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Individual Differences in Anterior EEG Asymmetry in Children with High Functioning Autism

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UNIVERSITY OF MIAMI

INDIVIDUAL DIFFERENCES IN ANTERIOR EEG ASYMMETRY IN CHILDREN
WITH HIGH FUNCTIONING AUTISM

By

Anne Pradella Inge

A DISSERTATION

Submitted to the Faculty
of the University of Miami
in partial fulfillment of the requirements for
the degree of Doctor of Philosophy

Coral Gables, Florida

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This study examined the moderating role of motivational tendencies for social approach and avoidance behavior, as measured by anterior EEG asymmetry, on symptom expression. In particular, this study aimed to replicate and extend previous findings that measures of anterior EEG asymmetry provide an important marker of subgroups of HFA children that significantly differ from each other, and controls, on measures of social communication impairment. EEG data were collected across two occasions on 51 HFA and 44 non-HFA children. EEG asymmetry was computed for homologous electrode pairs (e.g., lnF4-lnF3). More positive scores were indicative of relative left frontal asymmetry. Data on social and behavioral functioning were collected via parent- and self-report. Results of this short-term longitudinal study revealed moderate test-retest reliability for midfrontal asymmetry, $r(65) = .39, p < .01$. Results supported previous research demonstrating the differential relation of EEG asymmetry to symptom impairment among HFA children, such that parents of LFA-HFA children reported lower levels of impairment than RFA-HFA children on the SCQ Total Score, $F(3, 47) = 3.58, p = .065$, and Social Interaction Domain, $F(3, 47) = 4.59, p < .05$. Results also indicated that parents of LFA-HFA children reported higher levels of general communicative competence on the CCC-2, GCC, $F(3, 47) = 6.83, p = .01$, but greater impairment in pragmatic communication when compared to RFA-HFA children, SIDC, $F(3, 47) =$

4.41, $p < .05$. Additional analyses indicated that RFA was associated with early and more confident recognition of atypical (and stereotypically autistic) development based on retrospective parent-report (ADI-R #86), while LFA was associated with early, but less unambiguously autistic impairment, $X^2(51) = 3.75, p = .05$. This study demonstrates that anterior EEG asymmetry subgroups are reliable and useful markers of phenotypic variability that are meaningfully related to the experience and expression of symptoms of core autism impairment.

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CHAPTER 1: INTRODUCTION

The study of individual differences is integral to formulating a comprehensive understanding of clinical phenomenon (Underwood, 1975; Kosslyn et al., 2002). In particular, individual differences analysis is critical to an understanding of the pathophysiology of a disorder, including the multiple pathways to onset as well as individual differences in trajectory, outcomes, and treatment responsiveness. Thus data on individual differences in the expression of any form of pathology is essential to designing informed and individually-tailored treatment and intervention programs, as well as to identifying clinical subgroups or subtypes within a disorder (Wing & Gould, 1979; Dawson, Klinger, Panagiotides, Lewy, & Castelloe, 1995; Sutton et al., 2005; Burnette, 2005).

In research on Autism Spectrum Disorders (ASD), studies have begun to highlight the importance of observations of individual differences in social motivational tendencies. For example, within the intervention literature some researchers have suggested that a core area of impairment and focus for treatment in autism involves difficulties with spontaneous initiation of behaviors, which may implicate underlying motivational issues (Koegel, Carter, & Koegel, 2003). Indeed, a recent study examined the predictors of treatment responsiveness in young children with autism and observed that responders versus non-responders could be categorized, in part, based on distinct differences in social approach and avoidance behaviors in social/play situations (Sherer & Schreibman, 2005). This study suggests that information on individual differences within the social-motivational, approach-avoidance continuum may facilitate clinical decisions regarding the appropriateness of one form of intervention (e.g. Pivotal

Response Training, PRT) versus another (e.g., Discrete Trial Training, DTT) in work with children with autism (Sherer & Schreibman, 2005). Moreover, it suggests that motivational systems associated with approach and avoidance behaviors may be important to consider in research on autism.

Research on individual differences within the social motivation continuum is also supported by the Wing and Gould (1979) categorization of subgroups within ASDs based on variability in autistic children's behavioral profiles in social/play situations (i.e., "Active-but-odd; Passive; and Aloof" phenotypes). The repeated independent observations of variability within the social-motivational domain attest to the reliability and validity of this active-alooof/social-behavioral typology among children with autism (Borden & Ollendick, 1994; Dawson et al., 1995; Volkmar, Cohen, Bregman, Hooks, & Stevenson, 1989). Yet, few conceptual explanations of the meaning of these prominent behavioral differences among children with autism have been provided. A potentially useful viewpoint here is to think about the Wing and Gould categories in terms of motivational tendencies for action and approach behaviors (i.e., "Active-but-odd" children) versus inhibition and avoidance behaviors (i.e., "Passive to Aloof" children).

One way to look at differences in these axes of motivation is to employ research methods and theory related to the Behavioral Activation System (BAS) and the Behavioral Inhibition System (BIS). These fundamental dimensions of human behavior predispose an individual to engage in approach or withdrawal behaviors and are thought to underlie the global constructs of temperament and personality (Gray, 1972, 1994). The notion that differences in BIS/BAS related motivation might be expected to influence

social-emotional development in autism has been long suspected (Mundy, 1995) and has recently received empirical support (Burnette, 2005; Sutton et al., 2005).

Psychophysiological measures, and specifically EEG asymmetry, are one tool that has been used in research to measure these behavioral motivational systems (BIS/BAS). In its applications to the constructs of human behavior and personality, a relative increase in left frontal EEG asymmetry is associated with approach behavior and a relative increase in right frontal asymmetry is associated with withdrawal behaviors. In line with the BIS/BAS relation to psychopathology, specific patterns of EEG asymmetry also relate to individuals who are either at risk or diagnosed with psychopathology. In particular, studies have shown individuals with symptoms of depression and, in some cases anxiety, display right frontal asymmetry patterns (Schaffer, Davidson, & Saron, 1983; Henriques & Davidson, 1990; Sutton & Davidson, 1997; Schmidt, 1999). In this way, EEG asymmetry can be used as an index of an individual's predispositions on the BIS/BAS motivational continuums.

While the relation of a relative increase in right frontal asymmetry and psychopathology is well documented, there are also many instances of inconsistencies or contradictions in the literature (Baving, Laucht, & Schmidt, 2002; Sutton et al., 2005; Burnette, 2005). Further, there are competing theories in the literature with respect to the pattern of relations between anxiety symptoms and anterior and posterior asymmetry (Heller, Nitschke, Etienne, & Miller, 1997; Heller & Nitschke, 1998). In addition, age has been identified as a potential factor that can moderate the relation between asymmetry and symptoms of psychopathology (i.e., anxiety and depression) (Forbes, Fox, Cohn, Galles, & Kovacs, 2006; Pradella, 2006).

These inconsistencies apparent in the literature on EEG asymmetry and its relations to psychopathology and social-emotional status elucidate the very complex nature of the measure itself and its application to the study of development in children and adults. Nonetheless, psychophysiological investigation of motivational tendencies and/or temperament and personality factors remains a robust and unique method to examine temperament and personality traits by circumventing subjective report. As research continues to move forward and we learn more about the nature of the measure, sophisticated study design and methodological rigor are becoming the prerequisite to reliable assessment and valid interpretation of the results.

In this spirit, this study investigated the differential relation of EEG asymmetry to motivational bias and social-emotional status within a population of children and adolescents with high functioning autism (HFA). Past research in this area has shown a significant association between HFA children with left frontal asymmetry and self-reported anxiety (Sutton et al., 2005). This seemingly contradictory relation was observed in two independent studies (Sutton et al., 2005; Burnette, 2005). Interpretations of this finding support a motivational model of EEG asymmetry such that individuals with left frontal asymmetry are predisposed to motivational approach biases. In the context of the social communication impairments associated with autism, this motivational bias (as indexed by left frontal asymmetry) is thought to modify the expression of the disorder in such a way that leads to increased anxiety among these children and adolescents. The hypothesized interpretation is that the overlay of the impairments associated with autism on the individual's predisposed motivational bias to approach results in the experience of comorbid symptoms of anxiety (Mundy, Henderson, Inge, & Coman, 2007).

In an effort to continue to examine the findings of the relation of EEG asymmetry to comorbid psychopathology and motivational bias in populations of HFA children, this study aimed to replicate and extend the previously mentioned findings. Unique to this examination of EEG asymmetry in a population of HFA children and adolescents was the short-term longitudinal study design, allowing for two occasions of psychophysiological measurement. In this way, reliability of the measure itself could be examined, ultimately aiding in the valid interpretation of the results. Additionally, this study elaborated on previous self- and parent-reported findings of social impairment and comorbid social-emotional symptoms by including in vivo assessment of social interaction via the Autism Diagnostic Observational Schedule (ADOS) (Lord et al., 2000). In addition to the qualitative evaluation of social communication impairment, a quantitative approach to examining social approach/avoidance behaviors was also used.

In the sections that follow, a more complete discussion of the importance of the examination of individual differences within the diagnosis of high functioning autism will be provided. Specifically, the role of motivation as both an underlying deficit and pivotal area for intervention will be discussed (Mundy, 1995; Koegel, Koegel, & McNeerney, 2001). Specific applications to research in differential response to intervention in young children with autism will be reviewed (Schreibman, 2000; Ingersoll, Schreibman, & Stahmer, 2001; Sherer & Schreibman, 2005). In addition, research and theory on the Behavioral Activation and Inhibition Systems (BAS/BIS) will be provided along with its hypothesized role in social-emotional development and its application to psychophysiological research and specifically, EEG asymmetry (Gray, 1972, 1994; Mundy, 1995; Coan & Allen, 2003a). Next, the literature on the nature of

EEG asymmetry will be reviewed as well as its relation to adult and child psychopathology. Inconsistencies in the literature will be discussed. Finally, the application of EEG asymmetry in populations of HFA children and adolescents will be examined.

The Study of Motivation in Autism

Research on the phenomenology of Autism Spectrum Disorders (ASDs) indicates that variability is a characteristic of the phenotype. Beginning with the observations of Leo Kanner and Hans Asperger in the early twentieth century of children presenting with social communication impairments, the study of individual differences has shown that children within the same broad classification present with different competencies and deficits in the social communication domain. In an effort to capture the qualitative variance in clinical features of children with autism, Wing and Gould (1979) famously categorized children with ASDs into subgroups based on their behavioral profiles in social/play situations (i.e., Active-but-odd; Passive; and Aloof). In considering the etiology of these individual differences in social functioning, child characteristics and specifically, social motivational tendencies, have been identified as one theoretical axis along which children may differ (Mundy, 1995). Variability within the domain of social functioning is meaningful for course, outcome, and treatment responsiveness (Sigman & Ruskin, 1999; Charman et al., 2005; Mundy et al., 2007). In this light, it may be that a better understanding of individual differences is critical to identifying diagnostic subgroups within the spectrum of autistic disorders (Wing & Gould, 1979; Dawson et al., 1995; Sutton et al., 2005; Burnette, 2005).

Just as research on the phenomenology of ASDs highlights the variability in clinical presentation within the diagnoses, intervention research calls attention to the wide variability in response to treatment among individuals with autism. In considering differential response to treatment, a variety of factors come into consideration including child characteristics such as temperament and motivational bias. Koegel et al. (2001) have done extensive work in the area of intervention research examining what they identify as the *core pivotal areas* that appear to be most influential in interventions for autism. In doing this, they discuss the flawed strategies of traditional behavioral interventions (e.g., Discrete Trial Training) that target problem behaviors (one at a time) by providing external punishers and reinforcers in an isolated and highly structured environment.

