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CHANGES IN ELECTROENCEPHALOGRAM COHERENCE IN ADOLESCENTS
WITH AUTISM SPECTRUM DISORDER AFTER
A SOCIAL SKILLS INTERVENTION

by
Angela D. Haendel, BSE, MS, CCC-SLP

A Dissertation submitted to the Faculty of the Graduate School,
Marquette University,
In Partial Fulfillment of the Requirements for
the Degree of Doctor of Philosophy

Milwaukee, Wisconsin

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ABSTRACT
CHANGES IN ELECTROENCEPHALOGRAM COHERENCE IN ADOLESCENTS
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A SOCIAL SKILLS INTERVENTION

Angela D. Haendel, BSE, MS, CCC-SLP

Marquette University, 2018

Autism spectrum disorder (ASD) is a developmental disorder that affects social communication and behavior. There is a consensus that neurological differences present in individuals with ASD. Further, theories emphasize the mixture of hypo- and hyper-connectivity as a neuropathology in ASD (O'Reilly, Lewis, & Elsabbagh, 2017), however, there is a paucity of studies specifically testing neurological underpinnings as predictors of success on social skills interventions. This study examined functional neural connectivity (electroencephalogram, EEG, coherence) of adolescents with ASD before and after the Program for the Education and Enrichment of Relational Skills (PEERS[®]) intervention. Two groups were utilized in this randomized controlled trial (RCT): an Experimental ASD Group (EXP ASD; $n = 74$) and a Waitlist Control ASD Group (WL ASD; $n = 74$). The study had 2 purposes. Aim 1 was to determine whether changes in EEG coherence differed in adolescents with ASD receiving PEERS[®] compared to a waitlist control group of ASD adolescents that did not receive the intervention. Results revealed a statistically significant difference between groups in EEG coherence in the occipital left to temporal left pair; indicating an increase of connectivity between the occipital left and temporal left regions after intervention. Aim 2 was to determine if changes in EEG coherence related to changes in behavior, friendships, and social skills via the *Social Skills Improvement System (SSIS: Gresham, 2009)*, *Social Responsiveness Scale (SRS: Constantino, 2005)*, *Quality of Socialization Questionnaire-Adolescent (QSQ-A: Laugeson, 2010)*, and *Test of Adolescent Social Skills (TASSK: Laugeson, 2010)*. Results indicated a positive change in frontal right to parietal right coherence was linked to an increase in SSIS Social Skills scores at post-test. Positive changes in occipital right to temporal right coherence and occipital left to parietal left coherence were linked to an increase in the total number of get-togethers via the QSQ-A. Results of this study have implications for the importance of assessing response to treatment in ASD using neurobehavioral domains.

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Angela D. Haendel, BSE, MS, CCC-SLP

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Autism spectrum disorder (ASD) is a complex developmental disability with a wide range of severity. Individuals with ASD may have problems with thinking, feeling, language, and the ability to relate to others (American Psychiatric Association, 2013). Socially, people with ASD may have difficulty building age-appropriate friendships, responding appropriately in conversations, and reading nonverbal interactions (American Psychiatric Association, 2013), which can appear more evident during adolescence.

To address social impairments in adolescents with ASD, group-based social skills interventions (GSSIs) are often used (Gates, Kang, & Lerner, 2017) and are linked to improvement in social competence in youth with ASD (Reichnow, Steiner, & Volkmar, 2012). Traditional studies have used more subjective measures, such as parent report, to assess changes in adolescents with ASD. More objective measures of change over time of individuals with ASD are needed, as an atypical trajectory of brain maturation, including differences in neuroanatomy, functioning, and connectivity, mediate ASD symptoms and traits (Ecker, Brookheimer, & Murphy, 2015). Further, examining the brain in vivo, using EEG measures, could lead to the development of more individualized treatment approaches to ASD.

Electroencephalogram was one of the earliest measures used to investigate the neurobiology of autism (Minshew, 1991), and is a non-invasive, flexible tool to assess neural dysfunctions related to ASD (Coben, Mohammad-Rezazadeh, & Cannon, 2014). There are several methods to manipulate raw EEG data to index neural function, one of which is EEG coherence/connectivity. EEG coherence is a measure of how effectively two sites are able to communicate or link to share information, and is often referred to as neural synchronization (Nunez & Srinivasan, 2006).

Minshew and Keller (2010) established that autism, along with its signs and symptoms, is neurologic in nature and has been associated with abnormal neuroanatomy in imaging studies (Waiter, Williams, Murray, Gilchrist, Perrett, & Whiten, 2004). Further, a systematic review of neuroimaging studies revealed brain abnormalities in individuals with ASD (Pua, Bowden, & Seal, 2017). Differences in the neural connectivity of people with ASD has been established (Belmonte, 2004; Coben, Clarke, Hudspeth, & Barry, 2008; Just, 2004), however, there is a paucity of studies that look at brain connectivity before and after specific interventions for people with ASD. This study aimed to examine neural connectivity (EEG, coherence/ synchronization) of adolescents with ASD before and after the Program for the Education and Enrichment of Relational Skills (PEERS[®]) intervention. It compared those findings to a waitlist control group of adolescents with ASD. Although PEERS[®] is linked to decreases in adolescent anxiety and improved friendships (Schohl et al., 2014), and changes in EEG asymmetry patterns (Van Hecke et al., 2013) it is unknown how functional neurological connectivity in ASD is affected by treatment.

First, ASD in adolescence, social skill interventions, resting state EEG, and EEG coherence and connectivity theories will be reviewed. Then, a study which examined the following hypotheses will be presented: 1) does neural connectivity in adolescents with ASD show a significant change after the PEERS[®] intervention as compared to a waitlist ASD control group?; and 2) does the degree of change in EEG coherence link to changes in behavioral outcomes? Understanding the ways in which brain function can change over time, specifically, in response to interventions, will also be crucial for a complete understanding of the condition.

Autism Spectrum Disorder in Adolescents

The symptoms of ASD may change across development, with adolescence being one of the most dramatic transition periods (Anderson et al., 2011). Difficulties with social interactions and engagement are persistent in adolescence and into adulthood (See Schall & McDonough, 2010). Due to a rapid changing social landscape in adolescence, Sigman and Ruskin (1999) suggest that teens with ASD are severely impacted by the core symptoms of autism. Schall and McDonough (2010) go further to discuss that even though most teens with ASD show improvements in basic communication skills, impairments in social communication persist.

A study including a large group of adolescents and adults with ASD found that even though significant improvements of symptoms were noted over time, presence of friendships and presence of limited interests showed the least improvement with age (Seltzer, Krauss, Shattuck, Orsmond, Swe, & Lord, 2003). Further, individuals with ASD show greater risk for comorbid mental illnesses such as depression, anxiety, and ADHD (Park, Raznahan, Shaw, Gogtay, Lerch, & Chakravarty, 2018). About 40% of this population also meet criteria for anxiety disorder (Walsh et al., 2018), 30% for ADHD (Chantiluke et al., 2014) and also around 30% for depression (Buggink, Huisman, Vuijk, Kraaij, & Garnefski, 2016). Friendships have been found to be a protective factor against mental illness (Miller & Ingham, 1976); thus, by helping adolescents with ASD to make and keep friends, their ASD symptoms, as well as their comorbidities, may improve. In the past, ASD in adolescence has been understudied, however, research is now recognizing the importance of intervention at this critical developmental stage (Miller, Vernon, & Russo, 2014).

Adolescence is a time of maturational changes including social, emotional, cognitive, and physical development (Cridland, Caputi, Jones, & Magee, 2013). Along with these developmental changes, there are also transitions from middle school to high school. Making adjustments to these changes can lead to stress, anxiety, and other emotional issues in teens (Myles & Simpson, 1988), with greater impact on those with ASD (Erikson & Goosens, 2011). There is a dramatic change in social functioning during adolescence as social situations become more complex and societal expectations increase (Levesque, 2011). Adolescents may become more aware of their social differences and “fitting in” may have increased importance (Cridland et al., 2013; Blakemore, 2008), thus, this is a crucial time period to implement interventions targeting social skills.

Social Skills Interventions for Adolescents

Group-based social skills interventions (GSSIs) are widely used to address social impairments in adolescents with ASD (Gates, Kang, & Lerner, 2017) and are linked to improvement in social competence in youth with ASD (Reichnow, Steiner, & Volkmar, 2012). An analysis of existing studies of social skills interventions for teens found that the dependent variable in all studies was a measure of social change, with the majority (73%) using parent report questionnaires (Miller et al., 2014). Miller and colleagues (2014) reported that the parent measures that were most frequently used included the Social Skills Improvement System-Rating Scales (*SSIS-RS*: Gresham & Elliot, 2009), formerly known as the Social Skills Rating System (*SSRS*: Gresham & Elliott, 1990), and the Social Responsiveness Scale (*SRS*: Constantino, 2005). In addition, some studies also used adolescent report via questionnaires or direct assessments (Miller et al., 2014).

A strategy used in some GSSIs to promote generalization and maintenance of skills is to include a parent component. Involving parents directly in treatment and informing them about the skills being targeted may put them in a better position to assist their child with carryover outside of the group (Gates, Kang, & Lerner, 2017). Although it is clear that a better understanding of how treatments affect the brain in ASD is needed, it is also important to consider first whether the treatment in question is efficacious at the behavioral level. Treatments that are not efficacious behaviorally may not have as large, consistent, or distributed effect on brain activity or development.

Laugeson et al. (2009, 2012) developed and evaluated the Program for the Education and Enrichment of Relational Skills (PEERS[®]) intervention. PEERS[®] is a manualized, social skills training intervention for youth with social challenges that has a strong evidence-base for use with adolescents and young adults with ASD (Laugeson et al., 2012). The intervention includes both homework and parent components; more specifically, a parent group meets concurrently alongside an adolescent group where the parents are provided with the same skill curriculum as their children. The PEERS[®] intervention is designed and researched specifically for adolescents aged 11-17 years of age (Laugeson et al., 2012). PEERS[®] uses evidence-based practices to teach social skills, including explicit instruction, role-playing, modeling, rehearsal, coaching, and homework assignments. Studies of PEERS[®] have not only found significant changes in social functioning that maintained after treatment, but also generalization, reported by teacher measures, 14 weeks after intervention (Miller, 2014). Further, PEERS[®] has also been linked to decreased adolescent anxiety and improved friendships (Schohl et al., 2014). Although PEERS[®] has been associated with changes in neural activity, via a shift of EEG

power asymmetry after intervention (Van Hecke et al., 2015), it is unknown how functional neurological connectivity in ASD is affected by this treatment.

