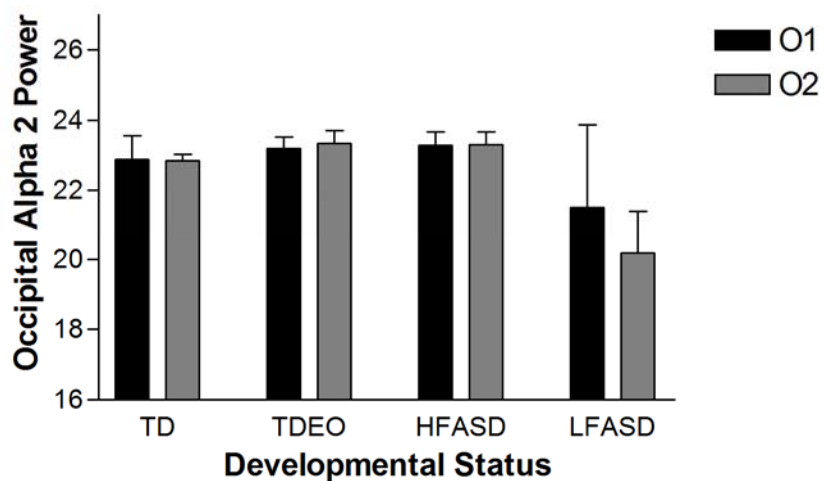


Figure 7. Simple effects of Developmental Status (TD, TDEO, HFASD, LFASD) X Occipital Region on Alpha 2 Power (Means). Although the TD, TDEO, and HFASD groups demonstrated greater power than the LFASD group, this was restricted to the right occipital hemisphere. Error bars reflect standard error of the mean.

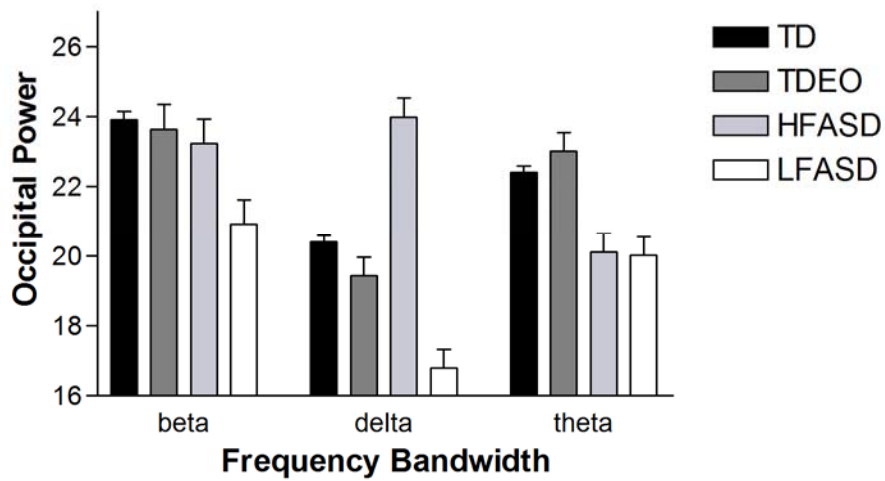


Figure 8. Main effect of Developmental Status (TD, TDEO, HFASD, LFASD) on Occipital Region Beta, Delta, and Theta Power (Means). The TD, TDEO and HFASD groups demonstrated greater beta power than the LFASD group. The HF ASD group demonstrated greater delta power than the TD, TDEO, and LFASD groups. The two TD groups also showed greater delta power than the LFASD group. The TD and TDEO groups demonstrated greater theta power than both ASD groups. Error bars reflect standard error of the mean.

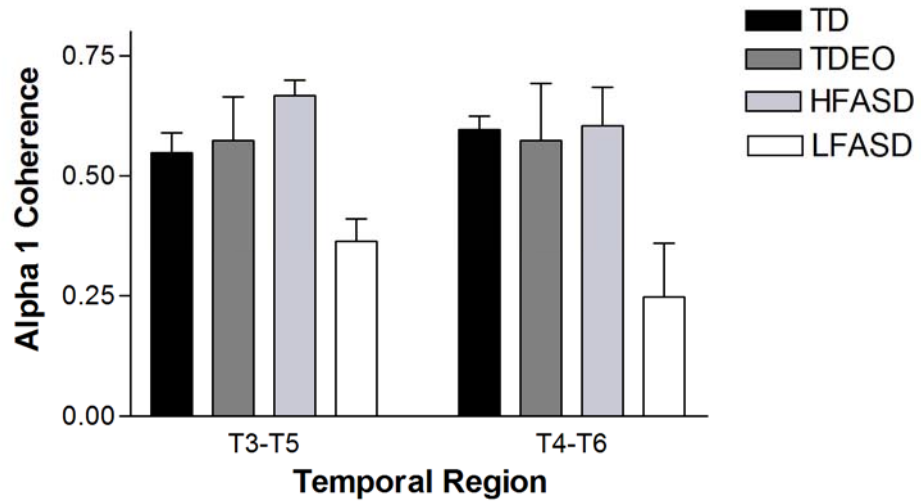


Figure 9. Simple effects of Developmental Status [Typically Developing (TD), TD eyes open (TDEO), High-Functioning ASD (HFASD), Low-Functioning ASD (LFASD)] X Temporal Region on Alpha 1 (5.5 – 9.5 Hz) Coherence (Means). The TD, TDEO, and HFASD groups displayed greater coherence values than the LFASD group, but only between channels T4-T6. Error bars reflect standard error of the mean.

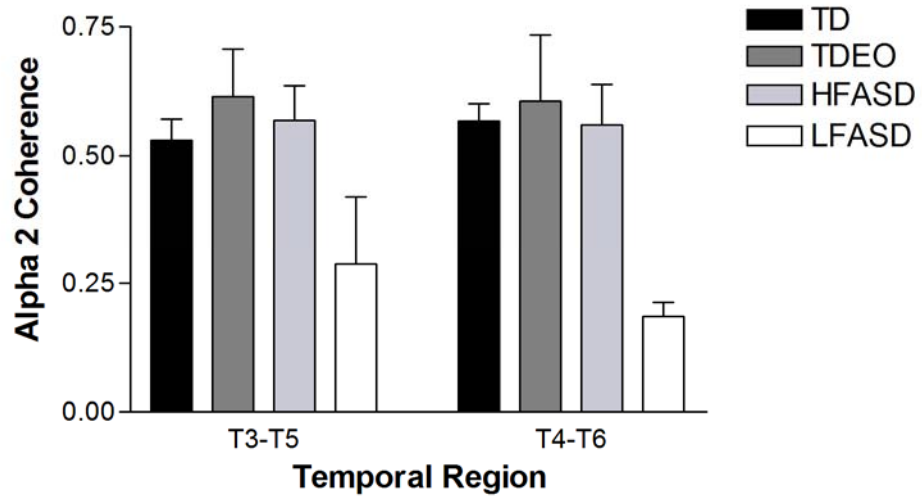


Figure 10. Simple effects of Developmental Status (TD, HF ASD, LFASD) X Temporal Region on Alpha 2 (7.5 – 12.5 Hz) Coherence (Means). Both of the TD groups and the HFASD group displayed greater coherence values than the low-functioning ASD group, but only between channels T4-T6. Error bars reflect standard error of the mean.

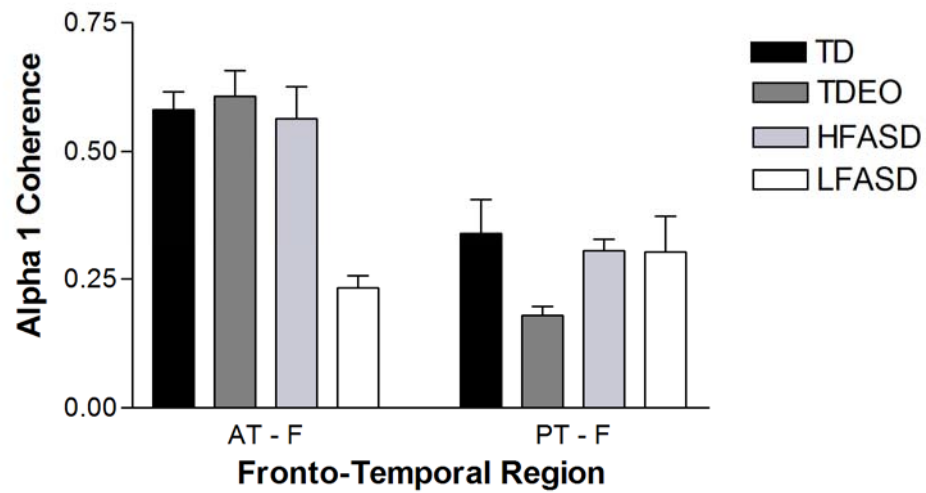


Figure 11. Simple effects of Developmental Status (TD, TDEO, HFASD, LFASD) X Frontal - Temporal Region on Alpha 1 Coherence (Means). The TD, TDEO, and HFASD groups demonstrated greater alpha 1 coherence between anterior temporal (AT) and frontal (F) EEG sites than the LFASD group. This pattern was not observed between posterior temporal and frontal EEG sites. Error bars reflect standard error of the mean.