Discrete trial interventions have proven to be successful in improving language, social, play, and academic skills, as well as decreasing problem behaviors; however, their generalizability and ecological validity are low (Lovaas, Koegel, Simmons, & Long, 1973). The Koegel's and their colleagues posit that the implementation of these techniques, using excessively restricted stimulus control, may have contributed to the failure to generalize skills experienced by many children receiving the intervention (Koegel et al., 2001; Rosenblatt, Bloom, & Koegel, 1995). In an effort to address the inherent inefficiency of targeting individual behaviors one at a time, researchers began to consider the utility of targeting certain core areas of the disorder, which if effectively treated could have widespread effects across non-targeted behaviors (Lovaas, 1977; Koegel, Camarata, & Koegel, 1994). These studies suggested that autism may involve primary and secondary factors, such that intervention for the primary (core) behavior

produced subsequent changes in proxy behaviors (e.g., ameliorate behavioral problems after treating early communication deficits), (Koegel et al., 2001; Newman, Tuntigian, Ryan, & Reinecke, 1997).

Research on *core pivotal areas* for intervention with children with autism identifies motivation and specifically, motivation to respond to social and environmental stimuli as a key pivotal area (Koegel et al., 2001). In targeting motivation, the intention is to increase children's ability to self-initiate and thereby increase their adaptive social, linguistic, and academic interactions. In doing this, the end result is increased child-initiated stimulus input and therefore, increased opportunities for learning (Koegel et al., 2001). This line of research has shown that motivation-targeted intervention has positive impacts across a variety of domains including behavioral, academic, language, and social (Koegel & Egel, 1979; Koegel, O'Dell, & Dunlap, 1988; Koegel, Carter, & Koegel, 1998; Koegel & Koegel, 1995). This type of intervention includes incorporating child choice, task variation and the interspersal of maintenance or previously mastered tasks. It also uses reinforcement of response attempts, not just reinforcement of responses that are "as good" or better than previous responses reinforced, and the use of natural and direct reinforcers.

Research on joint attention impairments in autism has also highlighted motivation, and specifically social-emotional motivation, as a core deficit in children with this syndrome. Mundy (1995) makes the distinction between nonverbal requesting skills, which are used relatively frequently by individuals with autism, and joint attention skills, which are used relatively infrequently by individuals with autism, in order to discuss the specific impairment in social-emotional motivation observed in children with

autism. Joint attention acts are distinguished from nonverbal requesting acts in their communicative function - joint attention acts involve the use of eye contact and gestures to show objects to others or share the experience of an event with others, while nonverbal requesting acts involve the use of eye contact and similar gestures with a social partner to request aid in obtaining an object or event (Mundy, 1995). Further, research has shown that the initiation of nonverbal joint attention acts involves the expression of positive affect to a greater degree than do nonverbal requesting acts (Kasari, Sigman, Mundy, & Yirmiya, 1990; Mundy, Kasari, & Sigman, 1992). This dissociation in the development of nonverbal communication skills observed in children with autism likely reflects a specific deficit in social-emotional behavioral motivation in these children (Mundy, 1995).

Motivational Bias and Intervention Response

Given that motivation, and specifically social motivation or motivation to initiate, has been identified in both the theoretical literature (Mundy, 1995) and the intervention literature (Koegel et al., 2001) as a core impairment in autism, researchers are beginning to examine the impact of child characteristics (i.e., motivational bias) on treatment responsiveness. One such study examined the behavioral profiles of children with autism in order to determine if pretreatment child characteristics could predict response to a child-directed intervention (Pivotal Response Training) (Sherer & Schreibman, 2005). Behavior profiles for responders vs. nonresponders were identified based on the following behaviors observed during a pretreatment structured lab assessment: toy play, approach and avoidance behavior, and verbal and nonverbal stimulation behaviors. Here,

approach behaviors were operationalized as physical movement towards the adult (i.e., including reaching to the adult), spontaneous looking at the adult's face, and approaching to take a toy. Avoidance behaviors were operationalized as physical movement away from the adult (i.e., including instances where the child pulled part of his/her body away from the adult's touch, resisted looking at the adult's face when the adult initiated a look, crawled under a table, and covered his/her ears or eyes in response to the adult speaking). Results of this study demonstrated that treatment responsiveness in young children with autism could be, in part, categorized based on distinct differences in social approach and avoidance behaviors in social/play situations (Sherer & Schreibman, 2005). This study highlights both the variability within the clinical presentation of children with autism on specific dimensions of social approach and avoidance, as well as the opportunity for child-matched (individually-tailored) treatment.

Further support for the observation of varying social-motivational behavioral profiles among children with autism and its implications for treatment responsiveness and treatment tailoring includes research from naturalistic, child-directed interventions. Koegel, Koegel, Harrower, & Carter (1999) examined the social-motivation profiles of children previously identified as having favorable outcomes (i.e., presence of functional speech before 5 years of age) before intervention. Interestingly, although all the children had the same prognosis, there was great variability in outcome after years of intensive intervention. Review of preintervention data indicated that the children who showed more favorable outcomes in response to the intervention exhibited more spontaneous self-initiations at preintervention. These results demonstrate that the presence of social approach motivation (i.e., evidenced by self-initiation behaviors pretreatment) predicted

treatment responsiveness among children with equivalent prognosis based on language measures.

Another study examined the behavior profiles of children with autism in an effort to identify the child characteristics that may affect the outcome of a particular treatment mode (i.e., an inclusion classroom) (Ingersoll et al., 2001). Inclusion classroom settings are highly regarded for the potential for social learning inherent in the model. In these classrooms children with autism are integrated with typically developing children who serve as intervention agents by modeling age-appropriate behaviors as well as providing opportunities for autistic children to practice appropriate social, play, and language skills. Results from this study indicated that there was significant variability in outcome among children with ASD, which could not be attributed to mental age equivalent or language level. Instead, peer social avoidance appeared to predict outcome for later peer social avoidance and language use (Ingersoll et al., 2001). Specifically, children with high peer social avoidance preintervention remained high at six month follow-up, while children with low peer social avoidance preintervention demonstrated a considerable decrease in this behavior after intervention. The authors concluded that peer social avoidance (a withdrawal-oriented behavior) may be a persisting (or trait-like) behavior in some children with autism that is not substantially reduced simply by access or proximity to peers (Ingersoll et al., 2001).

Research on individual differences within the social communication domain brings to bear the important observation that individual differences in social functioning exist (despite the pervasive social deficits in autism) and are meaningful for outcome, such that better social abilities (hypothesized to be mediated in part by social

motivational predispositions) are associated with better outcomes (Mundy, 1995; Sigman & Ruskin, 1999). This research highlights the importance of information on individual differences within the social-motivational continuum for making clinical decisions regarding the appropriateness of one intervention versus another (Sherer & Schreibman, 2005), as well as directing educators and administrators to the most appropriate learning environment for children with autism (i.e., inclusion classroom setting) (Ingersoll et al., 2001). Moreover, it suggests that motivational systems associated with approach and avoidance behaviors are important to consider in research on autism.

Behavioral Activation and Behavioral Inhibition Systems

Gray (1972, 1994) has suggested the existence of two hypothetical systems that underlie affect and personality, the Behavioral Inhibition System or BIS and Behavioral Activation System or BAS. In Gray's model, the BIS inhibits action and directs behavior towards removing or avoiding an undesirable stimulus, while the BAS responds to incentives and guides organisms toward attaining a desirable stimulus (Gray, 1972, 1994). These systems promote the organization of resources and execution of behaviors to either attain a desirable stimulus, or remove an undesirable stimulus (Sutton & Davidson, 1997; Coan & Allen, 2003a).

Gray's BIS/BAS constructs are frequently applied in psychophysiological research, and specifically EEG asymmetry. Here, the BIS/BAS constructs map on to the approach/withdrawal model of brain laterality, which states that each anterior hemisphere subserves a specific motivational brain system. Within this framework, the left anterior hemisphere is hypothesized to be specialized for approach behavior and therefore is

associated with BAS related functioning, while the right anterior hemisphere is hypothesized to be specialized for withdrawal behavior and therefore is associated with BIS related functioning (Davidson, 1984, 1992; Davidson & Tomarken, 1989). More detailed analysis of the relation of EEG asymmetry to Gray's motivational systems will be discussed in later sections.

The neurophysiological basis of the BAS and BIS systems is currently being examined in the literature. Recent work using source localization techniques in conjunction with EEG asymmetry measures during an approach/reward-oriented task has provided some support for the anatomical structures underlying the BAS system (Pizzagalli, Sherwood, Henriques, & Davidson, 2005). According to this research group, EEG asymmetry associated with reward-related behavior reflects differences in the activation patterns of the dorsolateral prefrontal cortex (DLPFC) and the orbital frontal cortex (OFC). They hypothesized that the former is involved in maintaining goal representations and in anticipating future rewards or loss relative to goal related behavior, while the latter is involved in the evaluation of the reward value of stimuli and in the learning of stimulus incentive associations (Pizzagalli et al., 2005). The identification of structures in the prefrontal cortex in the BAS system may have implications for assessing BAS related activity in children and adolescents where the prefrontal cortex has not matured (Pradella, 2006). Additional areas implicated in the BAS system involve catecholaminergic and especially dopaminergic, pathways (Stellar & Stellar, 1985).

There is some consensus regarding hypotheses about the neurophysiological basis of the BIS, although relatively few source localization studies exist. Theoretically, the research supports Gray's original hypothesis that the behavioral motivation systems

involve subcortical structures (i.e., including the amygdala) (Gray, 1981). Specifically, the BIS is thought to consist of the septohippocampal system, its monoaminergic afferents from the brainstem, and its neocortical projection in the frontal lobe (Carver & White, 1994). Because the BAS and the BIS represent distinct structures in the nervous system (being separable both pharmacologically and by brain lesions), their propensities or sensitivities are thought to be orthogonal (Quay, 1993). In this way, it follows that all human subjects should have the capacity for a combination of high and low BIS and BAS sensitivity resulting from the independent operation of the two systems (Carver & White, 1994).

The physiological mechanisms by which the structures implicated in the BIS and the BAS operate are not fully understood; however, Gray and others have argued that the BIS and the BAS function to regulate aversive and appetitive motivations (Carver & White, 1994; Coan & Allen, 2003b). The BIS refers to the aversive motivational system and its physiological mechanism is thought to control the experience of anxiety in response to anxiety-relevant cues (Gray, 1972, 1981, 1994). In this way, the BIS is responsive to signals of punishment, nonreward, and novelty. Activation of the BIS causes inhibition of movement towards goals inhibiting behavior that may lead to negative or painful outcomes. Gray has suggested that BIS functioning is responsible for the experience of negative feelings such as fear, anxiety, frustration, and sadness in response to these cues. With respect to individual differences in personality, greater BIS sensitivity should be reflected in greater proneness to anxiety when exposed to anxiety-related cues (Carver & White, 1994).

The BAS refers to the appetitive motivational system and its physiological mechanism is thought to regulate the experience of positive feelings such as hope, elation, and happiness (Gray, 1972, 1981, 1994). This system is thought to be responsive to signals of reward or reward-related stimuli, as well as signals related to nonpunishment and escape from punishment. Specifically, this system functions to initiate or direct movement towards goals and/or pleasurable experiences (Carver & White, 1994). In addition, the BAS is conceptualized as an approach-oriented system and in this way, the negatively valenced experience of anger (an approach-related emotion) is also subsumed under the BAS system (Harmon-Jones, 2004). With respect to individual differences in personality, greater BAS sensitivity should be reflected in greater propensities to engage in goal-directed activities and to experience positive feelings when exposed to cues of an anticipated reward.