Neural Correlates of Social Function in ASD

Neural correlates have been considered the underpinnings of the deficits of social communication for decades. Brain areas that have been associated with social communication and interaction are referred to as the “social brain areas,” which include the superior temporal sulcus (STS), middle and superior temporal gyri (Wernicke’s area), anterior cingulate cortex (ACC), fusiform gyrus/fusiform face area (FFA), amygdala, medial pre-frontal cortex (mPFC), and the inferior frontal gyrus (Broca’s area) (Adolphs, 2001; Kim et al., 2015; Blakemore, 2008). The STS is linked with the detection of social cues such as prosody, intention, and trustworthiness; and the mFC moderates the social brain in regards to social integration and approach (Tanimizu et al., 2017). The medial and superior temporal gyri, or auditory association cortex, is responsible for multisensory integration of spoken word recognition (Sokolov et al., 2017). Sokolov et al. (2017) indicated that the ACC plays an important role in the integration of neuronal circuitry as it lies between the emotional limbic system and the cognitive prefrontal cortex. The FFA is associated with facial recognition and links the inferior temporal cortex with the occipital (visual) cortex (Tanimizu et al., 2017). These aforementioned areas are the regions of interest (ROI) that were compared in this study. Processing social information requires attending to and integrating a great deal of information (Williams & Minshew, 2010). Imaging studies involving social attention have shown increased activation in the frontal premotor areas, the posterior parietal cortex, and the occipito-temporal regions (Greene, Mooshagian, Kaplan, Zaidel, & Iacoboni, 2009; Tipper, Handy, Giesbrecht, &

Kingstone, 2008). Further, adolescence is a critical time of significant functional development of the social brain, which can be attributed to changes in hormone levels and changes in social environment (Blakemore, 2008), as supported through evidence from social psychology (Steinberg & Morris, 2001).

Several functional imaging studies have suggested regions of unexpected hypo- or hyper-activity in social brain areas in individuals with ASD (Philip et al., 2012; Verhoeven et al., 2010; Just et al., 2012; Volkmar, 2011). Schultz et al. (2000) found that individuals with ASD had decreased activity in the middle portion of the right FFA, and this has been replicated many times (e.g., Critchley et al., 2000). Large differences have been found between typically developing (TD) and ASD groups, across varying task domains, with activation being greater in the posterior portion of Wernicke's area in those with ASD and greater activation in Broca's area in the TD group (Just et al., 2012). The findings of Just and colleagues (2012) seems to be a general phenomenon of the neural systems of people with ASD and unlikely specific to language tasks, as significant differences in brain activation were found in their compared studies across tasks in the domains of executive functioning, memory, and language, as well as resting state. These differences extend beyond activity and also are apparent via brain structural differences: Courchesne, Webb, and Schumann (2012) found that the frontal areas that mediate social functions are most developmentally abnormal in those with ASD. Even when correcting for brain size, the right amygdala and left hippocampus were found to be significantly larger in adolescents with ASD than a control group of typically developing adolescents, which could result in impaired affective behavior and emotion regulation (Groen, Teluij, Buitelaar, & Tendolkar, 2010). Further, amygdala enlargement has been suggested as a

predictor of the degree of social challenges in ASD; as a significant correlation has been found between amygdala volumes and increased social impairments (Juraneck, Filipek, Berenji, et al., 2006). ASD has been shown to be associated with larger grey matter volume in regions implicated in social cognition, such as: the superior, middle, and inferior gyri of the left frontal lobe, the left superior and middle temporal cortex, as well as the inferior aspects of the right medial frontal cortex (Waiter, Williams, Murray, Gilchrist, Perrett, & Whiten, 2004). Increased grey matter volume in individuals with ASD may be associated with a failure of apoptosis, or the normal pruning of cells (Waiter et al., 2004).

These structural differences between individuals with ASD and typically developing (TD) individuals have been shown across studies, and are different depending on age (Ha et al., 2015). Thus, observing brain function across the lifespan is imperative to relate different functions of the brain to structural differences (Ha, et al., 2015).

Neural Connectivity in ASD

Neural connectivity refers to the integration of spatially separated brain regions. Differences in the neural connectivity of people with ASD have been established (Belmonte, 2004; Coben, Clarke, Hudspeth, & Barry, 2008; Just, 2004). In fact, it has been suggested that “neural organization and connectivity may be a primary dysfunction of the autistic brain” (Coben et al., 2008, p. 1008). Research has focused on theories of connectivity in individuals with ASD, with specific hypotheses that long-range connectivity (brain regions segregated by greater distance both inter- and intra-hemispherically) is underdeveloped, and short-range connectivity (brain regions closer in proximity) is overdeveloped (Just et al., 2012).

A meta-analysis of studies using brain imaging techniques, such as functional Magnetic Resonance Imaging (fMRI) and Diffusion Tensor Imaging (DTI), identified abnormal brain connectivity in individuals with ASD (Hoppenbrouwers, Vandermosten, & Boets, 2014). The findings across 42 DTI studies partially supported the hypothesis that individuals with ASD show lower long-range and greater short-range cortical connectivity when compared to TD, with both the long-range and the local short-range connections showing differences between groups (Hoppenbrouwers, Vandermosten, & Boets, 2014). Wang and colleagues (2013) found that individuals with ASD exhibited a decrease in connectivity at rest between the medial prefrontal cortex and the left angular gyrus. Over-connectivity has been found between Broca's Area and the visual cortex that is mediated by the Precuneus and the Posterior Cingulate Cortex (Müller, 2007).

Results in the literature have found both hypo- and hyper-connectivity in ASD, however, hypo-connectivity has been more heavily represented, particularly for cortico-cortical and interhemispheric connectivity (Ha et al., 2015). The inconsistent and contradictory results can be attributed to researchers overlooking developmental changes in the brain across the lifespan (Hoppenbrouwers, Vandermosten, & Boets, 2014; Ha et al., 2015; Uddin, Supekar, & Menon, 2013). Several studies investigating very young children with ASD report greater structural connectivity, suggesting a developmental switch in white matter connectivity in the ASD brain (Hoppenbrouwers, Vandermosten, & Boets, 2014).

Prior studies have also examined resting state EEG connectivity, or coherence, in individuals with ASD (Murias et al., 2007; Coben et al., 2008; Mathewson et al., 2012). EEG is commonly characterized by breaking down oscillatory patterns into bands of

frequencies. Most typically, clinically relevant frequency bands of EEG range from 0.3 to 100 Hz (Wang et al., 2013), with focus on five frequency bands commonly broken down as follows: delta (0-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-31 Hz), and gamma (greater than 31 Hz). Respective frequency bands have been studied and linked to various cognitive processes (Basar, Basar-Eroglu, Karakas, & Shurmann, 2001) with alpha waves being present in relaxed, awake individuals (Klimesch, Sauseng, & Hanslmayr, 2007). In the middle range (alpha band) frequencies, compared to TD, individuals with ASD have shown reduced relative and absolute power across many brain regions, including the frontal, occipital, parietal, and temporal cortices (Wang et al., 2013; Cantor et al., 1986; Chan et al., 2007; Murias et al., 2007; Dawson et al., 1995).

Unlike evoked-response potential (ERP) studies, which are linked in time with either task performance or sensory stimulation, resting state EEG is used to monitor brain activity in the absence of a task. In most task-based evoked response potential studies, resting state activity is considered background noise, even though multiple studies have suggested that the brain operates intrinsically and involves a great deal of resting-state integration (Heunis, Deng, & De Vries, 2016; Wang, Bartein, Ethridge, Mosconi, Takarae & Sweeny, 2013; Fox & Raichle, 2007; Raichle & Snyder, 2007; Olshausen & Field, 2005). A resting state paradigm was chosen for this study because it allows for use with a wider range of participants in regard to age groups and developmental disability levels than ERPs (Wang et al., 2013). Increased power and coherence in the alpha band has been shown to be predominant in resting state EEG. (Quaedflieg et al., 2016; Gatzke-Kopp, Jetha, & Segalowitz, 2012). Pineda and colleagues (2008) linked changes in EEG

to specific neuro-feedback learning and stated that quantitative analyses of resting state EEG data has promise as an approach for monitoring treatment outcomes.

EEG coherence is a phase correlation of the electrical activity between various sensors on the scalp, thought to reflect functional connectivity and synchronization. Coherence measures evaluate the degree of similarity between two signals (Guevara & Corsi-Cabrera, 1996). Murias and colleagues (2006) found a combination of higher and lower EEG coherences across different regions of the brain in adults with ASD. Individuals with ASD have shown reduced long-range coherence patterns with significantly reduced coherences between the frontal lobe and the temporal, parietal and occipital lobes (Wang et al., 2013). Wang and colleagues (2013) also found that functional connectivity in the frontal lobe at low to mid frequency bands, such as alpha, is more significantly impaired in individuals with ASD. Further, in resting state EEG, individuals with ASD show functional under-connectivity in the anterior-posterior connections (Cherkassy et al., 2006). The most prominent functional disconnections in those with ASD can be observed in the alpha band, especially in the occipital and parietal lobes, both inter- and intra-hemispherically (Ye, Leung, Schafer, Taylor, & Doesburg, 2014).

Summary and Specific Aims

It is imperative that the scientific and clinical community examine neurophysiological measures to gain a better knowledge of brain function of individuals with ASD compared to typically developing individuals. Further, understanding the ways in which brain function can change over time, specifically, in response to interventions, is crucial for a complete understanding of the condition. More objective measures of change

over time of individuals with ASD is needed, which electroencephalogram (EEG) measures can provide.

Following review of the literature regarding connectivity, it is evident that there is a paucity of studies that examine EEG connectivity/coherence before and after specific social skills interventions for adolescents with ASD. Findings of such studies would influence future treatments for individuals with ASD, via demonstrating that effective intervention propagates functional neuronal change. Findings could also lead to expanded research in this area and improve the understanding of neural and behavioral plasticity in ASD.

The current study determined if the implementation of a randomized controlled trial (RCT) of an evidence-based intervention, PEERS[®], for adolescents with ASD, would alter brain connectivity via EEG coherence. This study had two main goals. The primary aim of this study was to examine whether changes in neural connectivity occurred in adolescents who participated in the PEERS[®] relationship-development program, versus a control group of age and gender matched individuals with ASD who did not complete PEERS[®] (randomized controlled trial design). A second aim of the study was to understand whether changes in EEG coherence were related to changes at the behavioral level.

Aim 1.1: Determine differences between the ASD EXP Group and the ASD WL Group at time 1 (pre).

It was hypothesized that no significant differences would be found between groups at pretest on Age, IQ, ADOS Total Score, SRS Total Score, TASSK, SSIS Problem Behaviors, SSIS Social Skills, Income, and Alpha Band Coherence Pairs (LF-

RF, LF-RP, LF-RT, LF-RO, LP-RF, LP-RP, LP-RT, LP-RO, LT-RF, LT-RP, LT-RO, LO-RF, LO-RP, LO-RT, LO-RO, LF-LP, LF-LT, LF-LO, LP-LT, LP-LO, LT-LO, RF-RP, RF-RT, RF-RO, RP-RT, RP-RO, RT-RO, RO-LO).