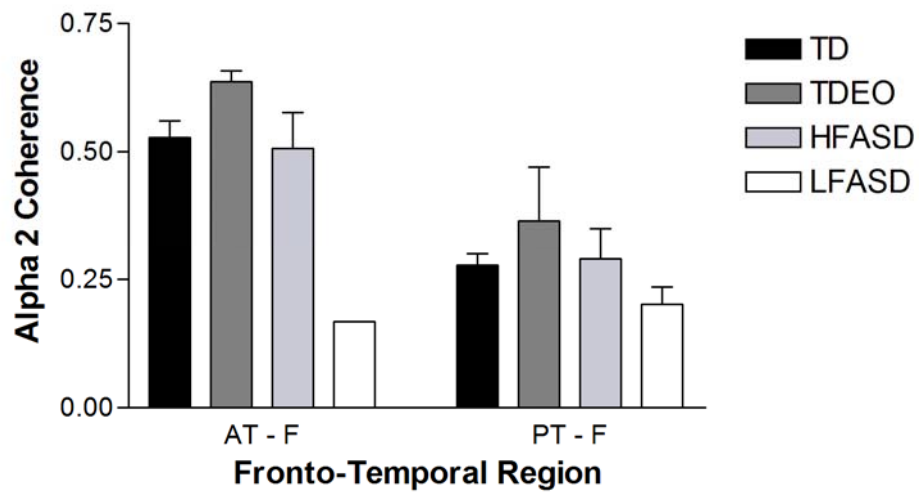


Figure 12. Simple effect of Developmental Status (TD, TDEO, HFASD, LFASD) X Frontal - Temporal Region on Alpha 2 Coherence (Means). The TD, TDEO, and HFASD groups demonstrated greater alpha 2 coherence between anterior temporal (AT) and frontal (F) EEG sites compared to the LFASD group. This pattern was not observed between posterior temporal and frontal EEG sites. Error bars reflect standard error of the mean.

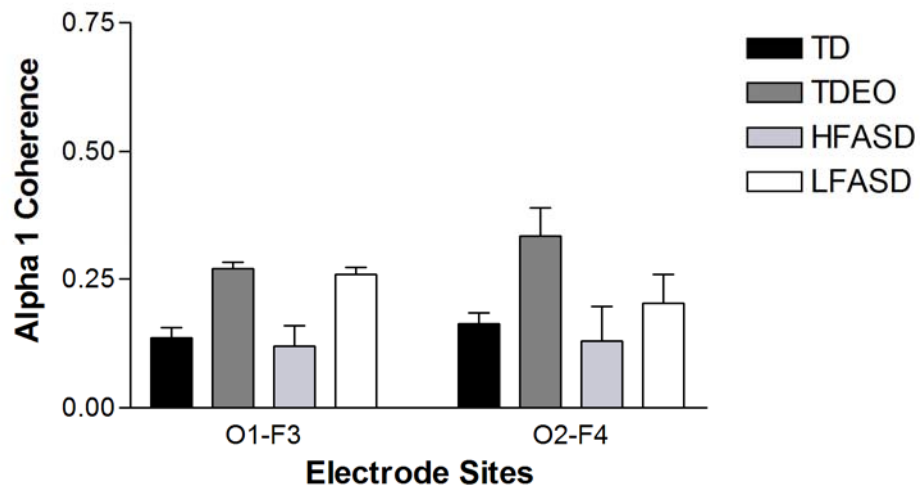


Figure 13. Simple effects of Developmental Status (TD, TDEO, HFASD, LFASD) X Occipital – Frontal Alpha 1 Coherence (Means). The TDEO and LFASD groups demonstrated greater alpha 1 coherence than the TD and HF ASD groups in the left hemisphere. In the right hemisphere, the TDEO group exhibited greater alpha 1 coherence than the TD and HFASD groups. Error bars reflect standard error of the mean.

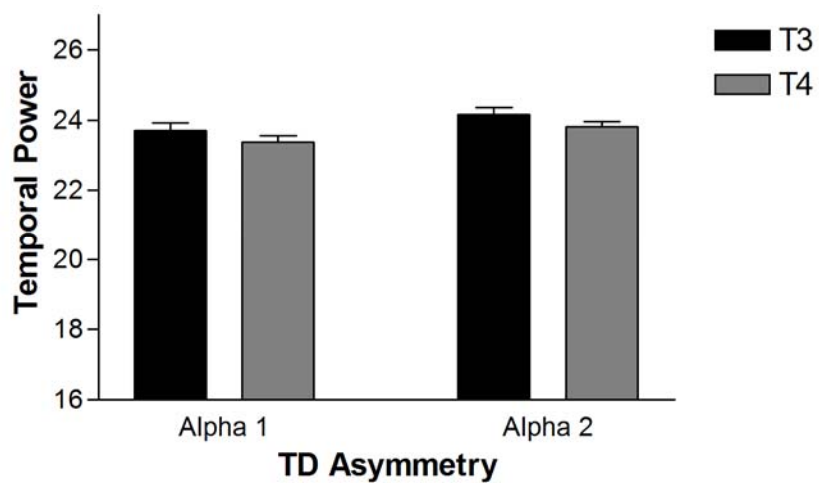


Figure 14. Mean difference values representing left alpha 1(5.5 – 9.5 Hz) and left alpha 2 (7.5 – 12.5 Hz) asymmetry for TD children in anterior temporal lobe. Error bars reflect standard error of the mean.

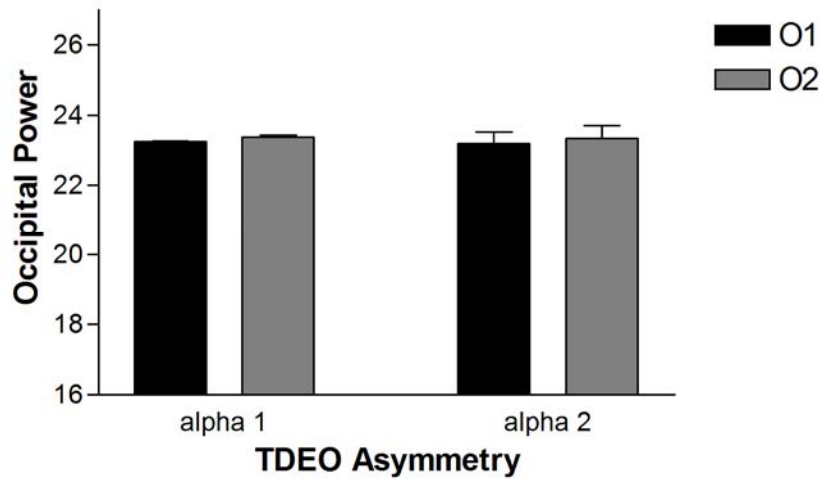


Figure 15. Mean difference values representing right alpha 1 (5.5 – 9.5 Hz) and alpha 2 (7.5 – 12.5 Hz) asymmetry for TDEO children in occipital lobe. Error bars reflect standard error of the mean.

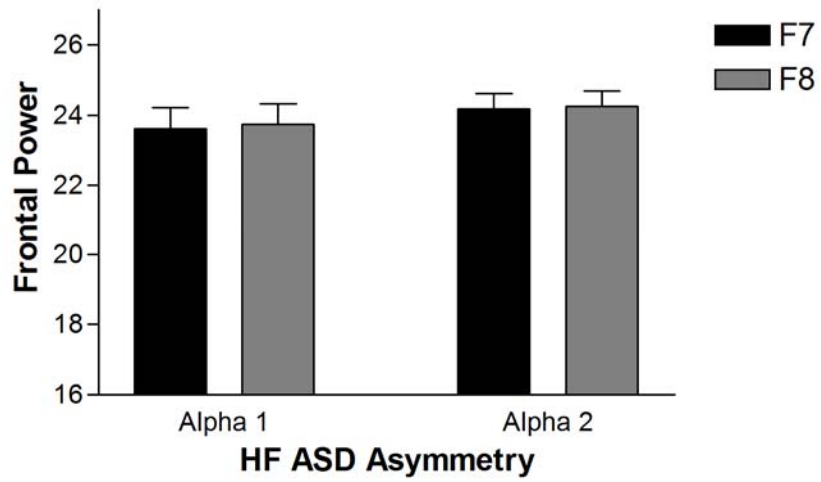


Figure 16. Mean difference values representing right alpha 1 (5.5 – 9.5 Hz) and alpha 2 (7.5 – 12.5 Hz) asymmetry for HFASD children in lateral frontal lobe. Error bars reflect standard error of the mean.