Applications of the Behavioral Activation and Inhibition Systems to Social-Emotional Development

Research and theory has suggested at least two ways that variability in BIS/BAS related motivational tendencies might be expected to influence social-emotional development in autism. The first hypothesizes that individual differences on the behavioral-motivational dimensions, such as a predisposition to experience extreme approach motivation/behavior or extreme avoidance motivation/behavior, interacts with the processes of social development in children with autism such as those involved in the acquisition of joint attention skills (Mundy, 1995). Research in this area hypothesizes that the neurological system that underlies the BIS/BAS constructs is compromised in children with autism resulting in an attenuation of the tendency to initiate affectively

positive social approach behaviors associated with initiation of joint attention (Mundy, 1995). Variability in this tendency for social approach in as much as it underlies the development of initiation of joint attention is associated with variability in developmental trajectories, where a bias towards social approach behavior is associated with a more promising developmental trajectory (i.e., acquisition of language and increased language functioning, decreased behavior problems, increased cognitive functioning, and increased social functioning) (Mundy, 1995; Koegel et al., 2001).

The hypothesized benefit of a predisposition for social approach involves the quality of stimulus input generated by and elicited by children. Specifically, it has been hypothesized that social- versus object-approach behaviors yield opportunities for different types of experiences and information that interact with the developing cognitive system of the young child (Loveland, 1991; Fischer & Bidell, 1991). This interaction of different experiences and information with emerging cognitive capacities may contribute to the development of different types of cognitive and social-cognitive skills (Fischer & Pipp, 1984; Karmiloff-Smith, 1992). Moreover, the experience of shared affect as evidenced in spontaneous initiation of joint attention is hypothesized to provide the developing child with crucial information about self and other affective experiences (Mundy, 1995). Developmental research and specifically the examination of joint attention development demonstrate the potential impact of motivational bias on social-emotional and social-cognitive development.

A second theoretical process through which individual differences in BIS and BAS may contribute to individual differences in social-emotional development involves the relation of dispositions on the dimensions of BIS and BAS to psychopathology (Gray,

1981; Carver & White, 1994). Evidence for this relation comes from research using Carver and White's BIS/BAS scales, which use self-report to assess individual differences in relation to the strength of the BIS and the BAS (Carver & White, 1994). Results from the validation of the scales indicate that the BIS scale predicted level of nervousness in response to threat-related cues and the BAS scale predicted happiness in response to impending reward (Carver & White, 1994). Research with clinical populations implicates BIS/BAS functioning in the experience of depression. In particular, depressed individuals are hypothesized to exhibit deficient BAS and overactive BIS functioning (Davidson, Ekamn, Saron, Senulis & Frieson, 1990; Henriques & Davidson, 1991; Kasch, Rottenberg, Arnow, & Gotlib, 2002). Additionally, anxiety research theorizes BIS dysfunction in the experience of anxiety symptoms and the expression of the disorder (Gray, 1981; Heller, Koven, & Miller, 2003). The relevance of the BIS/BAS construct to theoretical understanding of internalizing disorders is well documented in the literature.

The underlying model used to conceptualize the functionality of the BIS/BAS construct in predicting psychopathology is the diathesis-stress model. This model states that each individual has a particular set of vulnerabilities that when activated by stress lead to the emergence of a disorder. These vulnerabilities may be defined as inherited or acquired characteristics of functioning that render an individual susceptible to environmental stressors and arise from the influence of multiple risk factors, including biological, demographic, family, and social influences (Monroe & Simmons, 1991; Richters & Weintraub, 1990). In adapting this model to the construct of behavioral motivation systems, individual vulnerabilities are identified as motivational tendencies

and temperament attributes (BIS/BAS features), which predispose individuals to psychopathology. This model accounts for the fact that not all individuals who are predisposed develop psychopathology. Stressors (and or environmental threats) may be influential and increase the individual's vulnerability, or may act as a precipitant, triggering the onset of maladjustment or psychopathology (Richters & Weintraub, 1990). The diathesis-stress model of psychopathology illustrates the utility of the BIS/BAS construct in describing and identifying those individuals potentially at-risk for psychopathology.

Based on this research, there are at least two avenues by which individual differences in BIS and BAS may contribute to differences in social-emotional development and social behavior in children with autism. Historically, researchers have employed many methods to investigate the nature of these motivational systems. In adults, the primary assessment tool is self-report. In young children, parent report of BIS/BAS sensitivity and laboratory-based observational methods of approach and avoidance behavior have been used to study motivational bias. While these methods have proven quite useful for direct and efficient assessment of BIS/BAS orientation, they are not free from error given that they rely on self-report, which can be biased or inaccurate. Additionally, the measure of motivational predisposition is exceedingly more difficult in older children and adolescents where self-report may not be reliable and parent-report may not be accurate, especially for internalizing symptomatology. It is in this light that the utility of psychophysiological measures, which provide objective assessment of core motivational tendencies, can be best observed.

Motivation and EEG Asymmetry

Psychophysiological measures in alpha asymmetry are one tool that has been used in research to examine individual differences with respect to motivational tendencies. The hypothesized laterality of brain function specific to motivational processes is rooted in the neuropsychological observations of affective sequelae following brain lesions (Gainotti, 1972; Robinson, Kubos, Starr, Rao & Price, 1984; Hagemann et al., 1999). Based on these observations, Davidson and others proposed that each anterior hemisphere subserved a specific motivational brain system. Within this framework, the left anterior hemisphere was hypothesized to be specialized for approach behavior and associated with the experience and expression of positive emotion (e.g., elation and happiness). The right anterior hemisphere was hypothesized to be specialized for withdrawal behavior and associated with the experience and expression of negative emotion (e.g., sadness and anxiety) (Davidson, 1984, 1992; Davidson & Tomarken, 1989). From this approach/withdrawal model of brain laterality, Davidson and others hypothesized that cortical activity measured in terms of alpha asymmetry could serve as an index of motivational bias (Davidson & Tomarken, 1989; Davidson, 1992, 1998).

EEG asymmetry is measured in terms of alpha brain wave activity. Alpha waves represent non-arousal and are characterized as relatively slow brainwaves, 9 to 14 cycles or Hertz per second (Coan & Allen, 2003a). Alpha activity is thought to be inversely related to cortical activation, where a decrease in alpha power is observed when underlying cortical systems engage in active processing (Davidson, Chapman, Chapman, & Henriques, 1990; Pizzagalli et al., 2005). EEG alpha asymmetry is frequently reported using a hemispheric difference score, which is calculated by subtracting the natural log of

the left hemisphere (LH) sites alpha power from the natural log of the right hemisphere (RH) sites alpha power, ($[\ln]RH - [\ln]LH =$ hemispheric difference score). In this way, an asymmetry in alpha power (signified by a negative or positive overall alpha score) represents an asymmetry in the opposite direction in terms of cortical activity (Coan & Allen, 2003a). When the RH alpha power is greater than the LH alpha power, (representing less cortical activity in the RH and greater activity in the LH), a positive overall laterality score results; thereby signifying relatively greater left alpha power at the site. Conversely, when the RH alpha power is smaller than the LH alpha power (signifying more cortical activity in the RH) a negative overall laterality score results; thereby signifying relatively greater right alpha power. These calculated alpha asymmetries have been found to be both stable over time (indicative of a core trait) and malleable based on environmental conditions (indicative of state-related properties). Additionally, alpha asymmetries have been shown to correlate with behavioral and personality measures in child and adult studies.

Applications from developmental research examining EEG asymmetry in infants yield important information about the genetic and environmental components of alpha asymmetry. Infant studies have shown that individual differences in EEG asymmetries emerge early in life and are associated with behavioral differences along the approach-withdrawal continuum (Davidson, 1992; Fox and Davidson, 1986; Fox et al., 1995). Davidson and Fox (1989) showed that EEG asymmetry at 10 months could predict response to maternal separation such that right frontal asymmetry predicted negative affect and behavior (i.e., crying behavior) in response to maternal separation. Jones et al. (1997) highlighted the heritability of EEG asymmetry patterns by showing that infants of

depressed mothers displayed reduced left activation at one month of age. The genetic and environmental overlap inherent in parent-child dyads blurs the distinction between the contributions of variance from genes versus environmental factors (i.e., stress) in observed EEG asymmetry.

Familial studies have been integral in attempting to tease apart the relative influence of genes and environment in determining individual differences in EEG asymmetry patterns. Research in this area is sparse and mixed for the most part with some studies reporting heritability of frontal asymmetry (Anokhin & Rohrbaugh, 1998; MacDhomhail, Allen, Katsanis, & Iacono, 1999) and others reporting no heritability or gender differences in heritability (Coan & Allen, 2003a). The most recent study showed low but significant heritability for frontal asymmetry measured at midfrontal sites in adult female twin pairs (Anokhin, Heath, & Myers, 2006). Results from this study suggested that 27% of the observed variance in midfrontal EEG asymmetry could be accounted for by genetic factors. Interestingly, EEG asymmetry was not found to be heritable from lateral frontal sites. Familial studies have added to the ongoing discourse on genetic and environmental influences on EEG asymmetry. Given the current inconsistencies in the literature, more research is needed to explicate the manner in which EEG asymmetry originates and develops through organism-environment interactions.

Research from developmental and heritability studies demonstrates that the psychometric properties of anterior EEG asymmetry include trait components, where resting frontal EEG asymmetry is a property of the individual and is stable over time, such as temperament or risk for psychopathology (Urry, Hitt, & Allen, 1999; Coan & Allen, 2003a; Vuga et al., 2006). Sutton and Davidson (1997) showed resting frontal

EEG asymmetry to be stable in adults over a 6-week interval with good internal consistency ($\alpha = 0.86$) and moderate test-retest reliability (average intraclass correlation for 13 asymmetry measures = 0.57). Likewise, Jones et al. (1997) demonstrated that EEG asymmetry at 3 months of age was highly correlated with the same asymmetry at 3 years, ($r = 0.66, p < .01$). These reported statistical findings are comparable to other research investigating the reliability of EEG asymmetry (Tomarken, Davidson, Wheeler, & Kinney, 1992). A recent investigation of the stability of asymmetry in typical adults and adults with a history of depression indicated that alpha asymmetry was moderately stable over a 3 year span irrespective of sex and history of depression (intraclass correlations between 0.39 and 0.61) (Vuga et al., 2006). Given this and other research, it appears that EEG alpha asymmetries are relatively stable over time in both clinical and nonclinical populations, as well as adults, infants, and very young children. Absent from this literature is the examination of the stability of EEG asymmetry in older children and adolescents. This will be a crucial area for research given that this developmental period is characterized by rapid brain change and development, especially in the prefrontal cortex and frontal lobes (Huttenlocher, 1979; Durston et al., 2006; Blakemore & Choudhury, 2006).

Research has also shown that anterior EEG asymmetry can be manipulated in response to specific environmental conditions. In this research, experimental paradigms manipulating mood and/or motivational state have demonstrated state fluctuations in anterior EEG asymmetry. One study found that smiles that included the activation of the orbicularis pars lateralis muscles (the Duchenne smile) resulted in an increase in left frontal activation relative to smiles (characterized as “unfelt”) that did not include this

movement (Ekman & Davidson, 1993). Research examining EEG asymmetry response to a reward task found that a relative increase in left frontal asymmetry was associated with the propensity to respond with approach-related tendencies under incentive conditions (Pizzagalli et al., 2005). Findings from developmental research demonstrated this association in newborn infants (i.e., 2-3 days of age), where increased left frontal activation was observed in response to a desirable flavor (e.g., sucrose), while a relative increase in right frontal activity was observed in response to a neutral flavor (e.g., water) (Fox & Davidson, 1986). Additionally, results from research studying the psychophysiological effects of stress-states have shown that acute administration of cortisol results in a relative increase of right frontal activity (Tops et al., 2005). With this understanding of the malleability of anterior EEG asymmetry, resting frontal EEG asymmetry can be conceptualized as a stable indicator of trait phenomena (specific to the individual), which modulates state-dependent changes in response to specific environmental stimuli (Coan & Allen, 2003a).