Aim 1.2: Determine whether changes in EEG coherence existed in adolescents with ASD receiving PEERS[®] compared to a waitlist control group of ASD adolescents.

It was hypothesized that the experimental group that received the 14-week PEERS[®] intervention, versus the waitlist control group, would have significant change in their neural connectivity/coherence in at least one of the measured electrode pairs in the alpha band. Regions of interest (ROI) both intra-hemispherically and inter-hemispherically were examined. Based on the findings reviewed earlier (Wang et al., 2013; Ye et al., 2014), functional connectivity/coherence between averaged electrodes pairings in the following areas were compared: frontal-parietal (F-P), frontal-temporal (F-T), frontal-occipital (F-O), temporal-parietal (T-P), temporal-occipital (T-O), and parietal occipital (P-O) cortices, both intra-hemispherically and inter-hemispherically. Based on the findings of previous studies of over- and under-connectivity, it was predicted that long-range connections would show a positive change in coherence values (higher values) whereas the short-range connections would show a negative change in coherence (lower values).

Results specific to the group that completed intervention would indicate that provision of the PEERS[®] treatment had a unique effect on neural synchronization above and beyond the pattern of development seen over time (if any). It was hypothesized that the waitlist control group would show little to no change in their neural

coherence/connectivity after the 14-week waiting period without intervention across the measured electrode pairs in the alpha band. No findings in the waitlist control group would indicate that time and non-provision of the PEERS[®] treatment did not result in changing neural synchronization over time.

Aim 2: Determine how changes in EEG coherence relate to change in behavior.

It was **hypothesized** that significant changes in EEG coherence in the alpha band would link to improved behavioral outcome measures, via the *Social Skills Improvement System* (SSIS: Gresham, 2009), *Social Responsiveness Scale* (SRS: Constantino, 2005), *Quality of Socialization Questionnaire-Adolescent* (QSQ-A: Laugeson, 2010), and *Test of Adolescent Social Skills* (TASSK: Laugeson, 2010). It was **hypothesized** that changes in the coherence pairs involving the frontal-temporal, frontal-parietal, and frontal-occipital regions would predict changes in behavioral outcome measures. Further, significant changes in EEG coherence would be linked to an increased number of adolescent get-togethers, increased knowledge of social skills, and decreased adolescent problem behaviors.

METHODS

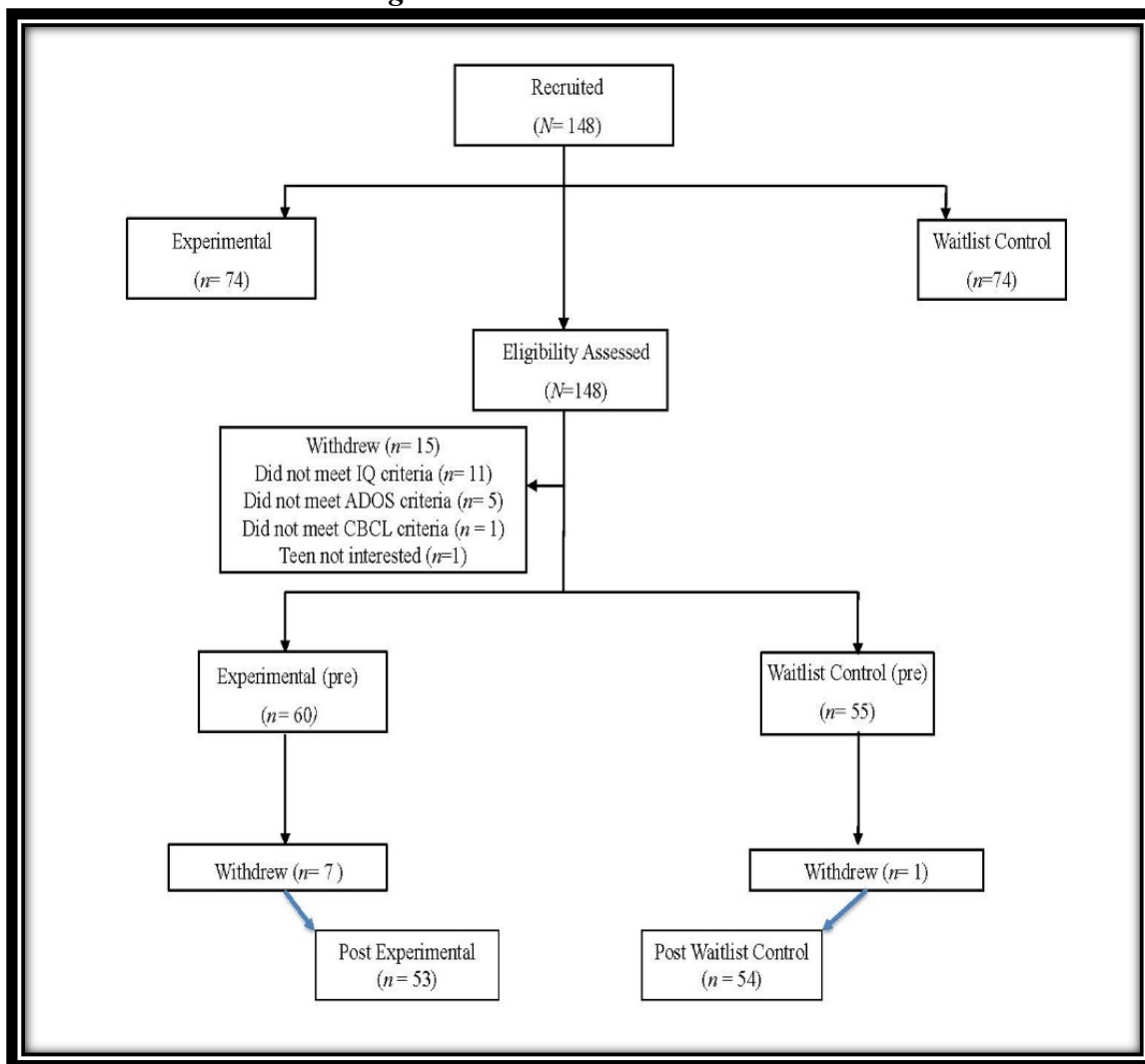
Data collection for this study was reviewed and continuously approved by the Marquette University Internal Review Board (IRB). Data was collected with collaboration with Amy Van Hecke's, PhD, laboratory, which included financial support from the Autism Society of Southeastern Wisconsin (ASSEW) and the Stackner Foundation.

Participants

Recruitment and eligibility. Participants (N=148) were recruited from local intervention agencies, an in-house waiting list for PEERS[®], and ASD support groups and advertisements in the community, which were approved by the Internal Review Board (IRB). This study includes a reanalysis of existing data sets (Schohl, et al., 2014; Van Hecke et al., 2015), augmented with 53 new participants. The participants were randomized into two groups: Experimental Group (EXP; $n=74$) and Wait-List Control Group (WL; $n=74$) See CONSORT Diagram (Figure 1). A graduate research assistant conducted a phone screening with the parent to determine if the teen was likely to meet criteria and if they were interested in the program. The research assistant then set up a 2.5 hour intake meeting if the family passed the screening. Intake criteria included: (a) adolescents with a previous and current diagnosis of Autism Spectrum Disorder (ASD) verified by scores of 7 or higher on Module 3 or 4 of the *Autism Diagnostic Observation Schedule-G* (ADOS-G: Lord et al., 1999); (b) both Verbal and Full Scale Intelligence Quotient (IQ) of 70 or higher on the *Kaufman Brief Intelligence Test Second Edition* (KBIT-2: Kaufman and Kaufman, 2005); (c) subjects were between 11 and 16 years of

age at intake; (d) no history of schizophrenia or bipolar disorder; (e) no history of hearing, physical, or visual impairments that would impede them from participating in PEERS[®]; and (f) express an interest in learning how to make and keep friends.

Figure 1. CONSORT DIAGRAM



For those who met criteria and chose to participate, PEERS[®] was provided at no charge and prizes valued around \$30 were given at graduation. These incentives were

designed to reduce attrition in the study.

Procedures

Events and participant assignment. After intake criteria were met the number of participants with ASD were randomized into two groups: the experimental ASD group, which received PEERS[®] immediately, and the waitlist ASD control group, which received PEERS[®] after completion of 2 research appointments approximately 14 weeks apart. The study controlled for age, gender, handedness, socioeconomic status, and IQ using covariates, as needed. Both ASD groups participated in an EEG session and filled out behavioral outcome measure questionnaires at two time points.

Electroencephalogram (EEG) Session. Data was collected using Electrical Geodesics Incorporated (EGI) Net Station 5 integrated software package for EEG acquisition. Subjects wore a 64 channel Geodesic Sensor Net Cap, appropriately sized for head circumference. Sensor placements were verified according to Electrical Geodesics Inc. technical specifications. Continuous resting EEG was recorded, amplified, and sampled at 1,000 Hz for a total of 3 minutes. During the recording, all impedances were maintained at or below 50 kOhm and a CZ reference was utilized.

Electroencephalograms were performed in an eyes-open, alert, resting state, while the adolescent participant looked at a fixation point (cross) with a black background on a 19-inch computer monitor for 3 minutes. Each participant was seated in a comfortable chair about 3 feet away from the computer monitor. The adolescents were videotaped during their session and monitored for alertness. Each session was also videotaped so the EEG measurements could be cross-referenced with the participant's movements.

Measures

Pre-test cognitive and diagnostic measures. *Kaufman Brief Intelligence Test-Second Edition (KBIT-2; Kaufman & Kaufman, 2005).* Intellectual functioning was assessed using the KBIT-2, which takes approximately 25 minutes to administer. Data is expressed as standard scores with a mean of 100 and a standard deviation of 15. All participants had a Verbal and Full Scale IQ of 70 or above. The KBIT-2 demonstrates good psychometric estimates, including an internal reliability for the IQ composite of 0.93, a test–retest reliability range of 0.88–0.89, and a standard error of measure of 4.3 points (Kaufman & Kaufman, 2005).

Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2001). The ADOS is a structured, interview-based observational assessment conducted with the teen and typically takes 30-45 minutes to administer. It has excellent test-retest reliability (.82) and inter-rater reliability (.92) (Lord et al., 2001). Activities and questions are presented to the teens which are designed to elicit communicative and social behaviors that are typically difficult for individuals with ASD. All participants enrolled in the study obtained a score of 7 or higher on the ADOS-G, which supported the likelihood of an ASD diagnosis.

Behavioral outcome measures. In addition to the pre and post EEG measures, core measures were taken before and after PEERS[®], or a 14-week waiting period, to assess changes in social skills. These behavioral measures included a variety of self and caregiver report surveys; which are listed as follows:

Test of Adolescent Social Skills Knowledge (TASSK; Laugeson & Frankel, 2006).