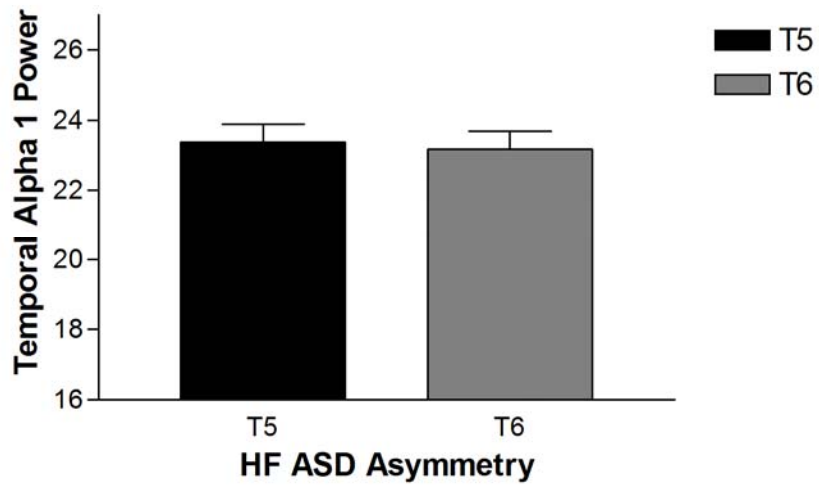


Figure 17. Mean difference values representing left alpha 1 (5.5 – 9.5 Hz) asymmetry for HFASD children in posterior temporal lobe. Error bars reflect standard error of the mean.

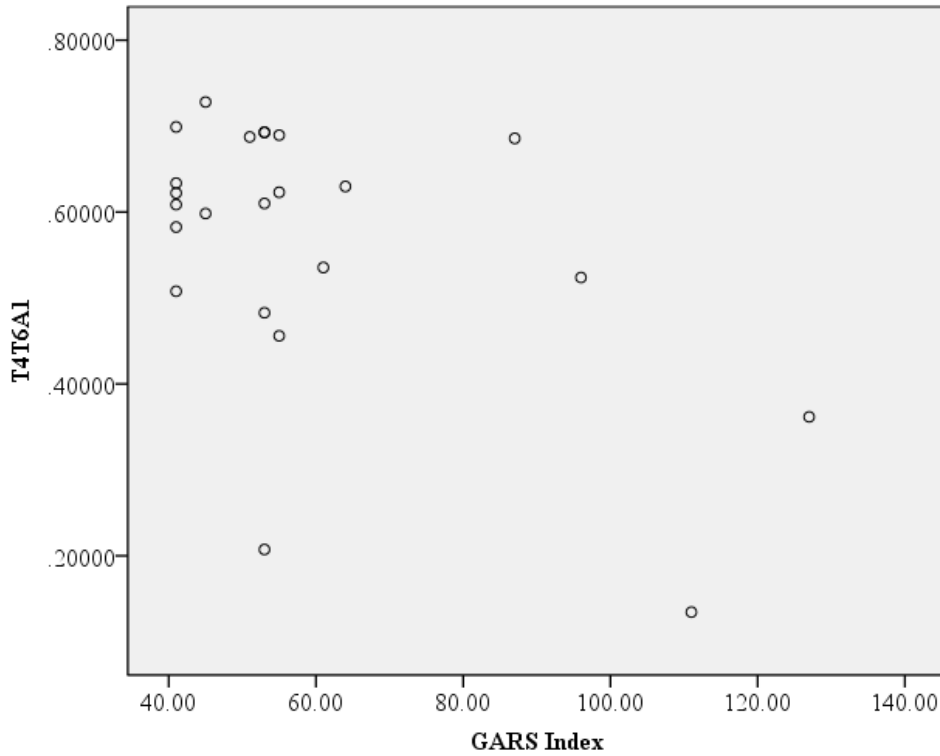


Figure 18. Scatterplot depicting Pearson correlation between ASD severity and T4-T6 alpha 1 coherence. As ASD severity increases, alpha 1 coherence values decrease indicating reduced functional connectivity between temporal regions of the right hemisphere.

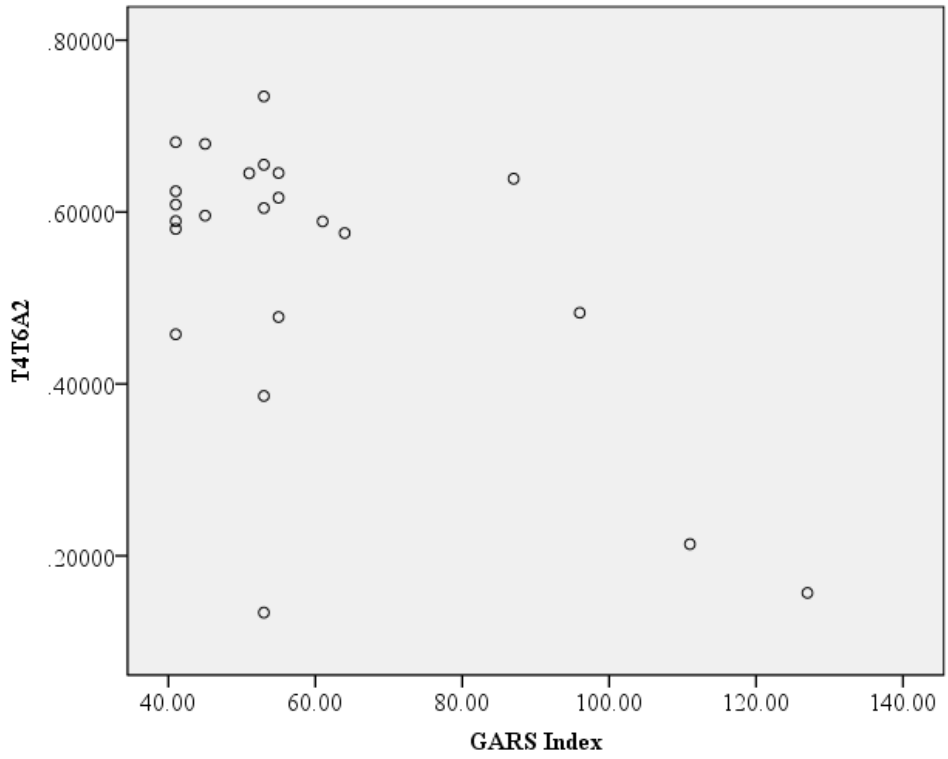


Figure 19. Scatterplot depicting Pearson correlation between ASD severity and T4-T6 alpha 2 coherence. As ASD severity increases, alpha 2 coherence values decrease indicating reduced functional connectivity between right temporal regions.

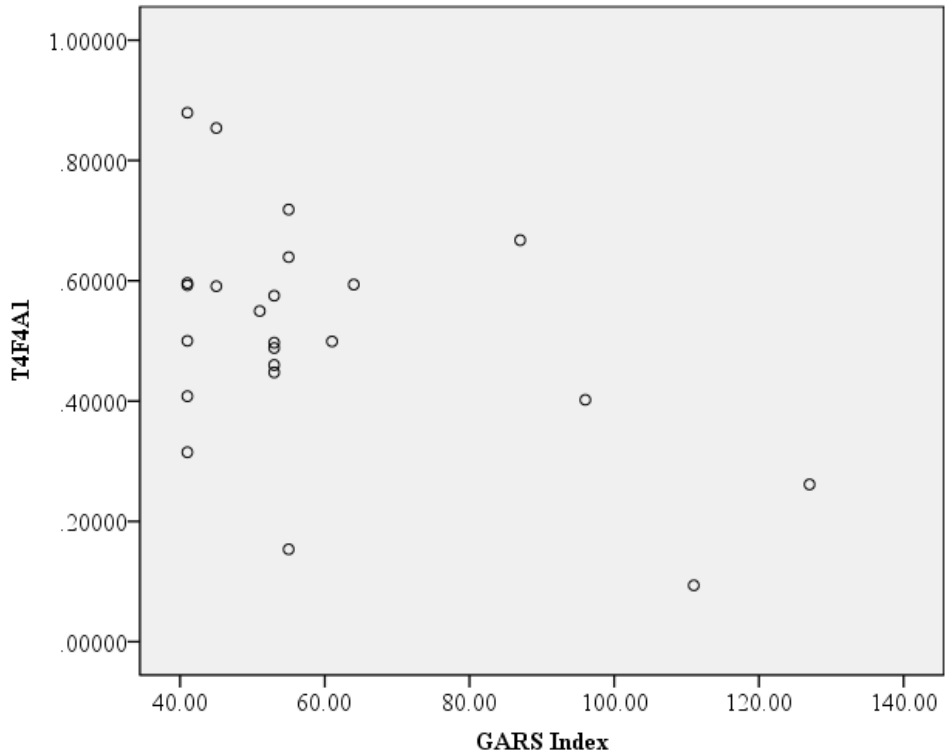


Figure 20. Scatterplot depicting Pearson correlation between ASD severity and T4-F4 alpha 1 coherence. As ASD severity increases, right anterior temporal - frontal alpha 1 coherence values decrease. Thus, increased ASD severity is associated with reduced alpha 1 functional connectivity between the anterior temporal and frontal regions.