Theoretical Understanding of Anterior EEG Asymmetry

Based on the current literature, the most useful model used to understand EEG asymmetry is the motivational direction model, which hypothesizes that relatively greater left frontal asymmetry is associated with approach-related emotions and intentions, including negatively valenced emotions (i.e., anger); while relatively greater right frontal asymmetry is associated with withdrawal-related emotions and intentions (Harmon-Jones, 2004). This model is supported by much of the research in EEG asymmetry including applications to Gray's BIS/BAS theory and research from studies examining

the relations of EEG asymmetry to anger (Gray, 1994; Harmon-Jones, 2004). Sutton and Davidson (1997) demonstrated the association of frontal EEG asymmetry and relative standing on BIS/BAS by showing that relative increases in left frontal activity was associated with higher BAS scores and higher BAS-BIS difference scores, while relative increases in right frontal activation was associated with higher BIS scores. Additionally, results from Harmon-Jones (2004) showed an association between certain types of anger and left frontal asymmetry, demonstrating that anger, an emotion with negative valence, can evoke approach behavior. In this way, current research with increasingly specific paradigms is helping to explicate the complex relationship of emotion, motivational bias, and asymmetry.

In reviewing the nature of resting state EEG asymmetry data, Coan and Allen (2003a) offered three systematic sources of variance to consider when conceptualizing the relationship between trait and state frontal EEG asymmetry: 1) trait frontal asymmetry that is consistent across multiple assessments, derived from resting EEG assessments; 2) occasion-specific but reliable variations in frontal asymmetry that characterize the variation in resting EEG assessments across multiple sessions of measurement (variations that are characteristic of the individual); and 3) state-specific changes in frontal asymmetry that characterize the difference between two conditions or between baseline resting levels and some condition.

Hagemann (2004) elaborated on the state-and trait-composition of resting asymmetry and concluded that resting asymmetry is not solely a trait variable. He suggested that asymmetry is in part due to the distinct state-dependence of the spontaneous EEG, which is evidenced by the moderate temporal stability of resting

asymmetry (resting asymmetry retest correlations of 0.50 or 0.60 for time intervals of 2 to 6 weeks in healthy subjects) (Sutton & Davidson, 1997; Debener et al., 2000; and Hagemann et al., 2002). In contrast, he notes the high annual stability coefficients for self-reported personality measures (0.98-0.99) (Costa & McCrae, 1992).

Researchers in the field have attempted to accommodate this inconsistency with the suggestion that resting EEG asymmetry represents a reflection of the joint contribution of a trait superimposed on state-like factors (Tomarken et al., 1992; Davidson, 1992). Hagemann et al. (2002) provided direct support for this hypothesis in their study that examined the reliability of EEG asymmetry over four time periods (each four weeks apart). They used structural equation modeling to decompose asymmetry measures into latent state and trait components within the framework of the latent state-trait (LST) theory (Steyer, Ferring, & Schmidt, 1992). They found that reliable occasion-specific fluctuations accounted for approximately 40% of overall explained variance in resting frontal asymmetry, while the consistency across multiple sessions (trait variation) accounted for approximately 60% of the variance (Hagemann et al., 2002). Hagemann, Hewig, Seifert, Naumann, and Bartussek (2005) replicated this study using a longitudinal design to assess EEG asymmetry on three measurement occasions. Results from this study showed that between 40% and 50% of the variance of anterior asymmetry measures was due to individual differences on a latent trait and therefore, approximately the same portion of the variance was due to occasion-specific fluctuations (Hagemann 2004; Hagemann et al., 2005). The work of Hagemann and others has demonstrated that EEG asymmetry has both state and trait properties, and consequently, the interpretation of the measure should be based on data from multiple occasions of assessment.

EEG Asymmetry and Psychopathology

The literature reviewed above suggests that EEG asymmetry over the frontal cortex can be viewed as a stable indicator of trait-like phenomena specific to approach and withdrawal motivations or behaviors, which map on to the principles of Gray's hypothesized behavioral motivation systems. The relevance of this construct as measured by EEG asymmetry to human behavior can be discussed with regard to the protective versus risk-related factors for psychopathology associated with individual frontal EEG asymmetry. Research has shown fairly consistent relations between EEG asymmetry and emotion-related psychopathology. Individuals with depression (symptoms or diagnosis) display greater relative right frontal asymmetry (or left frontal hypoactivation) (Henriques & Davidson, 1990, 1991; Tomarken et al., 1992; Coan & Allen, 2003a; Shankman, Klein, Tenke, & Bruder, 2007). Field, Fox, Pickens, and Nawrocki (1995) found that depressed mothers and their infants showed increased right frontal asymmetry when compared to a sample of mothers and infants without psychopathology. Another study looking at depressed and non-depressed mothers yielded a similar pattern of results where depressed mothers who displayed less affection behaviors displayed a greater decrease in left frontal asymmetry (Dawson et al., 1999). Yet another study using the Beck Depression Inventory (BDI) found that individuals with high scores on the BDI also showed increased relative right frontal asymmetry (Schaffer et al., 1983). Clearly, the pattern of increased right frontal EEG asymmetry and depression is well documented in the literature.

Research examining the relations of anxiety and anterior EEG asymmetry has yielded less consistent results. Some studies have shown that increased anxiety is

associated with a relative increase in right frontal activity (Wiedemann et al., 1999; Davidson, Jackson, & Larson, 2000), while other studies have shown that increased anxiety is related to a relative increase in left frontal activity and/or right posterior activity (Heller et al., 1997; Hofmann et al., 2005). Heller et al. (2003) posits that this inconsistency is due to the cognitive processing components that characterizes each type of anxiety disorder and both anterior and posterior asymmetries should be considered in order to accommodate the qualitative differences in symptoms. More somatic forms of anxiety called anxious arousal may be associated with right parietal activation whereas forms of anxiety with stronger verbal representation cognitive components, such as worry, are called anxious apprehension and associated with left frontal activation. In this way, Heller's group determined that the relation of EEG asymmetry to anxiety symptoms depended on the emotional valence and individualized characteristics of the individual's disorder. They found that by refining the motivational direction model to include cognitive processing features specific to the presentation of the pathology, they could better explain and accommodate the patterns of asymmetry observed. Certainly this idea argues for the considerable impact of individual differences within a diagnosis such as anxiety disorders and the importance of collecting EEG data across anterior and posterior brain regions.

The relation of anterior EEG asymmetry to psychopathology and/or symptoms of social-emotional impairment is further complicated by age differences in studies of children and adolescents. These apparent age effects have been observed in studies with typically developing and affected children (i.e., ADHD, ODD, Anxiety Disorder, at-risk for Depression, and High Functioning Autism) (Baving et al., 2002; Sutton et al., 2005;

Burnette, 2005; Forbes et al., 2006; Pradella, 2006). For example a study examining asymmetry responses to a disappointment task in children at-risk for depression found that age moderated the relation of affect to asymmetry such that younger children (ages 3-5) showed the hypothesized relation of relative right frontal activity and withdrawal behavior, however no effects were found in middle childhood (ages 6-9) (Forbes et al., 2006). In an effort to address the documented inconsistencies in the child/adolescent literature on EEG asymmetry, Pradella (2006) examined the relation of the measure to social-emotional symptoms in typically developing children. Results from this study indicated that age affected the pattern of relations between asymmetry and social-emotional status such that older children (mean age = 13.6 years) displayed the classic adult frontal activation pattern of associations between right frontal activity and anxiety, while younger children (mean age = 10 years) did not show this pattern. Conclusions from this and the aforementioned studies indicate that developmental factors must be considered in the interpretation of EEG asymmetry in children and adolescents.

EEG Asymmetry and High Functioning Autism

The inconsistencies apparent in the literature on EEG asymmetry and its relations to psychopathology and social-emotional status elucidate the very complex nature of the measure itself and its application to the study of development in children and adolescents. Nonetheless, psychophysiological investigation of motivational tendencies and/or temperament and personality factors remains a robust and unique method that circumvents the need for subjective report. The utility of applying this methodology to children and adolescents with autism is readily apparent when considering it can be used

in nonverbal populations. These methods also have implications for aiding in individualized treatment decisions. Theory on EEG asymmetry and the associated BIS/BAS motivation axes may help to explain approach and avoidance differences that are prominent in autism, as well as the role these differences play in the social development and intervention responsiveness of children with autism (Mundy, 1995; Sherer & Schreibman, 2005; Wing & Gould, 1979).

Sutton et al. (2005) provided the first study of EEG asymmetry and social development in autism. As expected in this study parents of higher functioning children with autism (HFA) who displayed left midfrontal asymmetry, and presumably exhibited more social approach tendencies (Mundy, 1995), reported fewer syndrome-specific symptoms of impairment than children with right midfrontal asymmetry. However, results from self-report data revealed the unexpected finding that HFA children with greater left frontal asymmetry self-reported more symptoms of depression, social anxiety, general anxiety, social stress, fear of negative evaluations by others, and less satisfaction with interpersonal relations than did right frontal HFA children. Interestingly, the opposite but expected pattern of right frontal associations with symptoms of dysphoria was observed in the control sample suggesting that EEG asymmetry displayed a syndrome specific pattern of associations with social-emotional variables in this study. However at least one previous study had reported that internalizing rather than externalizing symptoms may be associated with left frontal functioning in boys (Baving et al., 2002). So the pattern of asymmetry associations observed for the HFA sample was not without precedent in children without autism. Sutton et al. (2005) suggested that the enhanced tendency for social approach in left frontal HFA children in combination with

syndrome specific social deficits may lead to more frequent or more apparent failed bids for social interactions among left frontal children and these experiences heightened feelings of dysphoria and self appraisals of incompetence in this subgroup of children.

The findings from the Sutton et al. (2005) study demonstrate the utility of anterior EEG asymmetry in assessing underlying motivational bias. These results suggest that the hypothesized relations between anterior asymmetry and emotional impairment are inversely displayed in children with autism due to the mismatch between their motivational bias (i.e., approach) and their social communication impairments. In addition to the within-group differences observed in this study, group differences were observed in asymmetry such that HFA children displayed a relative increase in left frontal asymmetry at midfrontal and central regions, while the control group did not (Sutton et al., 2005).

A second examination of the relation of anterior EEG asymmetry and social-emotional symptoms was conducted in order to investigate the reliability and validity of these findings and interpretations (Burnette, 2005). This study attempted to improve upon the previously reported findings with larger samples and by including a more extensive diagnostic symptom assessment using items from the Autism Diagnostic Interview-Revised (ADI-R, Rutter, LeCouteur & Lord, 2003). Additionally, this study broadened the range of emotional symptoms assessed by including self-report measures looking at anger expression in order to demonstrate the theorized and empirically supported relation of anger symptoms and left frontal asymmetry (Harmon-Jones, 2004).

The results reported by Burnette (2005) largely replicated the previous research (Sutton et al., 2005). Specifically, Burnette (2005) observed that HFA children with left

midfrontal asymmetry reported more symptoms of social stress, obsessive-compulsive behaviors, external locus of control, and atypical thoughts and behaviors than those exhibiting right midfrontal asymmetry. Additionally, increased anger expression symptoms were related to left frontal asymmetry in this sample of HFA children. Corroborating this observation, parents of HFA children reported more symptoms of conduct disorder in left rather than right frontal HFA children.