The TASSK is designed to assess the teen's knowledge about the specific social skills taught in the intervention. The questionnaire has 22-items, which consist of sentence stems and two possible answers (e.g., "the goal of a conversation is to: make the other person like you or find common interests"). Total scores range from 0 to 22, with higher scores corresponding to greater knowledge of the social skills taught in the intervention. Reliability was not calculated for the TASSK due to the lack of subscales and range of topics on this questionnaire.

Social Skills Improvement System-Rating Scales (SSIS-RS) (Gresham & Elliot, 2009). The SSIS consists of standardized, norm-referenced rating scales and is designed for use with children ages 5-18 years old (Standard scores of 100 with SD of 15). The SSIS-RS measures seven domains of social skills functioning: Communication, Cooperation, Assertion, Responsibility, Empathy, Engagement, and Self-Control; and five domains of competing problem behaviors: Externalizing, Bullying, Hyperactivity/Inattention, Internalizing, and Autism Spectrum. Completion time for the SSIS-RS is about 15-20 minutes. The rating scale used is "N" (never), "S" (seldom), "O" for often, and "A" for almost always. Example of questionnaire items that the parent rates their teen on are "takes turns in conversation"; "follows your directions", "has temper tantrums", "tries to make others feel better", etc. The parent form shows high internal consistency (0.94), high test-retest reliability (0.84), and high validity (0.77) (Gresham et al. 2011). In the current study, Cronbach's alpha reliability was computed to be 0.86 for the total rating scale.

Social Responsiveness Scale (SRS) (Constantino, 2005). The SRS measures the severity of autism spectrum symptoms as they occur in natural settings. This 65-item rating scale takes approximately 15 to 20 minutes to complete. It is designed for use with children through adolescents from 4 to 18 years of age. Each item is rated on a scale from “0” (never true) to “3” (almost always true). The SRS includes items that ascertain social awareness (e.g., “Knows when he/she is too close to someone or invading someone’s space”), social information processing (e.g., “Concentrates too much on parts of things rather than ‘seeing the whole picture’ for patterns of behavior”), social anxiety/avoidance (e.g., “Does not join group activities unless told to do so”), and characteristic autistic preoccupations/traits (e.g., “Has repetitive, odd behaviors, such as hand flapping or rocking”). The SRS generates a total scale score that serves as an index of severity of social deficits on the autism spectrum, with higher scores on the SRS indicating greater severity of social impairment (t scores > 60 are in the clinical threshold). The psychometric properties of the SRS have been previously tested in children ages 4–15 years of age, and found to have high test-retest reliability among participants for Total Scale Scores (.88) (Constantino et al., 2000; Constantino & Todd, 2003). In addition, Cronbach’s alpha reliability, computed from data in this study, was 0.81 for the Total Score.

Quality of Socialization Questionnaire (QSQ) (Laugeson, 2010). The QSQ is administered to parents and teens independently and is comprised of 12 items to assess the frequency of get-togethers with peers, number of friends involved, and the level of

conflict during these get-togethers. In this study, only the teens' responses will be used (QSQ-A), as the teen measure has been shown to be more reliable showing significance from pre to post than parent report (Laugeson, Ellingsen, Sanderson, Tucci, & Bates, 2014). Two items ask for an estimate of the number of hosted and invited get-togethers the teen has had over the previous month, and this sum total of invited and hosted get-together will be used in this study. The QSQ-A was developed through factor analysis of 175 boys and girls. The coefficient alpha for the Conflict scale was 0.87 (Laugeson, 2010). Reliability was not calculated for the hosted and invited get-togethers since they are frequency counts, or sum scores if you add them together. The Conflict scale was not used in this study.

No statistically significant differences were found between groups at time 1 (pre) on Age, IQ, ADOS Total Score, SRS, TASSK, SSIS, QSQ-A, or Coherences Inter- and Intra- hemispherically in the Alpha-Band. *See Descriptive Statistics Table (Table 1).*

Table 1. Descriptive Statistics (Pre)

Variable	ASD EXP Group		ASD WL Group	
	Mean	SD	Mean	SD
Age (in years)	13.68	1.33	13.38	1.55
IQ	104.80	19.11	100.35	15.70
ADOS Total Score	10.86	3.32	10.69	3.30
SRS Social Awareness	12.59	3.73	12.81	3.46
SRS Social Cognition	19.07	5.35	18.89	6.08
SRS Social Communication	35.88	8.54	36.33	8.05
SRS Social Motivation	17.91	5.31	17.89	5.49
SRS Autistic Mannerisms	19.08	5.88	20.42	6.00
SRS Total	104.61	24.03	106.35	24.07
TASSK	12.75	2.88	13.12	2.62
SSIS Social Skills	112.31	14.23	110.96	19.33
SSIS Problem Behaviors	66.53	12.62	68.18	16.18
QSQ-A	2.91	7.10	2.81	5.99
Alpha Band Coherence				
Frontal Left-Frontal Right	.204	.200	.236	.219
Frontal Left-Temporal Right	.136	.194	.161	.213
Frontal Left-Parietal Right	.109	.197	.112	.194
Frontal Left-Temporal Left	.348	.168	.403	.188
Frontal Left-Parietal Left	.136	.196	.151	.196
Frontal Right-Temporal Right	.333	.198	.385	.175
Frontal Right-Parietal Right	.116	.207	.121	.182
Frontal Right-Temporal Left	.111	.153	.124	.180
Frontal Right-Parietal Left	.118	.201	.091	.168
Temporal Right-Parietal Right	.497	.165	.539	.167
Temporal Right-Temporal Left	.250	.158	.284	.213
Temporal Right-Parietal Left	.264	.181	.287	.201
Parietal Right-Temporal Left	.296	.188	.326	.197
Parietal Right-Parietal Left	.721	.152	.719	.122
Parietal Left-Temporal Left	.537	.194	.576	.168
Occipital Left-Temporal Left	.720	.180	.759	.147
Occipital Left-Parietal Left	.707	.154	.724	.140
Occipital Left-Frontal Left	.198	.175	.241	.209
Occipital Left-Temporal Right	.372	.174	.402	.202
Occipital Left-Parietal Right	.504	.183	.537	.177
Occipital Right-Frontal Right	.188	.183	.207	.180
Occipital Right-Temporal Right	.748	.100	.756	.108
Occipital Left-Frontal Right	.128	.186	.130	.176
Occipital Right-Temporal Left	.388	.154	.424	.198
Occipital Right-Parietal Left	.457	.177	.490	.161
Occipital Right-Frontal Left	.136	.179	.169	.212
Occipital Right-Parietal Right	.684	.160	.728	.136
Occipital Left-Occipital Right	.622	.144	.654	.156

Note. IQ=KBIT Total Score. ADOS=Autism Diagnostic Observation Scale. SRS=Social Responsiveness Scale. TASSK=Test of Adolescent Social Skills Knowledge. SSIS=Social Skills Improvement System. QSQ=Quality of Socialization Questionnaire. * denotes statistically significant difference between the group means at $p < .05$.

Provision of Intervention

The Program for the Education and Enrichment of Relational Skills (PEERS[®]) intervention was administered to the experimental group subjects over a 14-week period by individuals that held at least a Master's degree in psychology, speech-language pathology, or a related field, who were supervised by a certified PEERS provider. The control group did not receive PEERS[®] during that 14-week period. After the 14-week period, both groups of adolescents returned to the lab and repeated the eyes-open resting state EEG for 3 minutes as well as the social outcome measures. The same protocol was followed for this session as the first session, 14-weeks prior.

Intervention. PEERS[®] is a manualized intervention that is short-term in nature, supported by empirical research, and designed to address the development and maintenance of friendships in adolescents with ASD (see Laugeson et al., 2012). The PEERS[®] intervention consists of 14 weekly, small group sessions lasting 1.5 hours in duration (see *Table 2* for session information). Fidelity of the intervention was maintained throughout by including research assistants in each session. If participants missed a total of three sessions, they were counseled out of the group. A parent group is conducted at the same time in a separate room to support skill practice outside the group. Each week, a didactic lesson was presented and homework was given for the adolescents to practice. The following week, homework was reviewed and a new skill was presented using role plays and rehearsals. The fourteenth and final session of the PEERS[®] intervention consisted of a brief didactic review, a party for the adolescents, and a graduation ceremony.

Table 2. PEERS[®] Treatment Sessions

Session 1	Conversational Skills: Trading Information
Session 2	Conversational Skills: Two-Way Conversations
Session 3	Conversational Skills: Electronic Communication
Session 4	Choosing Appropriate Friends
Session 5	Appropriate Use of Humor
Session 6	Entering a Conversation
Session 7	Exiting a Conversation
Session 8	Get-Togethers
Session 9	Good Sportsmanship
Session 10	Rejection: Teasing and Embarrassing Feedback
Session 11	Rejection: Bullying and Bad Reputations
Session 12	Handling Disagreements
Session 13	Rumors and Gossip
Session 14	Graduation and Termination

Note. This table is adapted from “The PEERS[®] Treatment Manual” by E.A. Laugeson and F. Frankel, 2009, with permission of the author.

Data Preparation/Analysis

Statistical analyses were conducted using the *SPSS* 24.0 General Linear Model (SPSS, Inc., 2016) program and *M-Plus* (Version 6.11, Muthén & Muthén). Averaged electrode pairs were selected based on Homan et al. (1987) electrode placement correlates of cortical locations. Neural locations expected to be important in social information processing were compared. These included looking at the functional connectivity between averaged electrode pairs in the following areas: frontal (F), parietal (P), temporal (T), and occipital (O) cortices both between hemispheres (inter-hemispheric) and within each hemisphere (intra-hemispheric), indicated as right (R) and left (L); giving a total of 28 electrode pairings (LF-RF, LF-RP, LF-RT, LF-RO, LP-RF, LP-RP, LP-RT, LP-RO, LT-RF, LT-RP, LT-RO, LO-RF, LO-RP, LO-RT, LO-RO, LF-LP, LF-LT, LF-LO, LP-LT, LP-LO, LT-LO, RF-RP, RF-RT, RF-RO, RP-RT, RP-RO, RT-RO, RO-LO) .