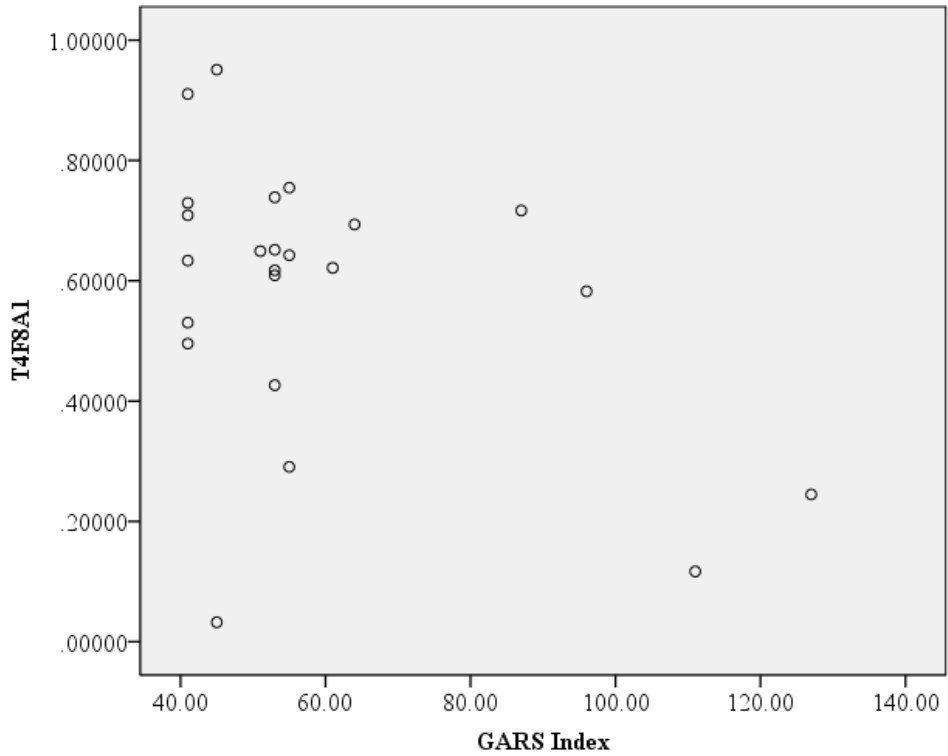


Figure 21. Scatterplot depicting Pearson correlation between ASD severity and T4- F8 alpha 1 coherence. As ASD severity increases, right anterior temporal - frontal alpha 1 coherence values decrease. Thus, increased ASD severity is associated with reduced alpha 1 functional connectivity between the anterior temporal and frontal regions.

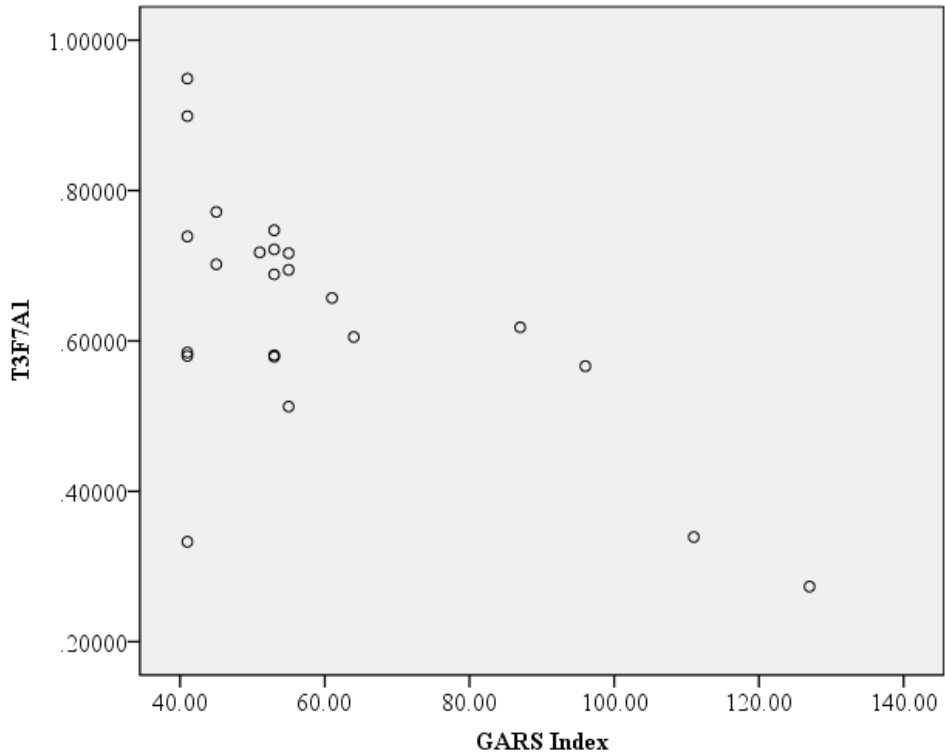


Figure 22. Scatterplot depicting Pearson correlation between ASD severity and T3- F7 alpha 1 coherence. As ASD severity increases, left anterior temporal - frontal alpha 1 coherence values decrease. This indicates that increased ASD severity is associated with reduced alpha 1 functional connectivity between the left anterior temporal and frontal regions.

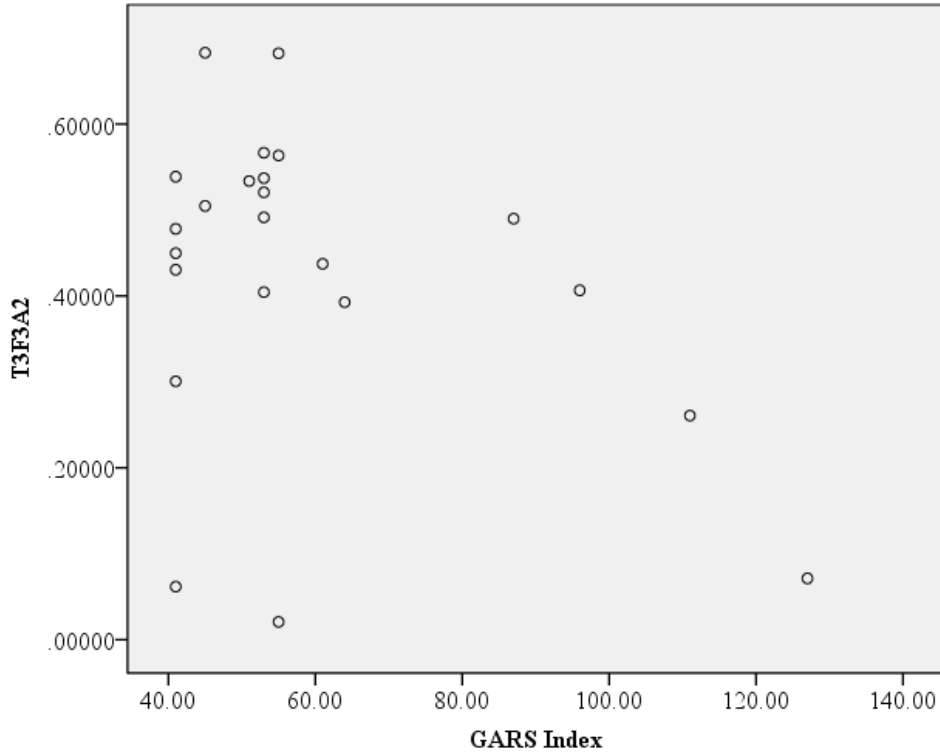


Figure 23. Scatterplot depicting Pearson correlation between ASD severity and T3- F3 alpha 2 coherence. As ASD severity increases, left anterior temporal - frontal alpha 2 coherence values decrease. Thus, increased ASD severity is associated with reduced alpha 2 functional connectivity between the left anterior temporal and frontal regions.