The data from Burnette (2005) also indicated that left frontal asymmetry was related to lower social symptom presentation in HFA children. Moreover, the data in this study suggested that anterior asymmetry was related to the course of symptom presentation in HFA children. Retrospective parent report indicated that HFA children with left frontal asymmetry had later onset of autism symptoms (at midfrontal or lateral frontal sites) and later age of parents' first concern about developmental progress (at midfrontal asymmetry sites). Age was also identified as a potential moderator of the relation of asymmetry and social impairment. Right lateral frontal asymmetry was associated with greater parent report of social symptom impairment on the SCQ among the younger (8- to 12-year old) but not the older (13- to 17-year-old) subgroups of HFA children. Group differences between HFA and control children were also examined and in this regard the results were inconsistent compared to results from the previous research (Sutton et al., 2005). Specifically, HFA and control children did not differ with respect to EEG asymmetry scores.

Interpretations of these findings support a motivational model of EEG asymmetry such that individuals with left frontal asymmetry are predisposed to motivational approach biases. In the context of the social communication impairments associated with

autism, this motivational bias (as indexed by left frontal asymmetry) is thought to modify the expression of the disorder in such a way that leads to decreased social symptom presentation in left rather than right frontal children, at least in preadolescent HFA children. However, increased social approach tendencies may come at a cost for left frontal children in that it precipitates more failed bids for social initiations which lead to anxiety and negative self appraisals among these children and adolescents. The hypothesized interpretation is that the overlay of the impairments associated with autism on the individual's predisposed motivational bias to approach results in the experience of comorbid symptoms of anxiety (Burnette, 2005; Mundy et al., 2007).

Study Purpose and Goals

Although prior research on EEG asymmetry and autism has been revealing, it is hardly conclusive. The samples sizes in previous studies have been modest at best. The data in these previous studies have also been limited to parent or self-report measures. Therefore, data on the relations between asymmetry and direct observation of social behaviors in HFA children are needed. Previous research has also failed to examine the degree to which the patterns of associations observed between anterior EEG asymmetry and social emotional measures is truly specific to HFA children or is also observed in children with elevated symptoms of anxiety and attention problems. Finally, if work in this arena is to continue on a firm scientific foundation, basic questions about the reliability estimates of EEG asymmetry in HFA children need to be addressed.

Therefore this study attempted to replicate and extend the previously reported findings of the relation of EEG asymmetry to comorbid psychopathology and

motivational bias in an effort to investigate the proposed theoretical framework from which these findings are interpreted (Mundy et al., 2007). Unique to this examination of EEG asymmetry in a sample of HFA children and adolescents is the short-term longitudinal study design, allowing for two occasions of psychophysiological measurement. In this way, reliability of the measure itself can be examined. Additionally, in order to examine the role of ADHD and anxiety symptoms in the associations between HFA status and EEG asymmetry, ADHD and anxiety symptoms were assessed in both the HFA sample and a non-HFA comparison sample. The effects of these continuous measures of comorbid symptoms were examined where there were significant correlations with independent measures through analyses of covariance.

Analysis of the reliability of EEG asymmetry in child and adolescent samples is greatly needed given the prevalence of inconsistent relations of anterior EEG asymmetry to social-emotional functioning and motivational bias in the literature. While research examining EEG asymmetry in children has shown that age is a potential moderator in the relation between asymmetry and social-emotional status (Pradella, 2006; Burnette, 2005; Forbes et al., 2006), past research has also shown asymmetry to relate inconsistently to social-emotional status across different diagnostic populations (i.e., typically developing children and children with ADHD, Anxiety Disorders, ODD, and those at-risk for depression) (Pradella, 2006; Forbes et al., 2006; Baving et al., 2000; Baving et al., 2002). Interestingly, in two studies examining the application of EEG asymmetry in populations of HFA children and adolescents, results have been consistent, albeit in the unexpected direction given the literature (Sutton et al., 2005; Burnette, 2005). Certainly, examining

the test-retest reliability of anterior EEG asymmetry in a population of children and adolescents with high functioning autism will aid in the valid interpretation of the results.

Additionally, this study elaborated on previously self- and parent-reported findings of social impairment and comorbid social-emotional symptoms by including in vivo assessment of social interaction via the Autism Diagnostic Observational Schedule (ADOS) (Lord et al., 2000). The ADOS is a diagnostic tool that yields qualitative information on social communication symptoms, which is then coded for level of impairment (e.g., absence, probably presence, and definite presence of abnormality). A drawback to this type of assessment is its relative insensitivity to important individual differences in social approach and avoidance behaviors among children with the diagnosis. To address this weakness, a quantitative adaptation of the ADOS (i.e., the Q-DOS), was developed to assess behaviors associated with prosocial interaction (i.e., sharing vs. non-sharing eye contact and social vs. nonsocial smiles). These target behaviors of shared eye contact and social affect were designed to assess an important symptom domain of autism (spontaneous sharing of experiences with others) that has been theoretically linked to approach motivation in autism (Mundy, 1995). This assessment method will increase power of measurement needed to detect these important individual differences in prosocial (i.e., approach-oriented) behaviors, and its underlying theoretical system (i.e., BIS/BAS).

Hypotheses

This study investigated the differential relation of EEG asymmetry to motivational bias and social-emotional status within a population of children and

adolescents with high functioning autism (HFA). In examining both the group differences between HFA and non-HFA comparison/control children and the within group differences among the HFA children and adolescents, six specific hypotheses were evaluated: 1) It is expected that the measures of anterior and posterior EEG asymmetry will display significant test-retest reliability in a large sample of HFA and non-HFA children, 2) HFA children with left frontal asymmetry will display significantly less impairment on both parent report and direct observation measures of social communication compared to children with right frontal asymmetry, 3) HFA children will demonstrate different patterns of hemispheric asymmetry when compared to children in the non-HFA comparison sample, 4) Based on theory, right frontal asymmetry is expected to be associated with heightened symptoms of anxiety and dysphoric social emotional status in non-HFA children; however, based on previous research, left frontal asymmetry is expected to be related to symptoms of anxiety and dysphoric emotional status in the HFA sample, 5) Based on previous research, children endorsing somatic symptoms of anxiety are expected to exhibit right parietal asymmetry, while children endorsing more cognitive/verbal symptoms of anxiety (i.e., worry) are expected to exhibit left frontal asymmetry in both HFA and non-HFA samples, and 6) Left frontal asymmetry is expected to be associated with increased symptoms of anger expression in both HFA and non-HFA children,.

Power Analyses

Power analyses were conducted for planned comparisons between the HFA and non-HFA groups and were based on a total sample size of 120 subjects. Previous research

using between group analyses (Burnette, 2005) compared a sample of individuals with HFA (N=37) and typically developing individuals (N=32) on the Compulsions subscale of the Leyton Obsessive Inventory (LOI) and indicated an effect size equal to .63. Based on this effect size, in order to reach a power of .80 for the proposed study, an a priori power analysis indicated that a sample size of 64 must be used. Since the current combined HFA and non-HFA comparison sample (N=95) is well above the required size for moderate to high power, it is expected that the samples involved in these analyses will yield sufficient power to observe comparable or larger effects with alpha set at 5% (two tailed) in multivariate and univariate tests (Kraemer & Thiemann, 1987; Stevens, 1992).

Power analyses were also conducted for the planned comparisons between the HFA asymmetry subgroups (Left Frontal Asymmetry HFA (LFA-HFA) group and the Right Frontal Asymmetry HFA (RFA-HFA)) and were based on a total sample size of 60 subjects. Previous research examining within group analyses compared a sample of LFA-HFA children (N=19) and RFA- HFA children (N=18) on the Compulsions subscale of the Leyton Obsessive Inventory (LOI). This analysis indicated an effect size equal to .85. Based on this effect size, in order to reach a power of .80 for the proposed study, an a priori power analysis indicated that a sample size of 36 must be used. Since the current combined HFA sample (N=51) is well above the required size for moderate to high power, it is expected that the samples involved in these analyses will yield sufficient power to observe comparable or larger effects with alpha set at 5% (two tailed) in multivariate and univariate tests (Kraemer & Thiemann, 1987; Stevens, 1992).

CHAPTER 2: METHODS

Participants and Procedure

In order to investigate the hypotheses of this study, two groups comprised of children between the ages of 8-16 were recruited: 51 High Functioning Autism (HFA) and 44 non-HFA children and adolescents. Given the considerable diagnostic ambiguity between High Functioning Autism and Asperger's Disorder, as well as the variability in social impairments experienced by children in both groups, children in the HFA group consisted of children who have either Asperger Disorder or High Functioning Autism (Volkmar & Klin, 2000). Additionally, given the high rates of comorbid anxiety and ADHD symptoms in populations of children with HFA, a portion of the HFA sample were elevated on measures of anxiety and ADHD (Farrugia & Hudson, 2006; Reiersen, Constantino, Volk, & Todd, 2007; Sutton et al., 2005; Burnette, 2005). In order to examine the role of comorbid anxiety and ADHD symptoms, the non-HFA comparison group consisted of typically developing children as well as children recruited specifically with elevated anxiety and ADHD symptoms. Expanding the control sample to include children with social-emotional impairment consistent with that experienced by HFA children and adolescents allowed for the sample distributions of the two groups to be more closely matched. Samples matched for comorbid symptoms allowed for the examination of the effects of primary diagnosis (i.e., HFA) on EEG asymmetry as well as any additional effects of comorbid anxiety and ADHD symptoms.

Elevations in anxiety were determined based on self-reported anxiety symptoms on the Multidimensional Anxiety Scale for Children (MASC). Elevations in attention and hyperactivity were determined based on parent-reported symptoms of attention and

hyperactivity problems on the Behavioral Assessment System for Children – Second Edition, Parent Report Scales (BASC-2 PRS). Children were excluded from the comparison sample if parent report indicated they had a significant history of developmental delay, sensory or motor impairment, a neurological or genetic disorder, psychotic symptoms disorder, or an identified syndrome in the six months prior to participation in this study. Children with learning problems and/or behavioral and emotional disturbance (e.g., ADHD or Anxiety Disorder) were included in the non-HFA comparison sample.

Children from the HFA group were recruited from the University of Miami Center for Autism and Related Disabilities (CARD) database based on their prior diagnosis of High Functioning Autism or Asperger Disorder by community clinicians. Participants in the non-HFA comparison group were recruited through Miami Dade County Public Schools and the West Lab School associated with the University of Miami. Additionally, in order to sample enough children with elevated anxiety and ADHD symptoms, children were recruited from families whose child received an assessment at the University of Miami Psychological Services Center, as well as community psychologists' offices.

Interested families voluntarily responded to recruitment letters and brochures by contacting the lab's project coordinator. At which time, they completed a phone screen and scheduled the visits. Data were collected over the course of three visits, which were approximately two hours in duration. On arrival for their first appointment, parents signed a consent agreeing to their child's participation in the study. Likewise, participants were asked to sign an assent before proceeding with testing.

Procedure

During the first testing session, subjects completed cognitive (Wechsler Intelligence Scale for Children - Fourth Edition subtests Similarities, Block Design, Vocabulary, and Matrix Reasoning; Wechsler Individual Achievement Test – Second Edition subtest Word Reading) and behavioral measures (Leyton Obsessive-Compulsive Inventory for Children, Social Anxiety Scale for Children – Revised, Multidimensional Scale for Children, and the Behavioral Assessment System for Children – Second Edition, Self-Report; BASC-2 SRP), and measures of anger/emotional expression (Pediatric Anger Expression Scale-Third Edition and Emotional Expression Scale for Children). In addition, research subjects completed the Autism Diagnostic Observation Schedule (ADOS). During this time, parents completed an abbreviated version of the Autism Diagnostic Interview – Revised (ADI-R) with one of the examiners. Participants received forty dollars compensation after completing each session.

The second visit consisted of an EEG session where the subject was asked to sit quietly for approximately seven minutes to collect baseline data, and then engage in a separate ERP task. Data from the former but not the later phase of EEG acquisition is relevant to this study. During this visit, the subject also completed the BASC-2 SRP and the Multidimensional Scale for Children (if they were not already completed after the first visit).