Recorded EEG data was filtered using NetStation (Electrical Geodesics, Inc.: Eugene, OR) software. The methods of Van Hecke et al. (2015), specifically, MATLAB scripts (2012a, The MathWorks Inc., Natick, MA) using EEGLAB functions (Delorme & Makeig, 2004) were followed for filtering and artifact handling. For EEG coherence, derived as magnitude squared coherence (MSC), Capon's approach was used, which is known as minimum variance distortionless response (MVDR) (Capon, 1969); as used in Benesty et al. (2005) and Dissanayaka et al. (2015); and outlined in Golińska (2011). The coherence function can be summed up by the following formula; where $Coh(f)$ is a coherence function, f is frequency, N is a number of EEG realizations involved in averaging, $F_1(f)$ and $F_2(f)$ are Fourier transforms of EEG signal in two different channels, and * symbol denotes complex conjugation:

$$Coh(f) = \frac{\left| \sum_{i=1}^N F_1(f) \cdot F_2^*(f) \right|^2}{\sum_{i=1}^N |F_1(f)|^2 \cdot \sum_{i=1}^N |F_2(f)|^2}$$

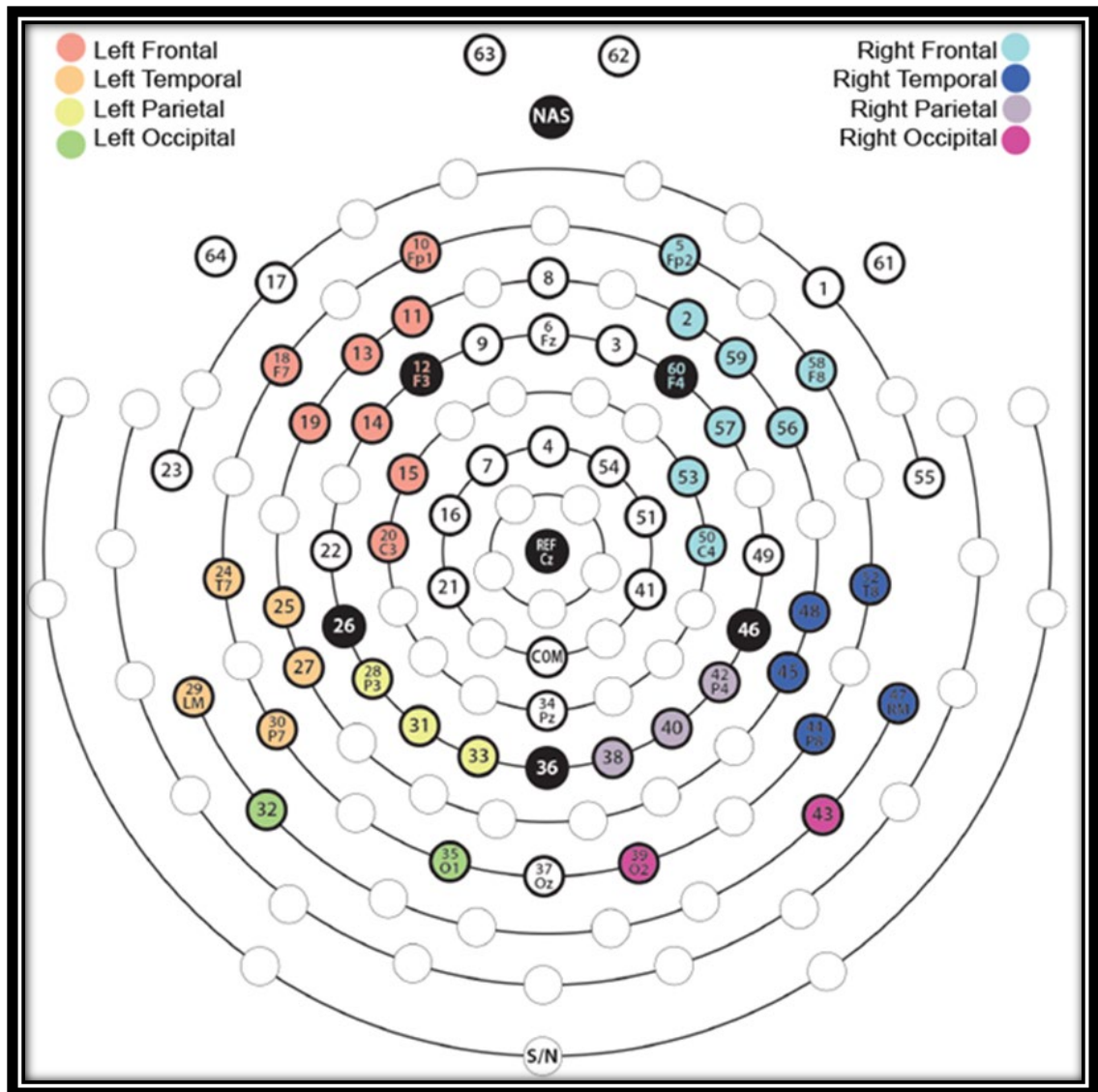
All programs were written in MATLAB using the *Coherence_MVDR* function (MathWorks Inc., Natick, MA). Coherence was calculated by dividing the numerical square of the cross-spectrum by the product of the autospectra, thus, is sensitive to both change in power and phase relationships (Guevara & Cors-Cabrera, 1996). Because squaring the signal is done in the calculation of coherence, all values are between 0-1. The MVDR method is best suitable for the estimation of functional connectivity, or coherence, because it is both data and frequency dependent and allows for higher spectral resolution (Dissanayaka, Ben-Simon, Gruberger, Maron-Katz, Sharon, Hendler, & Cvetkovic, 2015). Coherence function is based on the linear Fourier transform, although

the function itself is not linear (Golińska, 2011). This method was used to estimate the MSC between the selected averaged electrode region pairs within each data band.

As referenced in Van Hecke et al. (2015), Data bands were categorized as follows: Delta (0-4 waves per second), Theta (4-8 waves per second), Alpha (8-12 waves per second), Beta (12-31 waves per second), and Gamma (greater than 31 waves per second). Attention in this study was directed to the alpha band as research suggests that alpha power and coherences are increased during resting state EEGs (Quaedflieg et al., 2016; Wang et al., 2013; Srinivasan, Nunez, & Silberstein, 1998). To reduce the number of statistical comparisons, an average of absolute power indices from several electrodes in a region were used to gather a single value for each region of interest (ROI) in each hemisphere, as done by Coben et al. (2008).

Regions of Interest are: frontal lobe, parietal lobe, temporal lobe, and occipital lobe in both the right and left hemispheres respectively (*see figure 2*). For the left hemisphere: the frontal lobe value is the average power of electrodes 10, 11, 12, 13, 14, 15, 18, 19, and 20 (EGI labels). The Parietal lobe value is the average power of electrodes 28, 31, and 33. The temporal lobe value is the average power of 24, 25, 27, 29, and 30; and the occipital lobe is the average power of 32 and 35. For the right hemisphere: the frontal lobe value is the average power of electrodes 2, 5, 50, 53, 56, 57, 58, 59, and 60. The parietal lobe value is the average power of 38, 40, and 42. The temporal lobe value is the average power of electrodes 44, 45, 47, 48, and 52. Lastly, the occipital lobe is the average power of 39 and 43. All spectral/frequency resolutions were to 0.1 Hz. Coherence values were calculated using the MVDR method, as mentioned above.

Figure 2. Electrode Map of Averaged Regions of Interest



The proposed aims and hypotheses were:

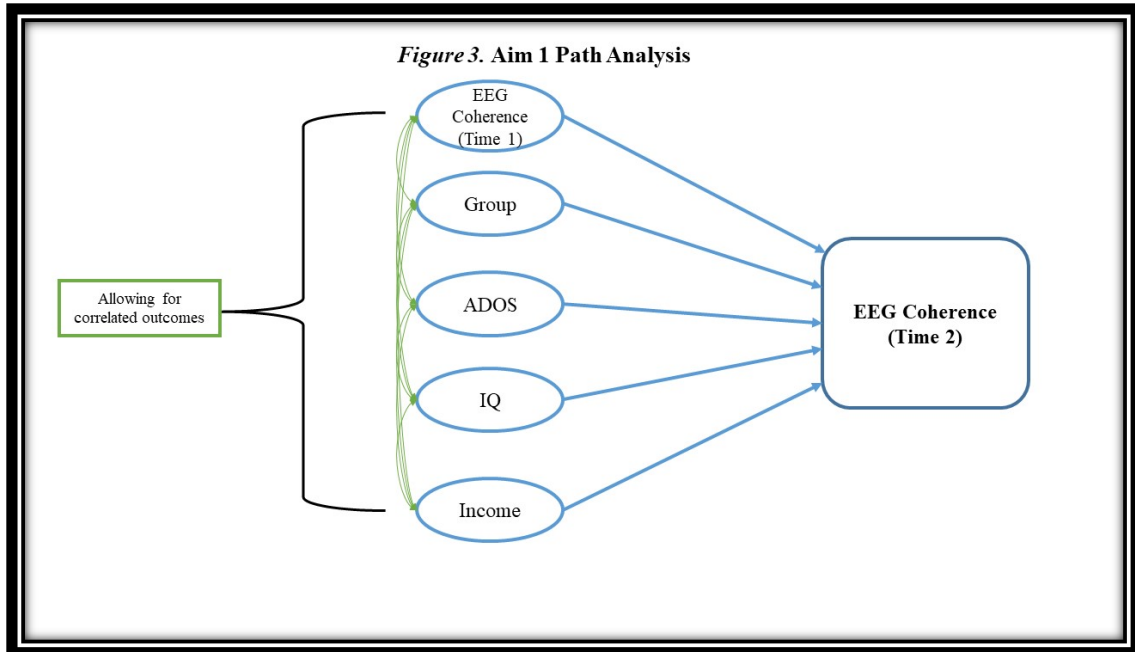
Aim 1.1: To determine differences between the ASD EXP Group and the ASD WL Group at time 1 (pre). It was **hypothesized** that no significant differences would be found between groups at pretest. Analysis consisted of ANOVA, allowing for covariates, in SPSS (IBM Corp., 2016) to indicate if there were any EEG coherence differences at time

one (pre) between groups (Waitlist-Experimental group). The within group factor consisted of averaged electrode coherence pair (LF-RF, LF-RP, LF-RT, LF-RO, LP-RF, LP-RP, LP-RT, LP-RO, LT-RF, LT-RP, LT-RO, LO-RF, LO-RP, LO-RT, LO-RO, LF-LP, LF-LT, LF-LO, LP-LT, LP-LO, LT-LO, RF-RP, RF-RT, RF-RO, RP-RT, RP-RO, RT-RO, RO-LO), and the between group factor was group condition (experimental versus waitlist ASD control).

Aim 1.2: To determine whether changes in EEG coherence existed between groups of adolescents with ASD receiving PEERS[®] compared to a waitlist control group of ASD adolescents. It was **hypothesized** that after receiving the 14-week PEERS[®] intervention, the experimental group, versus the waitlist control group, would have an improvement or positive change in their neural connectivity/coherence in at least one of the measured electrode pairs in the alpha band. Regions of interest (ROI) both intra-hemispherically and inter-hemispherically were examined. Results specific to the group that completed intervention would indicate that provision of the PEERS[®] treatment had a unique effect on neural connectivity above and beyond the pattern of development seen over time (if any). It was hypothesized that the waitlist control group would show little to no change in their neural connectivity after the 14-week waiting period without intervention across the measured averaged electrode pairs in the alpha band. Obtaining no significant findings in the waitlist control group would indicate that time and non-provision of the PEERS[®] treatment did not result in changing neural coherence over time.