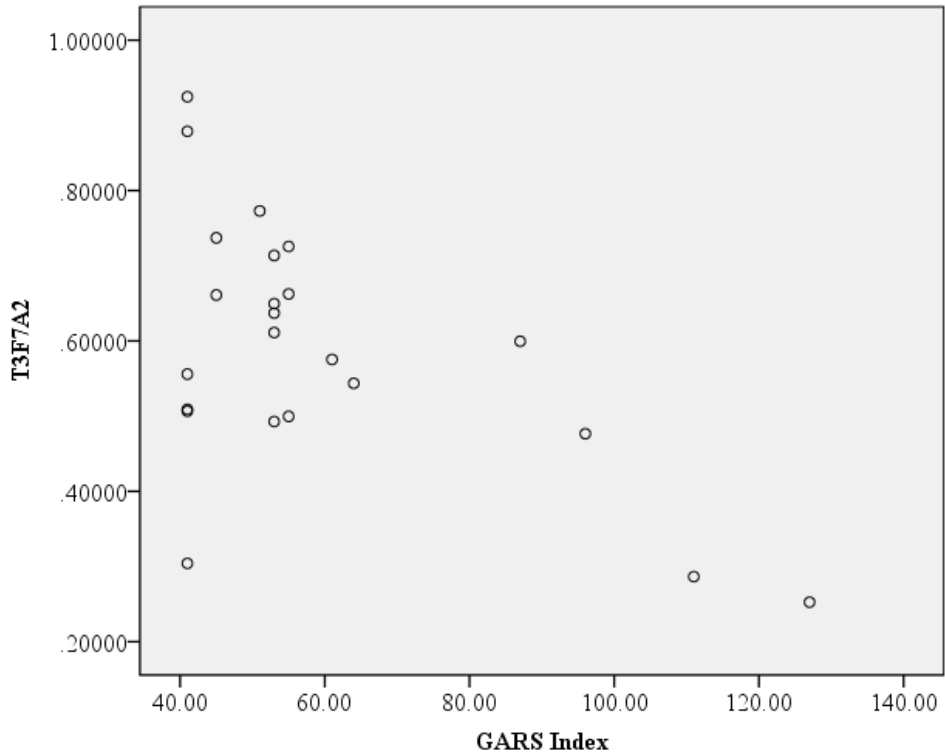


Figure 24. Scatterplot depicting Pearson correlation between ASD severity and T3- F7 alpha 2 coherence. As ASD severity increases, left anterior temporal -frontal alpha 2 coherence values decrease. This indicates that increased ASD severity is associated with reduced alpha 2 functional connectivity between the left anterior temporal and frontal regions.

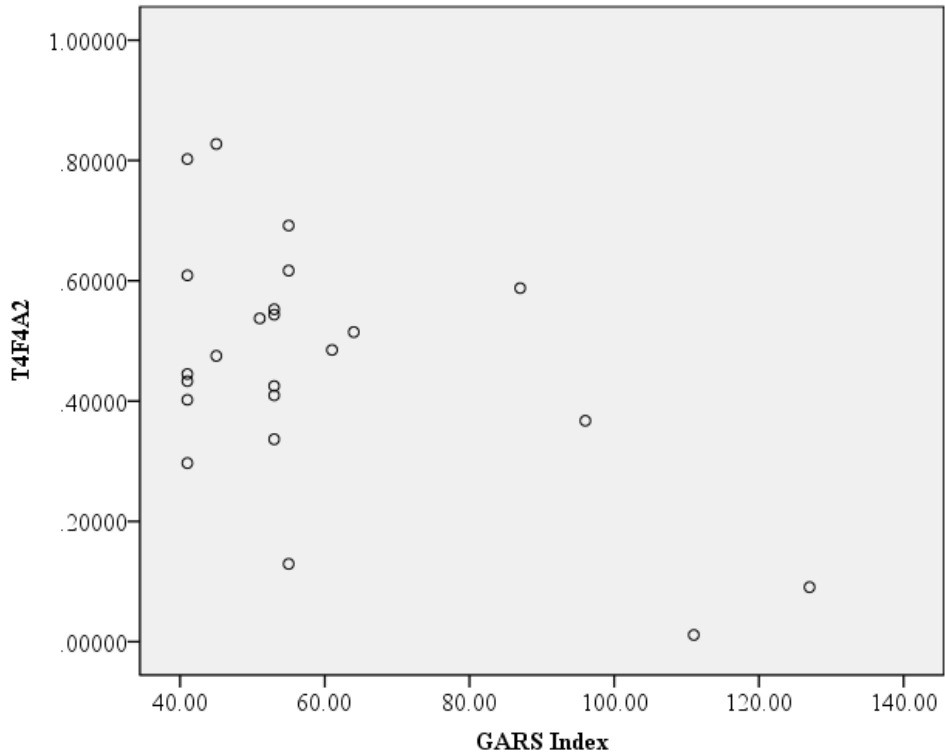


Figure 25. Scatterplot depicting Pearson correlation between ASD severity and T4- F4 alpha 2 coherence. As ASD severity increases, right anterior temporal - frontal alpha 2 coherence values decrease. Thus, increased ASD severity is associated with reduced alpha 2 functional connectivity between the right anterior temporal and frontal regions.

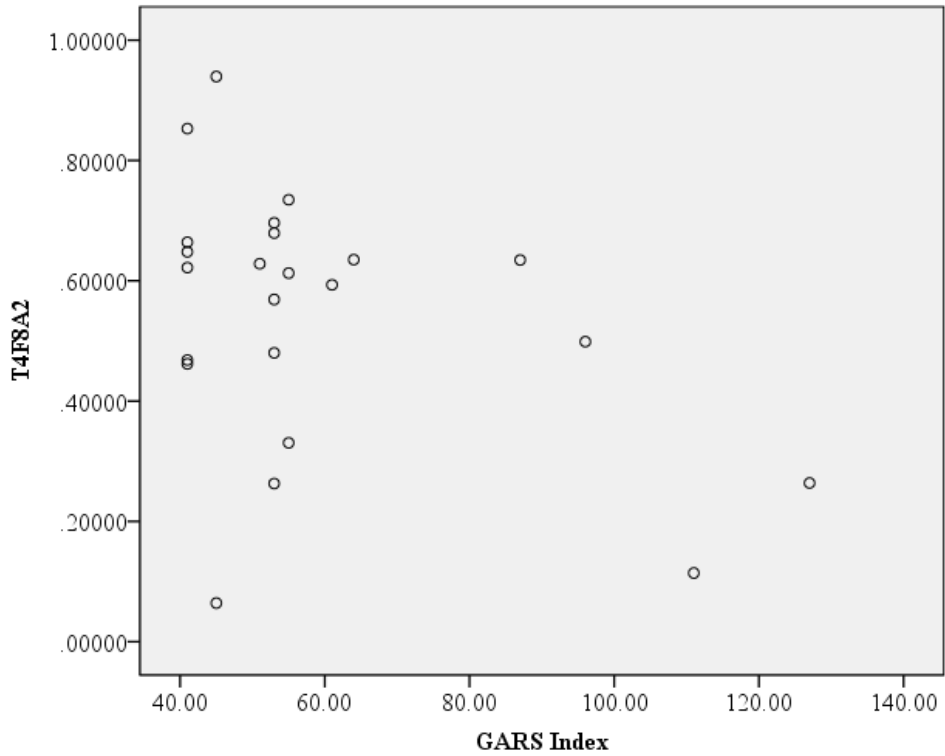


Figure 26. Scatterplot depicting Pearson correlation between ASD severity and T4- F8 alpha 2 coherence. As ASD severity increases, right anterior temporal - frontal alpha 2 coherence values decrease. Thus, increased ASD severity is associated with reduced alpha 2 functional connectivity between the right anterior temporal and frontal regions.

REFERENCES

- American Psychiatric Association. (4th Ed.). (1994). *Diagnostic and statistical manual of mental disorders*. Washington, DC: American Psychiatric Association.
- Autism Genome Project Consortium (2007). Mapping autism risk loci using genetic linkage and chromosomal rearrangements. *Nature Genetics*, 39, 319 – 328.
- Babiloni, C., Albertini, G., Onorati, P., Muratori, C., Buffo, P., Condoluci, C., ... Rossini, P. M. (2010). Cortical sources of EEG rhythms are abnormal in Down syndrome. *Clinical Neurophysiology*, 121(8), 1205 - 1212.
- Barry, R. J. & Clarke, A. R. (2009). Spontaneous EEG oscillations in children, adolescents, and adults: Typical development, and pathological aspects in relation to AD/HD. *Journal of Psychophysiology*, 23(4), 157 – 173.
- Barry, R. J., Clarke, A. R., & Johnstone, S. J. (2003). A review of electrophysiology in attention-deficit/hyperactivity disorder: I. Qualitative and quantitative electroencephalography. *Clinical Neurophysiology*, 114, 171–183.
- Barry, R. J., Clarke, A. R., Johnstone, S. J., & Brown, C. R. (2009). EEG differences in children between eyes-closed and eyes-open resting conditions. *Clinical Neurophysiology*, 120, 1806 – 1811.
- Başar, E., Başar-Eroglu, C., Karakaş, S., & Schürmann, M. (2001). Gamma, alpha, delta, and theta oscillations govern cognitive processes. *International Journal of Psychophysiology*, 39, 241 – 248.