The third visit consisted of a second EEG session where the subject was again asked to sit quietly for approximately seven minutes to collect baseline data, and then begin a separate (but different) ERP task. Again, only data from the baseline, resting state

condition is relevant for this study. Also during this visit, the subject had the opportunity to complete any unfinished self-report forms.

While the child is participating in the EEG sessions, the parents were asked to complete diagnostic (Autism Spectrum Screening Questionnaire, Social Communication Questionnaire), social communicative (Social Responsiveness Scale, Children's Communication Checklist – Second Edition) and behavioral (Social Anxiety Scale for Children – Revised Parent Form and the Behavioral Assessment Scale for Children – Second Edition, Parent Report Scales) questionnaires about their child. They were also asked to complete a demographic checklist, which included measures of ethnicity, parent education level, occupation, and estimated family income. Parents also completed several questionnaires about themselves that are not relevant to this study.

CHAPTER 3: MEASURES

Diagnostic Measures

Autism Spectrum Screening Questionnaire (ASSQ; Ehlers, Gillberg, & Wing, 1999)

The ASSQ was designed to be completed as a brief 27-item screening device to identify symptoms associated with either Asperger Disorder (AS) or other high-functioning autism spectrum disorders in children and adolescents of normal intelligence or mild mental retardation (Ehlers et al., 1999). Ehlers and colleagues (1999) recommend a cutoff score of 13 on the ASSQ for sensitivity in capturing those individuals who are positive for the disorder, while also identifying children with some degree of social impairment who are not in the autism spectrum. In our own evaluation of this scale a cutoff score of 13 correctly identified 100% of a HFA sample of 8 to 13-year-old children (N = 31), 100% of a typically developing sample (N = 16), and 80% of children with learning disabilities (N = 15) all matched for age, IQ and gender (Meyer et al., 2006).

Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003)

The SCQ is a 40-item parent-report screening measure that assesses autistic symptomatology in three domains: communication, reciprocal social interaction, and restricted, repetitive and stereotyped patterns of behavior. The SCQ items were chosen to match 40 of the 93 ADI-R items that were found to have the best discriminant diagnostic validity. The questionnaire is presented in a simple yes/no format and contains two forms, one that assesses lifetime prevalence of symptoms and another that assesses current behaviors. The Lifetime form was used in this study to determine if the specified behaviors have occurred at any point in the child's life. However, questions 20 to 40

focus specifically on the time frame from the age of 4-5 years old, as this is a crucial time period for diagnostic assessment. Research suggests that a cutoff score of 15 is adequately sensitive to capture children who demonstrate mild autistic symptoms beyond the realm of normal development.

Autism Diagnostic Interview-Revised (ADI-R; Rutter et al., 2003)

The ADI-R is a comprehensive 2-3 hour parent interview designed to assess a child's functioning in the three domains essential for autism diagnosis according to DSM-IV criteria: Qualitative Abnormalities in Reciprocal Social Interaction, Qualitative Abnormalities in Communication, and Restricted, Repetitive and Stereotyped Patterns of Behavior. For the purposes of this study, an abbreviated ADI was administered which includes the Restricted, Repetitive, and Stereotyped Patterns of Behavior domain as well as selected questions from the Qualitative Abnormalities in Communication domain to assess the child's age when they began speaking words and phrases, as well as to assess the child's current communicative abilities. Questions on the ADI assess current functioning as well as functioning between the ages of 4-5 years. According to DSM-IV criteria, children with Asperger disorder are distinguished from those with autism because they demonstrate a normal language development, and display evidence of fewer than six DSM-IV criteria for autism. The ADI-R has been shown to have good psychometric properties (LeCavalier et al., 2006) and good discriminative ability among children in a clinical setting (Mazefsky & Oswald, 2006).

Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 1999; Lord et al., 2000)

The ADOS is a semi-structured, standardized assessment of communication, social interaction, and play or imaginative use of materials to assess individuals with suspected autism. The ADOS provides a 45-minute observation period during which the examiner presents numerous opportunities for the individual being assessed to exhibit behaviors of interests in the diagnosis of an ASD through the use of standard “presses” for communication and social interaction. It consists of four modules which are graded based on an individual’s developmental and language level, ranging from no expressive or receptive language to verbally fluent. For the purposes of this study, only Modules 3 and 4 were administered, as study requirements demand fluent speech and adequate expressive and receptive language. Module 3 is intended for children for whom playing with toys is age appropriate (usually under 12-16 years of age), and who are verbally fluent. Verbal fluency is broadly defined as the expressive language skills of a typical 4-year-old child; producing a range of sentence types and grammatical forms, using language to provide information about events out of context, and producing some logical connections within sentences, although the child may make some grammatical errors. Module 4 includes socioemotional questions, as well as additional tasks and some interview items about daily living. The main difference between Modules 3 and 4 is that Module 3 employs observations during interactive play along with the use of interview questions to gather information about social communication, whereas Module 4 depends primarily on interview questions.

The ADOS is scored immediately after administration and these ratings can be used to formulate a diagnosis of an ASD through the use of the diagnostic algorithm

provided. The diagnostic algorithm is a set of rules that allow classification of individuals as having the social and communicative deficits of autism or ASD. The ADOS is broken down into three domains: Communication, Social Interaction, and Stereotyped Behaviors and Restricted Interests; however only the algorithm items for the Communication and Social Interaction domains are used in making the diagnosis of autism or ASD. The psychometric properties of the ADOS are well established. For Modules 3 and 4, interrater item reliability for exact agreement is high for codes related to social reciprocity, adequate for the “Stereotyped Behaviors and Repetitive Interests,” and somewhat variable for the codes related to the Communication domain. The relatively low interitem reliability for the Communication domain resulted in the elimination of some items from the original draft. Intraclass correlations across pairs of raters for algorithm subtotals and totals for each module were moderate to high: Social Interaction (range .88 to .97), Communication (range .74 to .90), and the Stereotyped Behaviors and Restricted Interests (range .84 to .98). The combined ADI-R and ADOS assessment is the gold standard method for assessing and diagnosing ASDs.

Quantitative ADOS Codes (Q-DOS)

The quantitative coding of the ADOS attempts to extend and validate parent and self-report of social motivation by coding frequency of prosocial interaction behaviors exhibited during the ADOS. The criteria for the coding system is based on the Early Social Communication Scales (Seibert, Hogan, & Mundy, 1982), which is a coding system used to rate eye contact and affect in very young children with autism. Like the ESCS, the quantitative codes consist of two social interaction dimensions, eye contact

and affect (i.e., smiles), on which individuals with autism are expected to differ based on research examining social-motivational tendencies in autism (Mundy, 1995). Frequencies of specific behaviors (i.e., eye contact and smiles, which are described in detail below) were recorded from taped administrations of the ADOS. The frequency counts were recorded over the course of four, 5-minute epochs: 5 minutes at the beginning and end of the administration and 2 consecutive 5-minute intervals in the middle of the administration (determined by dividing the total administration time in half and using the 5 minutes before and after the middle portion). Interrater reliability was established by having at least two trained coders overlap on 20 percent of cases for both HFA and non-HFA groups.

Within each dimension, the communicative function of each specified behavior was determined. Eye contact was rated as either sharing or non-sharing. In order for eye contact to be rated as sharing, the coder had to determine the functional degree to which the child initiated eye contact to spontaneously share his or her experience with the examiner. To help operationalize this subjective judgment, criteria for sharing versus non-sharing eye contact were established. Sharing eye contact was defined as all eye contact made while the subject is speaking provided that that the examiner is not moving or exhibiting behavior that could somehow elicit the eye contact. In addition, the examiner must be looking at the subject (and not taking notes) in order for the eye contact to be considered spontaneous and for the purpose of sharing. Non-sharing eye contact was defined as all eye contact made while the examiner is speaking, moving, or otherwise not looking at the subject. Non-sharing eye contact includes eye contact made for the purposes of checking (what the examiner is doing), responding (to the examiner's

request), and reacting (to task materials and/or task transitions). Any eye contact made during a requesting behavior (i.e., “Can I have more pieces?”) is coded as checking/reactive as the functional significance is not to spontaneously share his or her experience with the examiner, but to respond to the examiner’s task.

In addition to eye contact, the experience of positive affect was be rated by coding the frequency of smiles both directed to the examiner (social) and nondirected smiles (non-social). Again, in order for a smile to have been rated as sharing and social, the examiner must be looking at the subject simultaneously as the smile is shared. Additionally, if a smile begins as non-directed but then is directed to the examiner, it was counted as a sharing/social smile.

In order to examine the within-HFA group differences in the frequency of prosocial interaction behaviors observed during the ADOS, the proportion of social and nonsocial eye contact, the proportion of social and nonsocial smiles, and the overall sociability composite (social smile + social eye contact/social eye contact + nonsocial eye contact + social smile + nonsocial smile) were examined.

Social Communication Measures

The Children’s Communication Checklist - Second Edition (CCC-2; Bishop, 2003)

The CCC-2 is a 70-item parent-completed checklist designed to screen for language impairments, identify pragmatic impairments in children with communication problems, and to assist in identifying children who may have an autistic spectrum disorder. A specific function of this measure is to assess how children use language and to identify unusual features of language or communication such as stereotyped

conversation or over-literal comprehension. The CCC-2 has 10 scales, each consisting of 7 items. Four scales assess language structure, vocabulary, and discourse (i.e., Speech, Syntax, Semantics, and Coherence). Four scales assess pragmatic aspects of communication (i.e., Inappropriate Initiation, Stereotyped Language, Use of Context, and Nonverbal Communication). The last two scales assess behaviors that are usually impaired in children with autism (i.e., Social Relations and Interests). The CCC-2 is not used to diagnose autism, although disproportionately low scores on scales assessing pragmatics and evidence of impairment on the autism-specific scales, suggests a profile of communicative impairment that should be assessed for autism. Two composite scales are calculated: the General Communication Composite (GCC) and the Social Interaction Deviance Composite (SIDC). Poor performance on the GCC may be indicative of a clinically significant communication problem. The SIDC reflects a mismatch between the language scales and the pragmatic/autistic behavior scales and can be used to identify children with a communicative profile characteristic of autism. All scales have good internal consistency (above .65 for all scales), indicating that items cluster together coherently within each scale. In validation studies, the GCC was found to differentiate between controls and children with communication disorders. Additionally, the SIDC was found to be sensitive to ASDs.

Social Responsiveness Scale (SRS; Constantino et al., 2003; Constantino et al., 2004)

The SRS is a 65-item quantitative parent report measure that assesses autistic symptoms across the entire range of severity in which they occur in nature. It was developed using a sample of 1900 4- to 15-year-old children and has excellent short and

long term test-retest reliability (.83 to .88) and convergent multiple informant agreement between mothers, fathers and teachers (Constantino et al., 2003). Research using the SRS has shown that scores on the instrument were continuously distributed in the population, generally unrelated to IQ, and capable of distinguishing children with ASDs and those with other child psychiatric disorders (Constantino, Przybeck, Friesen, & Todd, 2000; Constantino & Todd, 2003; Towbin, Pradella, Gorrindo, Pine, & Leibenluft, 2005). Items from the SRS target a core domain believed to be impaired in children with ASDs, the ability to engage in emotionally appropriate reciprocal social interactions. Included in this complex ability is the child's awareness of the emotional and interpersonal cues of others, ability to appropriately interpret and respond to those cues, and motivation to engage in social interactions with others. It includes items that assess social awareness, social information processing, capacity for reciprocal social responses, and social anxiety/avoidance as well as characteristic autistic preoccupations/or repetitive behavior. The SRS generates a singular scale score that serves as an index of severity of social deficits in the autism spectrum. Higher scores on the SRS indicate greater severity of social impairment. Additionally, the SRS yields six subdomains: Social Cognition, Social Awareness, Social Motivation, Social Communication, and Autistic Mannerisms. Each item on the scale is rated from 0 ("never true") to 3 ("almost always true") resulting in a single factor score ranging from 0 to 195. This scale was included in this study because previous validity studies indicated that the SRS is sensitive to genetic influences on differences in social behavior in autistic children (Constantino & Todd, 2000) and because it yields a measure that is independent of IQ but distinguishes children with

autism, Asperger Disorder and PDD/NOS from control samples (Constantino et al., 2003).