Because it allows for correlated outcomes using a path analysis framework, *M-Plus* (Muthén & Muthén, 2007) was used to treat all outcome measures simultaneously while preserving power for Aim 1.2. Post coherence values were used as the outcome

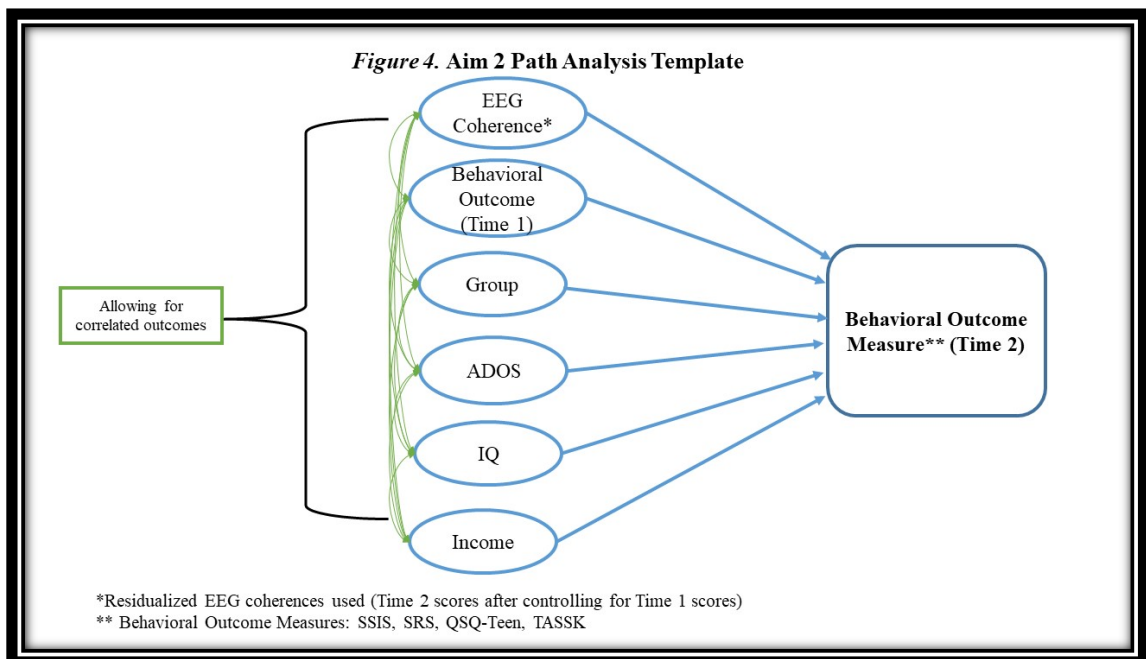
variable, and group was used as the independent variable. Pre coherence values were used as a covariate to determine if post connectivity differed between the two groups (EXP ASD vs. WL ASD), controlling for pre coherence values (*see Figure 3*). Other covariates included in the models were IQ, income, and ADOS total scores, as they were shown to have correlations with EEG coherences in the preliminary analysis of the data. The path analysis approach allows for multiple outcome variables to be considered simultaneously, and it also provides an estimate of the correlation among all of the post coherence values (LF-RF, LF-RP, LF-RT, LF-RO, LP-RF, LP-RP, LP-RT, LP-RO, LT-RF, LT-RP, LT-RO, LO-RF, LO-RP, LO-RT, LO-RO, LF-LP, LF-LT, LF-LO, LP-LT, LP-LO, LT-LO, RF-RP, RF-RT, RF-RO, RP-RT, RP-RO, RT-RO, RO-LO). It was **hypothesized** that after controlling for pre coherence values, the experimental group's post coherence values would be significantly higher (indicating more change) than the waitlist group. More specifically, it was predicted that greater change would be evident between the temporal-occipital regions as well as frontal-frontal regions.



Aim 2: To determine how changes in EEG coherence relate to changes in social behavior. It was **hypothesized** that significant changes in EEG coherence would also predict significant changes in behavioral outcome measures of *Social Skills Improvement System (SSIS: Gresham, 2009)*, *Social Responsiveness Scale (SRS: Constantino, 2005)*, *Quality of Socialization Questionnaire-Adolescent (QSQ-A: Laugeson, 2010)*, and *Test of Adolescent Social Skills (TASSK: Laugeson, 2010)*.

For Aim 2, path analyses, allowing for covariates, using *M-Plus* to allow for correlated outcomes, were used to determine whether a significant change in EEG coherence predicted a significant change in behavioral measures (*see Figure 4*). The model examined if the ROI with significant changes in EEG coherence would also show a significant change in their behavioral outcome scores, controlling for their EEG coherence scores and behavioral outcome scores at time one. Scores for the following coherence pairs were included as predictors: LF-RF, LF-RP, LF-RT, LF-RO, LP-RF, LP-

RP, LP-RT, LP-RO, LT-RF, LT-RP, LT-RO, LO-RF, LO-RP, LO-RT, LO-RO, LF-LP, LF-LT, LF-LO, LP-LT, LP-LO, LT-LO, RF-RP, RF-RT, RF-RO, RP-RT, RP-RO, RT-RO, RO-LO. Behavioral outcome measures at time 2 (*QSQ*, *TASSK*, *SSIS*, *SRS*) were used as the outcome measures, controlling for the behavioral measures at time 1 as a covariate. The other covariates that were used in the models were IQ and ADOS total score, as results from the author's previous study have shown both to be predictors of social skill outcome measures (Haendel et al., 2017). It was hypothesized that a statistically significant change in coherence value would also predict a statistically significant change in behavior outcome scores, while controlling for coherence measures and behavioral outcome measures at time one, in the experimental group, whereas the waitlist control group would show no significant change.



RESULTS

Results of the First Hypothesis of Aim 1: Differences between Groups at Pre-Test

In order to examine the hypothesis of Aim 1.1 - to determine differences between the ASD EXP Group and the ASD WL Group at time 1 (pre) - an analysis of variance (ANOVA) was performed using *SPSS*. Descriptive statistics presented in *Table 1* indicated no significant differences (2-tailed) were found between the two groups at time 1 (pre) in respect to age, race, income, handedness, gender, IQ, ADOS Total Score, SRS, TASSK, SSIS, QSQ-A, and coherences Inter- and Intra- hemispherically in the Alpha-Band (LF-RF, LF-RP, LF-RT, LF-RO, LP-RF, LP-RP, LP-RT, LP-RO, LT-RF, LT-RP, LT-RO, LO-RF, LO-RP, LO-RT, LO-RO, LF-LP, LF-LT, LF-LO, LP-LT, LP-LO, LT-LO, RF-RP, RF-RT, RF-RO, RP-RT, RP-RO, RT-RO, RO-LO). Preliminary analysis did not reveal any correlation of handedness, gender, or race with the outcome measures and were left out of the models (see Table 3 for demographic descriptive statistics). Income, IQ, and ADOS total score showed significant correlations with outcome measures and as such they were deemed as covariates in the models. As stated previously, the final sample sizes included 53 adolescents in the Experimental ASD Group ($n = 53$ ASD EXP) and 54 adolescents in the Waitlist Control ASD Group ($n = 54$ ASD WL); for a total sample size of 107. All variable distributions were examined for skewness, kurtosis, and sphericity when applicable. Based on these analyses, all domains were found to be within normal limits and transformations were not needed.

Table 3. Demographic Descriptive Statistics

	EXP Group	WL Group
Household Income (%)		
Less than 25K	6.7	9.1
25-50K	11.7	12.7
50-75K	26.7	14.5
75-100K	20	9.1
Above 100K	33.3	50.9
Not Reported	1.7	3.6
Race		
% Asian	3.3	3.6
% Hawaiian/islander	1.7	NA
% Black	NA	7.3
% White	88.3	81.8
% Multiracial	1.7	5.5
% Not Reported	5.0	1.8
Gender		
% Male	88.3	81.8
% Female	11.7	18.2
Handedness		
% Right	84.2	15.8
% Left	81.8	16.4

Results of the Second Hypothesis of Aim 1: Changes in EEG Coherence between Groups

For Aim 1.2, path-analyses were performed using *M-Plus* to examine if changes in EEG Coherence differed significantly between groups at time 2 (post). To minimize the number of tests, and to conserve power, data were run in 5 separate models. The models included: Left and Right Intra-hemispheric coherences (LF-LP, LF-LT, LF-LO, LP-LT, LP-LO, LT-LO, RF-RP, RF-RT, RF-RO, RP-RT, RP-RO, RT-RO), Inter-hemispheric Left-Frontal model (LF-RF, LF-RP, LF-RT, LF-RO), Inter-hemispheric Left-Parietal model (LP-RF, LP-RP, LP-RT, LP-RO), Inter-hemispheric Left-Temporal model (LT-RF, LT-RP, LT-RT, LT-RO), and Inter-hemispheric Left-Occipital model (LO-RF, LO-RP, LO-RT, LO-RO). A more stringent *p* value of .01 was used to correct

for multiple tests. Based on results of correlations run in SPSS, IQ, ADOS total score, and Income were used as covariates in all the models. After controlling for EEG coherence values at time 1, Income, IQ, and ADOS total score, statistically significant differences were found between the ASD EXP and the ASD WL groups at time 2 in OL-TL ($\beta = .202$, $SE = .08$, $p < .01$). See Table 3 for Descriptive Statistics at Post. No other significant effects of group were found in the 5 models.

After controlling for ADOS Total score, IQ, and EEG Coherences at time 1, significant effects of Income were found on EEG coherences at time 2 in OR-FR ($\beta = -0.13$, $SE = .04$, $p < .005$), OR-PL ($\beta = -.291$, $SE = .11$, $p < .01$), OR-TL ($\beta = -0.27$, $SE = .08$, $p < .003$), OR-FL ($\beta = -0.14$, $SE = .04$, $p < .001$), and OL-OR ($\beta = -0.30$, $SE = .10$, $p < .005$). After controlling for IQ, EEG Coherences at time 1, and Income; ADOS Total score was a predictor of EEG coherences at time 2 in TR-PR ($\beta = -0.27$, $SE = .10$, $p < .01$), OR-TR ($\beta = -0.25$, $SE = .09$, $p < .009$), OL-TL ($\beta = -0.27$, $SE = .10$, $p < .006$).