- Başar-Eroglu, C., Başar, E., Demiralp, T., & Schürmann, M. (1992). P300-response: Possible psychophysiological correlates in delta and theta frequency channels. A review. *International Journal of Psychophysiology*, *13*, 161 – 179.
- Bernier, R., Dawson, G., Webb, S., & Murias, M. (2007). EEG mu rhythm and imitation impairments in individuals with autism spectrum disorder. *Brain and Cognition*, *64*, 228 – 237.
- Boger-Meggido, I., Shaw, D. W. W., Friedman, S. D., Sparks, B. F., Artru, A. A., Giedd, J. N., ... Dager, S. R. (2006). Corpus callosum morphometrics in young children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *36*(6), 733 – 739.
- Brown, T. T. & Jernigan, T. L. (2012). Brain development during the preschool years. *Neuropsychology Review*, *22*, 313 – 333.
- Cantor, D. S., Thatcher, R. W., Hrybyk, M., & Kaye, H. (1986). Computerized EEG analyses of autistic children. *Journal of Autism and Developmental Disorders*, *16*(2), 169 – 187.
- Caplan, J. B., Madsen, J. R., Raghavachari, S., Kahana, M. J. (2001). Distinct patterns of brain oscillations underlie two basic parameters of human maze learning. *Journal of Neurophysiology*, *86*, 368 – 380.
- Centers for Disease Control and Prevention. (2012). Autism and developmental disabilities monitoring network surveillance year 2008. *Morbidity and Mortality Weekly Report*, *61*(3), 1 – 19.
- Chelly, J. & Mandel, J. L. (2001). Monogenetic causes of X-linked mental retardation. *Nature Reviews Genetics*, *2*(9), 669 – 680.

- Cherkassy, V. L., Kana, R. K., Keller, T. A., & Just, M. A. (2006). Functional connectivity in a baseline resting-state network in autism. *NeuroReport*, *17*(6), 1687 – 1690.
- Coben, R., Clarke, A. R., Hudspeth, W., & Barry, R. J. (2008). EEG power and coherence in autism spectrum disorder. *Clinical Neuropsychology*, *119*, 1002 – 1009.
- Cohen, J. (1988). *Statistical power analyses for the behavioral science (2nd Ed.)*. Hillsdale: Lawrence Erlbaum.
- Cohen, J. (1994). The earth is round ($p < .05$). *American Psychologist*, *49* (1), 997 – 1003.
- Dapretto, M., Davies, M. S., Pfeifer, J. H., Scott, A. A., Sigman, M., Bookheimer, S. Y., & Iacoboni, M. (2005). Understanding emotions in others: Mirror neuron dysfunction in children with autism spectrum disorders. *Nature Neuroscience*, *9*(1), 28 – 30.
- Davidson, R. J. & Fox, N. A. (1989). Frontal brain asymmetry predicts infants response to maternal separation. *Journal of Abnormal Psychology*, *98*, 127 – 131.
- Davidson, R. J., Ekman, P., Saron, C. D., Senulis, J. A., & Friesen, W. (1990). Approach-withdrawal and cerebral asymmetry: Emotional expression and brain physiology I. *Journal of Personality and Social Psychology*, *58*, 330 – 341.
- Dawson, G. (1994). Frontal electroencephalographic correlates of individual differences in emotion expression in infants: A brain systems perspective. *Monographs of the Society for Research in Child Development*, *59* (2/3), 135-151.

- Dawson, G., Carver, L., Meltzoff, A. N., Panagiotides, H., McPartland, J., & Webb, S. (2002). Neural correlates of face and object recognition in young children with autism spectrum disorder, developmental delay, and typical development. *Child Development, 73*(3), 700 – 717.
- De Fossé, L., Hodge, S. M., Makris, N., Kennedy, D. N., Caviness, V. S. Jr, McGrath, L., ... Harris, G. J. (2004). Language-association cortex asymmetry in autism and specific language impairment. *Annals of Neurology, 56*(6), 757 – 766.
- Dinstein, I., Pierce, K., Eyster, L., Solso, S., Malach, Rafael, M., Behrmann, M., & Courchesne, E. (2011). Disrupted neural synchronization in toddlers with autism. *Neuron, 70*, 1218 – 1225.
- Duffy, F. H. & Als, H. (2012). A stable pattern of EEG spectral coherence distinguishes children with autism from neuro-typical controls – a large case control study. *BMC Medicine, 10*(64), 1- 18.
- Elul, R. (1972). The genesis of the EEG. *International Review of Neurobiology, 15*, 228 – 263.
- Engel, A. K. & Fries, P. (2010). Beta-band oscillations – signaling the status quo? *Current Opinion in Neurobiology, 20*, 156 – 165.
- Engel, A. K., Fries, P., & Singer, W. (2001). Dynamic predictions: Oscillations and synchrony in top-down processing. *Nature Review Neuroscience, 2*, 704 – 716.
- Fatemi, S. H., Snow, A. V., Sary, J. M., Araghi-Niknam, M., Reutiman, T. J., Lee, S., Brooks, A. I., & Pearce, D. A. (2005). Reelin signaling is impaired in autism. *Biological Psychiatry, 57*, 777 - 787.

- Fecteau, S., Lepage, J.-F., & Théoret, H. (2006). Autism spectrum disorder: Seeing is not understanding. *Current Biology*, *16* (4), R131 – R133.
- Fell, J., Fernández, G., Klaver, P., Axmacher, N., Mormann, F., Haupt, S., & Elger, C. E. (2006). Rhinal-hippocampal coupling during declarative memory formation: Dependence on item characteristics. *Neuroscience Letters*, *407*(1), 37 – 41.
- Gasser, T., Bacher, P., & Steinberg, H., (1985). Test-retest reliability of spectral parameters of the EEG. *Electroencephalography and Clinical Neurophysiology*, *60*, 312 – 319.
- Gasser, T., Verleger, R., Bächer, P., & Sroka, L. (1988). Development of the EEG of school-age children and adolescents. I. Analysis of band power. *Electroencephalography and Clinical Neurophysiology*, *69*, 91 – 99.
- Gepner, B. & Féron, F. (2009). Autism: A world changing too fast for a mis-wired brain? *Neuroscience and Biobehavioral Reviews*, *33*, 1227 – 1242.
- George, M. S., Parekh, P. I., Rosinsky, N., Ketter, T. A., Kimbrell, T. A., Heilman, K. M., ... Post, R. M. (1996). Understanding emotional prosody activates right hemisphere regions. *Archives of Neurology*, *53*(7), 665 – 670.
- Ginsburg, D. A., Pasternak, E. B., & Gurvitch, A. M. (1977). Correlation analysis of delta activity generated in cerebral hypoxia. *Electroencephalography and Clinical Neurophysiology*, *42*(4), 445 – 455.
- Gloor, P., Ball, G., & Schaul, N. (1977). Brain lesions that produce delta waves in the EEG. *Neurology*, *27*(4), 326 - 333.
- Gmehlin, D., Thomas, C., Weisbrod, M., Walther, S., Resch, F., & Oelkers-Ax, R. (2011). Development of brain synchronisation within school-age – Individual

- analysis of resting (alpha) coherence in a longitudinal data set. *Clinical Neurophysiology*, *122*, 1973 – 1983.
- Graf, E. R., Zhang, X., Jin, S. X., Linhoff, M. W., & Craig, A. M. (2004). Neurexins induce differentiation of GABA and glutamate postsynaptic specializations via neuroligins. *Cell*, *119*, 1013 – 1026.
- Groen, W. B., Zwiers, M. P., van der Gaag, R.-J., & Buitelaar, J. K. (2008). The phenotype and neural correlates of language in autism: An integrative review. *Neuroscience and Behavioral Reviews*, *32*, 1416 – 1425.
- Hazlett, H. C., Gu, H., McKinstry, R. C., Shaw, D. W. W., Botteron, K. N., Dager, S. R., ... Piven, J. (2012). Brain volume findings in 6-month old infants at high familial risk for autism. *American Journal of Psychiatry*, *169*(6), 601 – 608.
- Herbert, M.R., Harris, G. D., Adrien, K. T., Ziegler, D. A., Makris, N., Kennedy, D. N., ... Caviness, V. S. Jr. (2002). Abnormal asymmetry in language association cortex in autism. *Annals of Neurology*, *52*, 588 – 596.
- Hughes, J. R. (2007). Autism: The first firm finding = underconnectivity? *Epilepsy & Behavior*, *11*, 20 – 24.
- Hughes, J. R. & Melyn, M. (2005). EEG and seizures in autistic children and adolescents: Further findings with therapeutic implications. *Clinical EEG Neuroscience*, *36*, 15 – 20.
- Jamain, S., Quach, H., Betancur, C., Rastam, M., Colineaux, C., Gillberg, I. C., ... Bourgeron, T. (2003). Mutations of the X-linked genes encoding neuroligins NLGN3 and NLGN4 are associated with autism. *Nature Genetics*, *34*(1), 27 – 29.