Intellectual Measure

Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV; Wechsler, 2003)

The WISC-IV is an updated version of the WISC-III and represents intellectual functioning in four cognitive domains including: Verbal Comprehension, Perceptual Reasoning, Working Memory, Processing Speed, and a combined Full Scale IQ. It also yields standardized scale scores for fifteen subscales (supplemental tests in italics) including five Verbal Comprehension scales (Similarities, Vocabulary, Comprehension, *Information*, and *Word Reasoning*), four Perceptual Reasoning scales (Picture Concepts, Block Design, Matrix Reasoning, and *Picture Completion*), three Working Memory scales (Digit Span, Letter Number Sequencing, and *Arithmetic*), and three Processing Speed scales (Coding, Symbol Search, and *Cancellation*). The following four subtests were used in this study: Vocabulary, Similarities, Block Design, and Matrix Reasoning. These four subtests were used to obtain estimated Verbal Comprehension and Perceptual Reasoning Index scores. These subtests were chosen because of their superior psychometric characteristics (i.e., Standard Error).

Wechsler Individual Achievement Test – Second Edition (WIAT-II; Wechsler, 2001)

The WIAT-II is an updated version of the WIAT and assesses functioning in four areas of achievement: Reading, Mathematics, Written Expression, and Oral Expression.

For the purposes of this study, only the Word Reading subtest from the WIAT-II was used to assess the child's reading level in order to ensure the child is capable of reading and understanding the questions on the self-report measures of behavior and social-emotional functioning. Data on the internal consistency, test-retest reliability, and interscorer reliability of the WIAT-II scores demonstrate consistently high levels of precision (Wechsler, 2001). Additionally, the Word Reading subtest of the WIAT-II has also demonstrated adequate concurrent validity with another measure of reading ability (i.e., WIAT-II Word Reading was correlated at .75 with the Reading subscale of the Wide Range Achievement Test – Third Edition) (Wilkinson, 1993).

Social-Emotional Functioning Measures

Behavioral Assessment System for Children - Second Edition, Self-Report (BASC-2 SRP; Reynolds & Kamphaus, 2004)

The BASC-2 SRP is a self-report measure used to evaluate the behavior and self-perceptions of children ages 8-18 years by asking them to respond true or false to a series of simple statements. Two forms are available depending on age level, child (ages 8-11) and adolescent (ages 12-18). Items load onto scales measuring Anxiety, Atypicality, Social Stress, Attention Problems, Depression, Interpersonal Relations, and Self Esteem. The adolescent version contains two scales not included on the child form, Sensation Seeking and Somatization. In addition, the BASC-2 includes composite scales measuring Internalizing and Externalizing Problems as well as adaptive scales such as Relations with Parents and Interpersonal Relations. For the purposes of this study, four scales were used: Anxiety (13 items, alpha = .86 for children and adolescents), Depression (13 items, alpha = .84 for children, and 12 items, alpha = .88 for adolescents), Social Stress (8

items, alpha = .81 for children, and 10 items, alpha = .85 for adolescents), and Interpersonal Relations (6 items, alpha = .81 for children, and 7 items, alpha = .79 for adolescents). The Anxiety and Depression scales were used to index aspects of internalizing distress including sadness and dysphoria, generalized fears, over-sensitivity, and worries that typically are irrational and poorly defined. The Social Stress and Interpersonal Relations scales were used to assess problematic social perceptions, an individual's success at relating to others, and the degree of enjoyment derived from this interaction. Detailed information on the convergent and discriminant validity, as well as test-retest reliability, is adequate and is reported in the manual. Norm-referenced T-scores (based on age and gender) were obtained for each scale. For all scales (with the exception of the Interpersonal Relations scale), higher scores index greater levels of impairment for the child/adolescent.

Social Anxiety Scale for Children-Revised (SASC-R; La Greca & Stone, 1993)

The SASC-R is a self-report measure which has been shown to relate to peer rejection and differentiate socially anxious from non-socially anxious children. Responses are rated on a scale from 1 ("not at all") to 5 ("all the time") based on the degree that the statement applies to the child. The scale contains 22 items and is comprised of 3 different subscales: Fear of Negative Evaluation from Peers (FNE), Social Avoidance and Distress-Specific to new situations (SAD-N), and Generalized Social Avoidance and Distress (SAD-G). Internal consistency for the SASC-R subscales is good with .86 for FNE, .78 for SAD-New, and .69 for SAD-General. Social anxiety on

this measure has been linked to impairments in social functioning (La Greca & Lopez, 1998).

Multidimensional Anxiety Scale for Children (MASC; March, Parker, Sullivan, Stallings, & Conners, 1997)

The MASC is a 39-item pediatric self-report anxiety scale that was designed to assess a wide spectrum of common anxiety symptoms in children across the elementary, junior, and senior high school age range. Children rate themselves on a 4-point Likert scale using the categories: “never true,” “rarely true,” “sometimes true,” and “often true.” The factors assessed by the MASC include Physical Symptoms (tense/restless and somatic/autonomic), Harm Avoidance (anxious coping and perfectionism), Social Anxiety (humiliation/rejection and public performance fears), and Separation Anxiety. The MASC factor structure has been cross-validated in clinical populations and population samples (March, Sullivan, & Parker, 1999) and in ADHD samples and is invariant across gender, race, and age (March et al., 1997). The instrument has been shown to have good internal consistency (.60 to .90) and test-retest reliability at 3 weeks and 3 months (.79 to .93) (March et al., 1997).

In addition to the empirically derived factors, the MASC also contains two embedded scales: one unifactorial short form intended for use in epidemiological and treatment outcome studies and a 12-item Anxiety Disorder Index (ADI) intended to discriminate anxious from both normal children and those with other types of psychopathology (March et al., 1999). Both the embedded scales have been shown to have excellent diagnostic efficiency (i.e., when used to discriminate anxious from normal children, the overall correct classification rate for the ADI subscale was 95%). When the

ADI was used to classify anxious and ADHD children, the overall classification rate was somewhat lower (71%), but still robust (Perrin & Last, 1992).

In order to examine the role of anxiety symptoms in the associations between HFA and frontal asymmetry, anxiety symptoms were assessed in both the HFA and non-HFA comparison group. Elevations in anxiety were determined based on self-reported anxiety symptoms on the MASC ADI and Total score. In addition to global level of anxiety, differences in cognitive processing components of individual anxiety disorders/symptoms (i.e., anxious arousal vs. anxious apprehension) are of interest in this study due to their hypothesized relation to anterior and posterior EEG asymmetry (Heller et al., 2003). Therefore, anxious arousal was measured using the following subscales of the MASC: Tense Restless Scale, Somatic Autonomic Scale, and the Physical Symptoms Total Scale, while anxious apprehension was measured using three different subscales of the MASC: Perfectionism Scale, Anxious Coping Scale, and the Harm Avoidance Total Scale.

Leyton Obsessional Inventory for Children and Adolescents (LOI; Berg, Whitaker, Davies, Flament, & Rapoport, 1988)

The LOI-Child Version is a 20-item questionnaire measuring symptoms of Obsessive Compulsive Disorder (OCD). Questions assess compulsions, obsessions, and the level of interference experienced by the child. The child is asked to respond yes or no to a question, and for the yes questions, to rate how much the thought or behavior interferes with their life based on a 4-point scale (i.e., 1 = This habit does not stop me from doing things vs. 4 = This habit stops me from doing many things). A total score is calculated, in addition to scores representing obsessions and compulsions. Internal

reliability is high ($\alpha = .81$). Further, the compulsions and obsessions scales reliably discriminated clinical cases of OCD from controls.

Anger Expression Measures

Pediatric Anger Expression Scale-Third Edition (PAES-III; Jacobs, Phelps, & Rohrs, 1989)

The PAES-III has been used to assess anger expression styles in children. The PAES-III includes three scales that measure anger turned inwardly, anger expressed outwardly, and anger controlled cognitively or behaviorally. The PAES-III consists of fifteen items read aloud to the child. The child responds verbally to each question by stating that the behavior occurs “hardly ever,” “sometimes,” or “often.” A card with the response choices is placed in front of the child as a visual reminder. In previous studies (Hagglund, Clay, Frank, & Beck, 1994), the three scales of the PAES-III demonstrated adequate internal consistency (Cronbach’s alpha ranging from .54 to .72). The PAES-III has also demonstrated adequate concurrent validity with other measures of anger expression.

Emotional Expression Scale for Children (EESC; Penza-Clyve & Zeman, 2002)

The EESC is a self-report scale designed to examine two aspects of problematic emotional expression: poor emotional awareness and reluctance to express negative emotion. Children read each statement to him/herself and respond using a 5-point Likert scale ranging from 1 (not at all true) to 5 (very true). The scale consists of 16 items and two factors: poor emotional awareness and expressive reluctance. On a community sample of 208 school age children, the two scales of the EESC showed good internal

consistency (Cronbach's alpha ranging from .81 to .83), and adequate test-retest reliability (Pearson's Correlation ranging from .56 to .59) after a two-week interval (Penza-Clyve & Zeman, 2002).

Convergent Data on Emotional Functioning from Parent Report of Child

Behavioral Assessment System for Children - Second Edition, Parent Rating Scale (BASC-2 PRS; Reynolds & Kamphaus, 2004)

The BASC-2 PRS is a parent-report questionnaire used to assess a parent's perception of a child's emotions, behaviors, and beliefs by asking them to choose how often a particular behavior occurs for their child (Never, Sometimes, Often, Always). Two forms are available depending on age level, child (6-11) and adolescent (12-18). Questions load onto scales measuring Hyperactivity, Aggression, Conduct Problems, Anxiety, Depression, Somatization, Atypicality, Withdrawal, and Attention Problems, Social Skills, and Leadership. In addition, composite scales measuring broad domains include Externalizing and Internalizing Problems, as well as adaptive scales measuring Relations with Parents and Interpersonal Relations are included. The child version contains one scale not included on the adolescent form, Adaptability. For the purposes of this study, the following scales were used: Hyperactivity (10 items, alpha = .86 for children, and 8 items, alpha = .82 for adolescents), Aggression (11 items, alpha = .87 for children, and 10 items, alpha = .87 for adolescents), Attention Problems (6 items, alpha = .87 for children, alpha = .88 for adolescents), Anxiety (14 items, alpha = .85 for children, and 11 items, alpha = .81 for adolescents), Depression (14 items, alpha = .88 for children, and 13 items, alpha = .86 for adolescents), Withdrawal (12 items, alpha = .81 for children, and 8 items, alpha = .82 for adolescents) and Social Skills (8 items, alpha = .87

for children, $\alpha = .88$ for adolescents). Detailed information on convergent and discriminant validity, as well as test-retest reliability, is adequate and reported in the manual. Age and gender norm-referenced T-scores were obtained for each scale. For all scales (with the exception of the Social Skills scale), higher scores index greater levels of impairment for the child/adolescent.

In order to examine the role of ADHD symptoms in populations of HFA children and adolescents, ADHD symptoms were assessed in both the HFA and non-HFA comparison group. Elevations in attention and hyperactivity were determined based on parent-reported symptoms of attention and hyperactivity problems on the BASC-2 PRS Attention Problems scale and/or the Hyperactivity scale.