Table 4. Descriptive Statistics (Post)

Variable	ASD EXP Group		ASD WL Group	
	Mean	SD	Mean	SD
SRS Social Awareness	10.92	3.93	12.80	3.73
SRS Social Cognition	14.82	5.30	17.98	5.54
SRS Social Communication	27.78	8.20	34.45	8.09
SRS Social Motivation	14.02	5.12	16.67	5.61
SRS Autistic Mannerisms	15.47	5.52	18.86	5.82
SRS Total	83.02	23.78	100.76	23.2
TASSK	21.19	3.51	13.53	2.77
SSIS Social Skills	122.27	14.92	113.85	19.83
SSIS Problem Behaviors	60.41	10.54	66.85	14.61
QSQ	4.76	4.70	2.39	5.10
Alpha Band Coherence				
Frontal Left-Frontal Right	.236	.166	.252	.220
Frontal Left-Temporal Right	.141	.135	.151	.189
Frontal Left-Parietal Right	.079	.127	.101	.179
Frontal Left-Temporal Left	.394	.177	.394	.189
Frontal Left-Parietal Left	.114	.127	.135	.187
Frontal Right-Temporal Right	.358	.191	.349	.205
Frontal Right-Parietal Right	.119	.168	.123	.194
Frontal Right-Temporal Left	.140	.157	.135	.196
Frontal Right-Parietal Left	.099	.164	.114	.190
Temporal Right-Parietal Right	.484	.184	.470	.210
Temporal Right-Temporal Left	.296	.180	.259	.295
Temporal Right-Parietal Left	.247	.193	.262	.190
Parietal Right-Temporal Left	.326	.179	.300	.200
Parietal Right-Parietal Left	.697	.144	.711	.136
Parietal Left-Temporal Left	.555	.145	.562	.172
Occipital Left-Temporal Left	.777	.085	.730	.135
Occipital Left-Parietal Left	.669	.172	.699	.140
Occipital Left-Frontal Left	.224	.142	.212	.196
Occipital Left-Temporal Right	.385	.202	.357	.196
Occipital Left-Parietal Right	.502	.167	.495	.180
Occipital Right-Frontal Right	.203	.170	.197	.202
Occipital Right-Temporal Right	.722	.161	.718	.123
Occipital Left-Frontal Right	.144	.155	.137	.191
Occipital Right-Temporal Left	.434	.183	.397	.222
Occipital Right-Parietal Left	.435	.199	.472	.192
Occipital Right-Frontal Left	.147	.134	.161	.191
Occipital Right-Parietal Right	.688	.162	.689	.160
Occipital Left-Occipital Right	.640	.192	.623	.181

Note. SRS=Social Responsiveness Scale. TASSK=Test of Adolescent Social Skills Knowledge. SSIS=Social Skills Improvement System. QSQ=Quality of Socialization Questionnaire. * denotes statistically significant difference between the group means at $p < .05$

Results of Aim 2: Changes in EEG Coherence related to Social Outcomes

For Aim 2, path analyses (*see Figure 4*) allowing for correlated outcomes and covariates were performed using *M-Plus* to determine whether a significant change in EEG coherence predicted a significant change in behavioral measures (SSIS, SRS, QSQ, TASSK). Coherences at time 2 were regressed onto coherences at time 1 in each model in order to calculate a residualized EEG coherence score for Time 2. Five separate models (as outlined in Aim 1.2) were conducted for each behavioral dependent outcome measure to decrease the number of tests and to maintain continuity between Aims.

Social Skills Improvement System (SSIS)

SSIS Intra-hemispheric Left and Right. After controlling for SSIS scores at time 1, residualized EEG coherences, IQ, ADOS, and Income, statistically significant differences between groups were found at time 2 (post) on the SSIS-Social Skills subtest ($\beta = .185$, $SE = .05$, $p < .001$) and the SSIS-Problem Behaviors subtest ($\beta = -0.178$, $SE = .05$, $p < .001$). The Residualized time 2 score in the Frontal Right-Parietal Right (FR-PR) coherence pair at was significantly related to the Social Skills subtest of the *SSIS* at time 2 ($\beta = .303$, $SE = .10$, $p < .002$).

SSIS Inter-hemispheric. After controlling for SSIS scores at time 1, residualized EEG coherences, IQ, ADOS, and Income, statistically significant differences were found between groups at time 2 on the SSIS Social Skills subscale in all 4 models; LF model (LF-RF, LF-RP, LF-RT, LF-RO) ($\beta = .182$, $SE = .06$, $p < .007$); LP model (LP-RF, LP-RP, LP-RT, LP-RO) ($\beta = .183$, $SE = .06$, $p < .004$); LT model (LT-RF, LT-RP, LT-RT,

LT-RO) ($\beta = .184$, $SE = .06$, $p < .005$); LO model (LO-RF, LO-RP, LO-RT, LO-RO) ($\beta = .182$, $SE = .06$, $p < .006$) as well as with the Problem Behaviors subscale; LF model (LF-RF, LF-RP, LF-RT, LF-RO) ($\beta = -0.179$, $SE = 0.5$, $p < .001$); LP model (LP-RF, LP-RP, LP-RT, LP-RO) ($\beta = -0.183$, $SE = .05$, $p < .001$); LT model (LT-RF, LT-RP, LT-RT, LT-RO) ($\beta = -0.174$, $SE = .05$, $p < .003$); LO model (LO-RF, LO-RP, LO-RT, LO-RO) ($\beta = -0.175$, $SE = .06$, $p < .01$). An effect of income on SSIS Social Skills at time 2 was found in the LT model (LT-RF, LT-RP, LT-RT, LT-RO) after controlling for SSIS scores at time 1, residualized EEG coherences, IQ, and ADOS ($\beta = -0.157$, $SE = .05$, $p < .002$). No significant relationships were found between the SSIS Social Skills or Problem Behavior subtests at time 2 and residualized Inter-hemispheric coherence values.

Social Responsiveness Scale (SRS)

SRS Total Intra-hemispheric Left and Right. An effect of group ($\beta = -0.307$, $SE = .06$, $p < .000$) was found after controlling for IQ, residualized EEG coherences, ADOS total score, income, and SRS total score at time 1, on SRS total score at time 2. No statistically significant effects of residualized intra-hemispheric coherences were found on SRS at time 2.

SRS Total Inter-hemispheric. After controlling for IQ, residualized EEG coherences, ADOS total score, income, and SRS total score at time 1, a significant effect of group was present in every model [LF model (LF-RF, LF-RP, LF-RT, LF-RO) ($\beta = -0.33$, $SE = .06$, $p < .000$); LP model (LP-RF, LP-RP, LP-RT, LP-RO) ($\beta = -0.32$, $SE = .06$, $p < .000$); LT model (LT-RF, LT-RP, LT-RT, LT-RO) ($\beta = -0.31$, $SE = .06$, $p < .000$); LO model (LO-RF, LO-RP, LO-RT, LO-RO) ($\beta = -0.31$, $SE = .06$, $p < .000$)].

.000); LO model (LO-RF, LO-RP, LO-RT, LO-RO) ($\beta = -0.31$, $SE = .06$, $p < .000$)] on SRS total score at time 2. No statistically significant effects of residualized inter-hemispheric coherences were found on the SRS at time 2.

Quality of Socialization Questionnaire-Adolescent (QSQ-A)

QSQ-A Intra-hemispheric Left and Right. After controlling for IQ, ADOS total score, Income, and QSQ at time 1, significant effects of group ($\beta = .357$, $SE = .07$, $p < .000$), OL-PL residualized coherence ($\beta = .318$, $SE = .13$, $p < .002$), and OR-TR residualized coherence ($\beta = .36$, $SE = .10$, $p < .008$) were found on QSQ-A scores at time 2. A significant effect of ADOS total score was found after controlling for group, QSQ at time 1, residualized EEG coherences, IQ, and Income ($\beta = -0.264$, $SE = .08$, $p < .002$) on QSQ-A at time 2.

QSQ-A Inter-hemispheric. Significant effects of group were found across all 4 models [LF model (LF-RF, LF-RP, LF-RT, LF-RO) ($\beta = .255$, $SE = .10$, $p < .01$); LP model (LP-RF, LP-RP, LP-RT, LP-RO) ($\beta = .259$, $SE = .08$, $p < .003$); LT model (LT-RF, LT-RP, LT-RT, LT-RO) ($\beta = .305$, $SE = .07$, $p < .000$); LO model (LO-RF, LO-RP, LO-RT, LO-RO) ($\beta = .285$, $SE = .07$, $p < .000$)] on QSQ-A at Time 2. After controlling for IQ, QSQ-A at time 1, Income, and IQ, ADOS was a found to be a predictor of QSQ-A scores at time 2 in the LP model (LP-RF, LP-RP, LP-RT, LP-RO) ($\beta = .230$, $SE = .06$, $p < .003$); LT model (LT-RF, LT-RP, LT-RT, LT-RO) ($\beta = .305$, $SE = .07$, $p < .000$); and LO model ($\beta = .285$, $SE = .07$, $p < .000$). No statistically significant effects of residualized inter-hemispheric coherences were found on the QSQ-A at time 2.

Test of Adolescent Social Skills (TASSK)

TASSK Intra-hemispheric Right and Left. There was a significant effect of group ($\beta = .758$, $SE = .04$, $p < .000$) on TASSK scores at time 2 when controlling for IQ, ADOS total score, Income, residualized EEG coherences, and TASSK at time 1. When controlling for IQ, Income, TASSK at time 1, and residualized EEG coherences, ADOS total score was a predictor of TASSK scores at time 2 ($\beta = -0.137$, $SE = .05$, $p < .01$). No statistically significant effects of residualized intra-hemispheric coherences were found with the TASSK at time 2.

TASSK Inter-hemispheric. After controlling for IQ, ADOS total score, Income, residualized EEG Coherences, and TASSK at time 1, a significant effect of group was found on TASSK scores at time 2 in all four models; LF model (LF-RF, LF-RP, LF-RT, LF-RO) ($\beta = .776$, $SE = .04$, $p < .00$), LP model (LP-RF, LP-RP, LP-RT, LP-RO) ($\beta = .768$, $SE = .04$, $p < .00$), LT model (LT-RF, LT-RP, LT-RT, LT-RO) ($\beta = .772$, $SE = .05$, $p < .00$), and LO model (LO-RF, LO-RP, LO-RT, LO-RO) ($\beta = .59$, $SE = .12$, $p < .00$). ADOS total score was a predictor TASSK scores at time 2 when controlling for IQ, Income, residualized EEG coherences, and TASSK at time 1 in the LP model ($\beta = -0.130$, $SE = .05$, $p < .01$). When controlling for ADOS total score, Income, residualized EEG coherences, and TASSK at time 1, IQ was found to have a statistically significant effect on TASSK scores at time 2 in the LO model ($\beta = .29$, $SE = .08$, $p < .01$). No statistically significant effects of residualized inter-hemispheric coherences were found with the TASSK at time 2.

DISCUSSION

This study investigated EEG coherences in the alpha band of adolescents with ASD before and after a specific social skills intervention by examining changes between groups, as well as linking EEG coherence changes to changes at the behavioral level. The first hypothesis of Aim 1 predicted no significant differences between the EXP Group and WL Group at time 1 (pretest) on Age, IQ, Income, handedness, ADOS Total Score, SRS Total Score, TASSK, SSIS Social Skills, SSIS Problem Behaviors, QSQ, and Alpha Band Coherence Pairs. The hypothesis of Aim 1.1 was fully supported as the results indicated that there were no significant differences between the two groups at pre-test.