- Jasper, H. H. (1958). The ten-twenty electrode system of the international federation. *Electroencephalography and Clinical Neurophysiology*, *10*, 371-375.
- Jenson, O. & Tesche, C. D. (2002). Frontal theta activity in humans increases with memory load in a working memory task. *European Journal of Neuroscience*, *15*, 1395 – 1399.
- Jones, N. A., Field, T., Davalos, M., & Pickens, J. (1997). EEG stability in infants/ children of depressed mothers. *Child Psychiatry and Human Development*, *28*, 59 – 70.
- Jones, N. A., Field, T., Fox, N. A., Davalos, M., & Gomez, C. (2001). EEG during different emotions in 10-month old infants of depressed mothers. *Journal of Reproductive and Infant Psychology*, *19*, 295 – 312.
- Just, M. A., Cherkassy, V. L., Keller, T. A., & Minshew, N. J. (2004). Cortical activation and synchronization during sentence comprehension in high-functioning autism: Evidence of underconnectivity. *Brain*, *127*(8), 1811 – 1821.
- Just, M. A., Cherkassky, V. I., Keller, T. A., Kana, R. K., & Minshew, N. J. (2007). Functional and anatomical cortical underconnectivity in autism: Evidence from an fMRI study of an executive function task and corpus callosum morphometry. *Cerebral Cortex*, *17*, 951 – 961.
- Just, M. A., Keller, T. A., Malave, V. L., Kana, R. K., & Varma, S. (2012). Autism as a neural systems disorder: A theory of frontal-posterior underconnectivity. *Neuroscience and Biobehavioral Reviews*, *36*, 1292 – 1313.

- Kana, R. K., Libero, L. E., & Moore, M. S. (2011). Disrupted cortical connectivity theory as an explanatory model for autism spectrum disorders. *Physics of Life Reviews*, 8, 410 – 437.
- Kandel, E. R., Schwartz, J. H., & Jessell, T. M. (2000). *Principles of neural science*, 4th ed. New York: McGraw-Hill.
- Kaneko, W. M., Phillips, E. L., Riley, E. P., & Ehlers, C. L. (1996). EEG findings in fetal alcohol syndrome and Down syndrome children. *Electroencephalography & Clinical Neurophysiology*, 98(1), 20 – 28.
- Kleinmans, N. M., Richards, T., Johnson, L. C., Weaver, K. E., Greenon, J., Dawson, G., & Aylward, E. (2011). fMRI evidence of neural abnormalities in the subcortical face processing system in ASD. *Neuroimage*, 54(1), 697 – 704.
- Kleinmans, N. M., Richards, T., Sterling, L., Stegbauer, K. C., Mahurin, R., Johnson, L. C. ... Aylward, E. (2008). Abnormal functional connectivity in autism spectrum disorders during face processing. *Brain*, 131, 1000 – 1012.
- Kleinmans, N. M., Richards, T., Weaver, K., Johnson, L. C., Greenon, J., Dawson, G. & Aylward, E. (2010). Association between amygdala response to emotional faces and social anxiety in autism spectrum disorders. *Neuropsychologia*, 48, 3665 – 3670.
- Klimesch, W., Doppelmayr, M., Russegger, H., Pachinger, T., & Schwaiger, L. (1998). Induced alpha band power changes in the human EEG and attention. *Neuroscience Letters*, 244(2), 73 – 76.
- Klostermann, F., Nikulin, V. V., Kühn, A. A., Marzinzik, F., Wahl, M., Pogosyan, A., ... Curio, G. (2007). Task-related differential dynamics of EEG alpha- and beta-band

- synchronization in cortico-basal motor structures. *European Journal of Neuroscience*, 25, 1604 – 1615.
- Knyazev, G. G. (2007). Motivation, emotion, and their inhibitory control mirrored in brain oscillations. *Neuroscience and Biobehavioral Reviews*, 31, 377–395.
- Knyazev, G. G. (2012). EEG delta oscillations as a correlate of basic homeostatic and motivational processes. *Neuroscience and Biobehavioral Reviews*, 36, 677 – 695.
- Kumar, R. & Christian, S. (2009). Genetics of autism spectrum disorders. *Current Neurology and Neuroscience Reports*, 9, 188 – 197.
- Levy, S. E., Mandell, D. S., & Schultz, R. T. (2009). Autism. *The Lancet*, 374, 1627 – 1638.
- Lopes da Silva, F. (1991) Neural mechanisms underlying brain waves: From neural membranes to networks. *Electroencephalography and Clinical Neurophysiology*, 79, 81 – 93.
- Lüchinger, R., Michels, L., Martin, E., & Brandeis, D. (2011). EEG-BOLD correlations during (post-)adolescent brain maturation. *NeuroImage*, 56(3), 1493 – 1505.
- Lushchekina, E. A., Podreznaya, E. D., Lushchekin, V. S., Novototskii-Vlasov, V. Yu., & Strelets, V. B. (2013). Characteristics of the spectral power of EEG rhythms in children with early childhood autism and their association with the development of different symptoms of schizophrenia. *Neuroscience and Behavioral Physiology*, 43(1), 40 – 45.
- Mariosi, E., Harmony, T., Sanchez, L., Becker, J., Bernal, J., Reyes, A., ... Fernandez, T. (1992). Maturation of the coherence of EEG activity in normal and learning-

- disabled children. *Electroencephalography and Clinical Neurophysiology*, 83, 350 – 357.
- Marshall, T. R., Bar-Haim, Y., & Fox, N. A. (2002). Development of the EEG from 5 months to 4 years of age. *Clinical Neurophysiology*, 113, 1199–1208.
- Mattson, S. N., Riley, E. P., Jernigan, T. L., Ehlers, C. L., Delis, D. C., Jones, K. L., ... Bellugi, U. (1992). Fetal alcohol syndrome: A case report of neuropsychological, MRI, and EEG assessments of two children. *Alcoholism: Clinical and Experimental Research*, 16(5), 1001 – 1003.
- Michels, L., Muthuraman, M., Lüchinger, R., Martin, E., Anwar, A. R., Raethjen, J., ... Siniatchkin, M. (2013). Developmental changes of functional and directed resting-state connectivities associated with neuronal oscillations in EEG. *NeuroImage*, 81, 231 – 242.
- Muhle, R., Trentacoste, S. V., & Rapin, I. (2004). The genetics of Autism. *Pediatrics*, 113, 472 – 486.
- Murias, M., Webb, S. J., Greenson, J., & Dawson, G. (2007). Resting state cortical connectivity reflected in EEG coherence in individuals with autism. *Biological Psychiatry*, 62, 270 – 273.
- Niedermeyer, E. (1982). The normal EEG of the waking adult. In E. Niedermeyer & F. Lopes da Silva (Eds.) *Electroencephalography* (2nd Ed., pp. 17 – 34). Munich: Urban & Schwarzenberg.
- Nunez, P. L., Srinivasan, R., Westdorp, A. F., Wijesinghe, R. S., Tucker, D. M., Silberstein, R. B., & Cadsuch, P. J. (1997). EEG coherency I: Statistics, reference electrode, volume conduction, Laplacians, cortical imaging, and interpretation at

- multiple scales. *Electroencephalography and Clinical Neurophysiology*, 103, 499 – 515.
- Okazaki, M., Kaneko, Y., Yumoto, M. & Arima, K. (2008). Perceptual change in response to a bistable picture increases neuromagnetic beta-band activity. *Neuroscience Research*, 61, 319 – 328.
- O’Roak, B. J. & State, M. W. (2008). Autism genetics: Strategies, challenges, and opportunities. *Autism Research*, 1, 4 – 17.
- Ozonoff, S., Iosi, A., Baguio, F., Cook, I. C., Hill, M. M., Hutman, T., ... Young, G. S. (2010). A prospective study of the emergence of early behavioral signs of autism. *Journal of the American Academy of Child and Adolescent Psychiatry*, 49, 256 – 266.
- Pickens, J., Field, T., & Nawrocki, T. (2001). Frontal EEG asymmetry in response to emotional vignettes in preschool age children. *International Journal of Behavioral Development*, 25(2), 105 – 112.
- Pierce, K., Müller, R.-A., Ambrose, J., Allen, G., & Courchesne, E. (2001). Face processing occurs outside of the fusiform ‘face area’ in autism: Evidence from functional MRI. *Brain*, 124, 2059 – 2073.
- Pivik, R. T., Broughton, R. J., Coppola, R., Davidson, R. J., Fox, N., & Nuwer, M. R. (1993). Guidelines for the recording and quantitative analysis of electroencephalographic activity in research contexts. *Psychophysiology*, 30, 547 – 558.
- Pizzagalli, D. (2007). Electroencephalography and high-density electrophysiological sources localization. In *Handbook of psychophysiology* (pp. 56 – 79).

- Raghavachari, S., Kahana, M. J., Rizzuto, D. S., Caplan, J. B., Kirschen, M. P., Bourgeois, B., ... Lisman, J. E. (2001). Gating of human theta oscillations by a working memory task. *Journal of Neuroscience*, *21*(9), 3175 – 3183.
- Ramachandran, V. S. & Oberman, L. M. (2006, November). Broken mirrors: A theory of autism. *Scientific American*, 63 – 69.
- Rippon, G., Brock, J., Brown, C., & Boucher, J. (2007). Disordered connectivity in the autistic brain: Challenges for the ‘new psychophysiology.’ *International Journal of Psychophysiology*, *63*, 164 – 172.
- Rizzolatti, G. & Fabbri-Destro, M. (2010). Mirror neurons: From discovery to autism. *Experimental Brain Research*, *200*, 223 – 237.
- Rosenthal, J. A. (1996). Qualitative descriptors of strength of association and effect size. *Journal of Social Science Research*, *21*(4), 37 – 59.
- Rosenthal, R. & Rosnow, R. L. (2008). *Essentials of behavioral research: Methods and data analysis* (3rd Ed.). New York, NY: McGraw Hill.
- Sarnthein, J., Petsche, H., Rappelsberger, P., Shaw, G. L., von Stein, A. (1998). Synchronization between prefrontal and posterior association cortex during human working memory. *Proceedings of the National Academy of Sciences of the United States of America*, *95*, 7092 – 7096.
- Scher, M. S. (2008). Ontogeny of EEG-sleep from neonatal through infancy periods. *Sleep Medicine*, *9*, 615 – 636.
- Sebat, J., Lakshmi, B., Malhotra, D., Troge, J. Lese-Martin, C., Walsh, T., ... Wigler, M. (2007). Strong association of de novo copy number mutations with autism. *Science*, *316*, 445 – 449.

- Speckmann, E.-J. & Elger, C. E. (1982). Neurophysiological basis of the EEG and of DC potentials. In E. Niedermayer & F. Lopes da Silva (Eds.), *Electroencephalography: Basic principles, clinical applications, and related fields* (pp. 1 – 14). Baltimore: Urban & Schwarzenberg.
- Srinivasan, R., Nunez, P. L., & Siberstein, R. B. (1998). Spatial filtering and neocortical dynamics: Estimates of EEG coherence. *IEEE Transactions on Biomedical Engineering*, 45 (7), 814 – 826.
- Srinivasan, R., Winter, W. R., Ding, J., & Nunez, P. L. (2007). EEG and MEG coherence: Measures of functional connectivity at distinct spatial scales of neocortical dynamics. *Journal of Neuroscience Methods*, 166, 41 – 52.
- Stroganova, T. A., Nygren, G., Tsetlin, M. M., Posikera, I. N., Gillberg, C., Elam, M., & Orekhova, E. V. (2007). Abnormal EEG lateralization in boys with autism. *Clinical Neurophysiology*, 118, 1842 – 1854.
- Sutcliffe, J. S. (2008). Insights into the pathogenesis of Autism. *Science*, 321, 208 – 209.
- Sutton, S. K. & Davidson, R. J. (1997). Prefrontal brain asymmetry: A biological substrate of the behavioral approach and inhibition systems. *Psychological Science*, 8, 204 – 210.
- Swann, N., Tandon, N., Canolty, R., Ellmore, T. M., McEvoy, L. K., Dreyer, S., ... Aron, A. R. (2009). Intracranial EEG reveals a time- and frequency-specific role for the right inferior frontal gyrus and primary motor cortex in stopping initiated responses. *Journal of Neuroscience*, 29, 12675 – 12685.

- Tabuchi, K., Blundell, J., Etherton, M. R., Hammer, R., Liu, X., Powell, C. M., & Südhof, T. C. (2007). A neuroligin-3 mutation implicated in autism increases inhibitory synaptic transmission in mice. *Science*, *318*, 71 – 76.
- Tottenham, N., Tanaka, J., Leon, A. C., McCarry, T., Nurse, M., Hare, T. A., Marcus, D. J., Westerlund, A., Casey, B. J., Nelson, C. A. (2009). The NimStim set of facial expressions: Judgments from untrained research participants. *Psychiatry Research*, *168*(3), 242-249.
- Takeichi, M. (2007). The cadherin superfamily in neuronal connections and interactions. *Nature Reviews Neuroscience*, *8*, 11 – 20.
- Tuchman, R. & Rapin, I. (2002). Epilepsy in autism. *Lancet Neurology*, *1*(6), 352 – 358.
- Tyszka, J. M., Kennedy, D. P., Paul, L. K., & Adolphs, R. (2013). Largely typical patterns of resting-state functional connectivity in high-functioning adults with autism. *Cerebral Cortex*. Advance online publication. doi: 10.1093/cercor/bht040
- Varoquaux, F., Aramuni, G., Rawson, R.L., Mohrmann, R., Missler, M., Gottman, K., Zhang, W., Südhof, T. C., & Brose, N. (2006). Neuroligins determine synapse maturation and function. *Neuron*, *51* (6), 741 – 754.
- Veenstra-Vanderweele, J., Christian, S. I., & Cook, E. H. Jr. (2004). Autism as a paradigmatic complex genetic disorder. *Annual Review of Genomics and Human Genetics*, *5*, 379 – 405.
- Vidal, C. N., Nicolson, R., DeVito, T. J., Hayashi, K. M., Geaga, J. A., Drost, D. J., ... Thompson, P. M. (2006). Mapping corpus callosum deficits in autism: An index of aberrant cortical connectivity. *Biological Psychiatry*, *60*(3), 218 – 225.

- Vladimirova, G. (1991). Development of the electroencephalographic rhythms of wakefulness in healthy infants during their first year. *Acta Physiologica et Pharmacologica Bulgarica*, 17, 13 – 20.
- Vuga, M., Fox, N. A., Cohn, J. F., George, C. J., Levenstein, R. M., & Kovacs, M. (2006). Long-term stability of frontal electroencephalographic asymmetry in adults with a history of depression. *Journal of Psychophysiology*, 59, 107 – 115.
- Vuga, M., Fox, N. A., Cohn, J. F., Kovacs, M., & George, C. J. (2008). Long-term stability of electroencephalographic asymmetry and power in 3 to 9 year-old children. *International Journal of Psychophysiology*, 67, 70 – 77.
- Wallace, S., Coleman, M., & Bailey, A. (2008). Face and object processing in autism spectrum disorders. *Autism Research*, 1, 43 – 51.
- Wang, K., Zhang, H., Ma, D., Bucan, M., Glessner, J. T., Abrahams, B. S., ... Hakonarson, H. (2009). Common genetic variants on 5p14.1 associate with autism spectrum disorders. *Nature*, 459, 528 – 533.
- Wass, S. (2011). Distortions and disconnections: Disrupted brain connectivity in autism. *Brain and Cognition*, 75, 18 – 28.
- Wolf, J. M., Tanaka, J. W., Klaiman, C., Cockburn, J., Herlihy, L., Brown, C., ... Schultz, R. T. (2008). Specific impairment of face-processing abilities in children with autism spectrum disorder using the Let's Face It! Skills Battery. *Autism Research*, 1, 329 – 340.
- Wolff, J. J., Gu, H., Gerig, G., Elison, J. T., Styner, M., Gouttard, S., ... Piven, J. (2012). Differences in white matter fiber tract development present from 6 to 24 months in infants with autism. *American Journal of Psychiatry*, 169 (6), 589 – 600.

Zikopoulos, B. & Barbas, H. (2010). Changes in prefrontal axons may disrupt the network in autism. *Journal of Neuroscience*, 30 (44), 14595 – 14609.

Zwaigenbaum, L., Bryson, S., Rogers, T., Roberts, W., Brian, J., & Szatmari, P. (2005). Behavioral manifestations of autism in the first year of life. *International Journal of Neuroscience*, 23, 143 – 152.