The second hypothesis of Aim 1 predicted that group EEG coherence differences would be found at time 2; more specifically, in regions involving the frontal to temporal, frontal to parietal and the frontal to occipital lobes both within hemispheres and between the hemispheres.

Results of the hypothesis of Aim 1.2 revealed group differences in the occipital left to temporal left coherence (OL-TL) pair. Adolescents in the experimental group that received the PEERS[®] intervention, showed a greater positive change in their EEG coherence at time 2, after taking into account time 1 coherences, than the adolescents in the waitlist control group, which did not receive intervention. These results indicated that changes in the connectivity between the occipital left and temporal left regions were linked to delivery of PEERS[®]. Even though significant differences were not found among all the pairings, this one observed change in coherence in response to PEERS[®] may prove to be clinically significant. These findings provide further support for studies that have

suggested that the decrease of structural connectivity at resting state in the occipital cortex impacts social development (Jung et al., 2017; Di Martino et al., 2014; Libero et al., 2014). Moreover, the social brain areas associated with the connectivity of the OL-TL regions are the Superior Temporal Sulcus (STS), Wernicke's area, and the visual cortex, which are responsible for multisensory integration of information (Spirey, Joanisse, & McRae, 2012; Straube, Wroblewski, Jansen & He, 2018). Wernicke's area, located in the left temporal lobe of most individuals, is implicated in semantic processing of language, speech articulation, and auditory perception (Spirey, Joanisse, & McRae, 2012). The occipital lobe, often referred to as the visual cortex, is linked with visual perception (Duncan 1998). Further, individuals with increased language skills have shown an increase in EEG signals in the occipital regions (Bedney, Pascual-Leone, Dodel-Feder, Fedorenko, & Saxe, 2011). The STS modulates connectivity between areas related to visual gestures, such as eye contact, and audition of speech (Straube, Wroblewski, Jansen, & He, 2018) providing support that the STS is implicated in social perception, via constructs, such as theory of mind and joint attention (Binder, 2015).

Changes in the brain have been previously shown as a response to PEERS[®], more specifically, adolescents displayed a shift of greater activity from the right hemisphere to the left hemisphere after receiving the intervention (Van Hecke et al. 2015). Greater activation in the left hemisphere has been linked to constructs such as happiness and well-being; whereas greater activation in the right hemisphere has been linked with withdrawal, anxiety, and depression (McAdams, 2015; Li, Xu, & Chen 2015). This study offers exciting findings as it goes further to link increases in social relationships not only to changes in the brain, but how connections in the brain can change. Further

investigation is warranted to compare those findings. The hypothesis of Aim 1.2 was partially supported as statistically significant group differences were found in one of the pairings.

Further investigation of the results of Aim 1.2, indicated a negative relationship with ADOS total score and coherences within the same hemisphere, both right and left respectively. Lower ADOS scores, indicative of lower ASD symptom severity, were related to higher coherences within the right hemisphere (temporal right to parietal right and occipital right to temporal right) and left hemisphere (occipital left to temporal left). These results seemingly provide conflicting evidence of previously documented theories that cortical areas closer in proximity are over-connected in the autistic brain (Coben, Mohammed-Rezazadeh, & Cannon, 2014). The findings of this study indicate individuals with greater ASD symptom severity show less connectivity in short-range connections in the “social brain,” involving the temporal to parietal regions in the right hemisphere, as well as the occipital to temporal regions in both the right and left hemispheres. When interpreting these results, it is important to remember both groups in this study consisted of adolescents with ASD. Theories of over- and under-connectivity have compared groups of individuals with ASD to groups of typically developing (TD) individuals. It could be derived from this study that autism severity is a factor that affects connectivity.

Along with ADOS scores, income was found to be a predictor of EEG coherences at time 2 between hemispheres. Adolescents with lower family incomes exhibited greater change in post coherences in long range-connections across the right and left hemispheres involving the occipital right region (occipital right to frontal left; occipital right to parietal left; occipital right to occipital left). This finding could be due to brain

differences related to socio-economic background. Less gray matter in the occipital regions of individuals from lower economic classes have been a robust finding across multiple studies (Mackey et al., 2015; Hanson et al., 2013; Lawson et al., 2013; Jednoróg et al., 2012; Hackman & Farah, 2009). These differences could be attributed to greater deprivation of opportunities and increased family stress, leading to lower pre-coherence scores. PEERS[®] fosters social relationships and increases interaction opportunities, which could be linked to an increase in the connectivity in the occipital lobes across the corpus callosum. Previous studies have also shown occipital cortex abnormalities in individuals with ASD (Jung et al., 2017; Di Martino et al., 2014; Wallace et al., 2013). Findings of this study provide further support of the role of the occipital cortex in the neuropathology of ASD and in children at-risk for poor outcomes due to socioeconomic challenge, but also emphasize the possibility of neuroplasticity and resilience pertaining to these concerns, when evidence-based treatments are provided to this population.

The hypothesized results of Aim 2 were that changes in EEG coherences from pre to post would be linked to changes in behavioral outcome measures from pre to post. This study observed similar robust changes in outcome measures between groups as seen in Van Hecke et al. (2015), Karst et al. (2015), and Schohl et al. (2014). These results are not surprising given some overlap of participants across all studies. Adolescents in the experimental group, that received the PEERS[®] intervention, showed significant changes on all four behavioral outcome measures (SSIS, SRS, QSQ-A, and TASSK), whereas the adolescents in the waitlist control group did not. These findings indicated that changes in social behavioral outcome measures are linked to provision of PEERS[®].

The effect of change in EEG coherences on changes in behavioral outcome scores were evident in within-hemisphere predictions for the SSIS Social Skills outcome measure utilizing the “long-range” frontal right to parietal right (FR-PR) coherence pair. This finding suggests that increases in frontal right to parietal right connectivity is linked to increases in social skills. These findings support studies that have suggested frontal-parietal regions to be responsible for social cognition and socioemotional processing (Schaer, 2013; Ecker et al., 2012; Rojas et al., 2006). Further, results of this study indicated change in EEG coherence predicted change in behavioral outcome measures after the PEERS[®] intervention.

Similarly, the change in EEG coherence in the “short-range” occipital left to parietal left (OL-PL) pair and occipital right to temporal right (OR-TR) pair were found to have significant effects on the QSQ-Adolescent outcome measure at time 2. These results suggest an increase of EEG coherence in the occipital left to parietal left and occipital right to temporal right regions were linked to increases in the total number of adolescent get-togethers. These findings support the research of Jung et al. (2017) and Hubbard et al. (2012), which suggested decreased structural connectivity in the occipital lobe during resting state impacts social development due to the decreased ability to integrate verbal and non-verbal communication cues. Further, results of the current study indicated an increase in short-range connections in the social brain, in individuals with ASD, are related to improved social behaviors. These findings may seem contradictory to the studies supporting the under-connectivity theory, however, “short-range” versus “long-range” connections have not been solidly established in the literature, especially when averaging electrodes within regions.

No statistically significant effects were found in predicting behavioral change via change in long range connections across the two hemispheres. Even though robust group differences were found across all four behavioral outcome measures at time 2 (SSIS, SRS, QSQ-A, and TASSK), the same was not the case for the latter portion of Aim 2, linking behavior change to change in EEG coherence in inter-hemispheric long-range connections.

Further investigation of the results from Aim 2 revealed a relationship of ADOS total score with QSQ-A and TASSK scores at time 2. Higher ADOS scores, indicative of greater symptoms of autism severity, were linked to fewer number of total get-togethers and lower adolescent social skills knowledge. Adolescents that exhibited lesser autism severity symptoms had more get-togethers and had greater social skill knowledge on the TASSK. An effect of IQ was also found on the TASSK scores at time 2 in the coherence pairs involving the left occipital region (LO-RF, LO-RP, LO-RT, LO-RO). Environmental factors, such as socio-demographics, have been related to intelligence (Ripke, 2015) as well as cortical gray matter in the occipital regions (Haier, Jung, Yeo, Head, & Alkire, 2004). As stated previously, less gray matter in the occipital regions have been linked to socioeconomic challenge. Moreover, findings of this study go further to relate IQ to the occipital region. Lower IQ scores were linked to lower adolescent social skills knowledge. The author found similar effects of ADOS and IQ scores predicting social skill outcome measures after the PEERS[®] intervention in preliminary research done with fewer participants (Haendel et al., 2017).

Although the current study offers findings to contribute to the literature regarding neurobiology after a social skills intervention, it does present with limitations. All the

participants used in this study were adolescents with ASD. Having a group of neuro-typical adolescents (TYP) could offer greater possibilities. Comparing EEG coherences at pre and post adding a TYP group could provide a typical trajectory of EEG coherences in adolescents over time. It could also allow for investigation to determine if the EEG coherences of the EXP ASD group are more like the TYP group at post than the EXP WL group. This study recruited a large sample size, but due to the number of coherence pair comparisons, the analyses were split to avoid saturated models. A p value of .01 was still used to determine statistical significance, however, that may have shown to be too conservative given the decrease in findings in the models used.

Exciting preliminary results reflected a change in the connectivity of the adolescent brain after PEERS[®]. Further investigation is warranted to determine if EEG coherence could be a predictor of social outcomes in other intervention programs, and at other ages. Analyzing the data differently and with a wider age range holds great possibility of linking EEG coherence and social competency on behavioral outcome measures. Further, no other studies (to the author's knowledge) have specifically tested neurological underpinnings as predictors of success on social skills interventions, leading to a lack of literature on which to base the findings of this study. Due to the mixed findings and exploratory nature of this study, the author suggests further analyses to determine if a bi-directional effect is occurring as a result of PEERS[®]. Pre-coherence values could determine the effect as well as the direction of the effect the social skills intervention has on the brain.

The results of this study partially supported the hypothesized aims and valuable information about future directions of EEG and social outcome research were gained.

Linking increased social relationships after the PEERS[®] intervention to changes in the connectivity of the brain in adolescents provides an exciting basis for future studies.

Follow up studies are planned to gain insights into the neuroplasticity of the brain areas associated with social functioning and the impact of social skills interventions in individuals with ASD.

In summary, results of this study first indicated that adolescents exhibiting more severe symptoms of ASD showed less coherence in “short-range” EEG pairings in social brain areas. After receiving PEERS[®], those same adolescents exhibited changes in an exemplar “short-range” coherence pair that was linked to changes in their social knowledge and behavior. This study provides objective neural evidence for the initial brain differences and risks in ASD being affected by treatment, indicating support of neuroplasticity. Further, the captivating results of changes in connectivity after intervention could afford the adolescents with more opportunities of social interactions, leading to a more positive trajectory over the course of their lifetime.

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