Social Anxiety Scale for Children-Revised-Parent Version (SASC-R; La Greca & Stone, 1993)

The SASC-R Parent version assesses parents' perceptions of their child's social interactions including peer rejection and symptoms of social anxiety. Responses are rated on a scale from 1 ("not at all") to 5 ("all the time") based on the degree that the statement applies to their child. The scale contains 22 items and is comprised of 3 different subscales: Fear of Negative Evaluation from Peers (FNE), Social Avoidance and Distress-Specific (SAD-N), and Social Avoidance and Distress-General (SAD-G). Internal consistencies were satisfactory for mothers' and fathers' FNE, SAD-New, and SAD-G subscales, as well as the Total SASC-R/Parent scores (mothers' alphas were .93, .88, .78, and .94 respectively; fathers' alphas were .92, .88, .76, and .93 respectively) (Epkins, La Greca, & Steidnitz, 2004). Social anxiety on this measure has been linked to impairments in social functioning (LaGreca & Stone, 1993).

Electrophysiological Recordings

Resting EEG Asymmetry (Sutton et al., 2005)

Data collection procedures followed the same protocol as those described in Sutton et al. (2005). EEG was collected using a Lycra stretch electrocap with tin electrodes embedded in positions corresponding to the international 10-20 electrode system. EEG was recorded from 16 scalp sites (F7, F3, Fz, F4, F8, and FCz [frontal], C3, Cz, C4 [central], T7, T8 [anterior temporal], P3, Pz, P4 [parietal], O1, O2 [occipital]), with a ground electrode at site AFz. This electrode array is similar to that used in other studies (Henderson, Marshall, Fox, & Rubin, 2004; Sutton et al., 2005), and enables efficient cap placement and scalp preparation with children and adolescents (Sutton et al., 2005). Since source localization is not a goal of this study, a larger electrode array is not necessary. Prior to each recording session, a 50- μ V 10 Hz calibration signal will be inputted into each of the channels. During electrode placement children were allowed to watch a video or play a hand-held electronic game. A small amount of abrasive Omni-Prep was inserted into each of the active sites. Following gentle abrasion, impedances were measured at each site and considered acceptable if each site is at or below 5000 ohms and pairs of homologous sites are within 2000 ohms. EEG signals were referenced to the left ear lobe (A1). In order to derive an averaged-ears reference for analyses, an electrode was also placed on the right ear lobe (A2, referenced to A1). This reference scheme has support for use in the literature given a sufficiently large array of electrodes (Allen, Coan, & Nazarian, 2004). Eye movements (electro-oculograms, EOG) were recorded with electrode pairs placed vertically above and below one eye and horizontally to the right and left of each eye. During data acquisition children were instructed to

minimize head movements during a sequence of twelve 30-second trials in which they alternated between having their eyes closed and having their eyes open (fixating on a single dot on a blank wall four feet in front of the data acquisition chair).

CHAPTER 4: RESULTS

Data Preparation

Data accuracy in scoring and data entry were double checked by research staff. The means and distributions of all variables were examined for data entry errors, univariate outliers and odd distributions. Outliers were determined using a greater than three standard deviation from the mean criterion. Data that met or exceeded this criterion were removed from the dataset. Examination of the distribution determined no substantial skew or distribution anomalies; therefore, no transformations were necessary, (Kline, 1998; Cohen & Cohen, 1983).

Missing scores were observed for less than 5% of the data in this study (only four subjects). In order to maintain consistent sample sizes for all analyses, group mean substitution (HFA, N=51; CON, N=44) was used for two behavioral measures (BASC-PRS and SASC-R Parent Version) and one direct observation measure (i.e., ADOS). This procedure was used on four occasions: for subjects 124 and 46, group means were used for all BASC-PRS scale scores. Additionally, for subject 46, the group mean was used for the parent report SASC-R Total Score. For subjects 37 and 86, group means were used for ADOS domains scores (i.e., Communication Domain, Reciprocal Social Interaction Domain, and Repetitive Behaviors and Stereotyped Patterns Domain). For analyses where group means were substituted, results were computed both with and without group means to ensure that the substitution method did not artificially alter the results. For measures where greater than 5% of the data was missing (i.e., Q-DOS), mean substitution was not used and instead, analyses were run with less subjects (N = 33 subjects). All subjects included in the analyses had at least one occasion of useable EEG data. Subjects

with missing Time 2 EEG data were not included in the reliability analyses. Due to the qualitative nature of some items on the ADI-R, specified scores were recoded (i.e., from 990's codes to an estimate of age in months) so that the age of first disturbance could be better gleaned from the item.

Preliminary Analyses

Diagnostic Group Matching Analyses

Preliminary analyses were conducted to examine differences in chronological age, estimated Verbal Comprehension Index (VCI) and Perceptual Reasoning Index (PRI), and gender ratio between the diagnostic groups: HFA versus CON (non-HFA comparison sample). Where group differences were apparent, the measure was correlated with both midfrontal and parietal EEG asymmetry. Table 1 presents the means, standard deviations, F values, and p values on these variables for the HFA and CON samples respectively.

Results of an independent samples t -test indicated a near significant group difference on chronological age where children in the HFA sample were younger ($M=155$ months, $SD=30$ months) than children in the CON sample ($M=165$ months, 24 months), $t(93) = -1.83, p = .07$. Follow-up correlation analyses between age and midfrontal and parietal asymmetry indicated no significant relation in either diagnostic group, HFA: $F3/F4, r(51) = -.01, ns$; $P3/P4, r(51) = .10, ns$; CON: $F3/F4, r(44) = -.05, ns$; $P3/P4, r(44) = .02, ns$. Despite this apparent non-significant relation, chronological age was used as an independent factor in all primary analyses given the specific hypotheses related to the moderating effect of age on the association between EEG asymmetry and social-

emotional symptoms. Age groups were defined using a sample based median split at 163 months, as this statistic best divided the samples into comparable older and younger groups (Young $M = 135.30$ (17.54); Old $M = 182.34$ (10.92)). Group matching analyses specific to age are presented in the “Analyses Examining Associations of EEG Asymmetry, Age, and Social-Emotional Symptoms” section.

Results of a Chi Square analysis indicated significant differences on gender where the CON group consisted of more females (28 male/16 female) when compared to the HFA group (44 male/7 female), $X^2(1, 95) = 6.60, p = .01$. In order to examine the association between gender and midfrontal and parietal asymmetry in both diagnostic groups, a 2 (Diagnostic groups: HFA vs. CON) X 2 (Gender: Male vs. Female) MANOVA on midfrontal (F3/F4) and parietal (P3/P4) asymmetry was computed. Results indicated no significant effect of gender, Wilks' Lambda = .96, $F(3, 91) = 1.87, ns$, or the interaction between gender and group, Wilks' Lambda = 1.0, $F(3, 91) = .15, ns$, on asymmetry. Therefore, gender was not included as a covariate in the analyses.

Results of an independent samples t-test indicated significant group differences on the WISC-IV VCI such that children in the CON sample scored higher ($M=107$, $SD=12.88$) than children in the HFA sample ($M=100.59$, $SD=14.41$), $t(93) = -2.27, p < .05$. Follow-up correlation analyses between WISC-IV VCI and midfrontal and parietal asymmetry indicated no significant relation in either diagnostic group, HFA: F3/F4, $r(51) = .16, ns$; P3/P4, $r(51) = .07, ns$; CON: F3/F4, $r(44) = -.02, ns$; P3/P4, $r(44) = .02, ns$. Therefore, VCI was not included as a covariate in the analyses. No group differences were found on nonverbal cognitive functioning; WISC-IV PRI, $t(93) = .06, ns$.

Analyses of Attention/Hyperactivity and Anxiety Symptoms

The elevated occurrence of ADHD symptoms in populations of children with HFA, as well as research showing associations between externalizing symptoms and anterior EEG data, suggested that the correlation of parent report of ADHD symptoms (i.e., BASC-2 PRS Attention Problems Scale and Hyperactivity Scale) with midfrontal asymmetry be examined separately in both groups. Within the HFA group, results of correlation analyses indicated marginally significant associations between parent report of hyperactivity symptoms and midfrontal asymmetry, $r(51) = -.27, p = .06$, but no significant relations between parent report of attention problems and midfrontal asymmetry, $r(51) = -.18, ns$. In the CON group, results of correlation analyses indicated no significant associations between parent report of ADHD symptoms and midfrontal asymmetry, Attention Problems Scale, $r(44) = .08, ns$; Hyperactivity Scale, $r(44) = .16, ns$. Given these marginally significant associations, hyperactivity symptoms were controlled for in all HFA within group analyses.

Likewise, given the high occurrence of comorbid anxiety symptoms experienced by children with HFA and the documented association of anxiety and EEG asymmetry, the correlation of self-reported anxiety symptoms (i.e., MASC Anxiety Disorder Index and MASC Total Score) with midfrontal and parietal asymmetry was examined separately in both groups. Interestingly, results of correlation analyses indicated no significant associations between midfrontal asymmetry and self-reported anxiety in the HFA and CON groups. However, associations between parietal asymmetry and self-reported anxiety were significant in only the HFA sample, HFA: MASC Total Score, $r(51) = .29, p < .05$; MASC ADI, $r(51) = .27, p = .056$; CON: MASC Total Score, $r(44)$

= .25, *ns*; MASC ADI, $r(44) = .20$, *ns*. The relation of posterior asymmetry and anxiety will be examined in primary analyses investigating the effect of anxiety subtypes on the relation of symptoms to posterior asymmetry.

Medication Effects

Parent report on children's psychotropic medication was categorized. Children exposed to specific classes of medication ($N = 20$) vs. no medication ($N = 75$) were compared to examine possible effects on the EEG asymmetry predictor variables (i.e., F3/F4 and P3/P4). No systematic effects of medication were revealed, $t(93) = .35$, *ns* for F3/F4, and $t(93) = -.43$, *ns* for P3/P4.

Primary Analyses

Analysis of Reliability of Midfrontal and Parietal EEG Asymmetry

To examine the reliability of midfrontal and parietal EEG asymmetry in HFA and CON children and adolescents, zero-order Pearson correlations for midfrontal and parietal asymmetry scores at Time 1 and Time 2 were computed for the entire sample, and then separately for each diagnostic and age group. To account for the possible effect of time interval between Time 1 and Time 2 EEG assessments, follow-up partial correlations controlling for time interval were also computed on the specified groups. Table 2 presents EEG midfrontal and parietal asymmetry reliability data for the entire sample, and separately for the diagnostic and age groups.

Results indicated significant test-retest reliability for midfrontal and parietal asymmetry scores across the entire sample, $r(65) = .39$ at F3/F4, $p < .01$; $r(65) = .60$ at

P3/P4, $p < .01$ (See Figure1 for midfrontal asymmetry scatter plot). These associations were unchanged after controlling for time interval, $r(65) = .39$ at F3/F4, $p < .01$; $r(65) = .61$ at P3/P4, $p < .01$.

To examine diagnostic group differences in test-retest reliability, zero-order Pearson correlations for midfrontal and parietal asymmetry at Time 1 and Time 2 were computed separately for each diagnostic group (see Figures 2 and 3 for midfrontal asymmetry scatter plots for each diagnostic group). Results indicated significant test-retest reliability of midfrontal and parietal asymmetry within the HFA sample, $r(35) = .43$ at F3/F4, $p = .01$; $r(35) = .66$ at P3/P4, $p < .01$. These associations were unchanged after controlling for time interval, $r(35) = .42$ at F3/F4, $p = .01$; $r(35) = .66$ at P3/P4, $p < .01$. Within the CON sample, results indicated significant test-retest reliability for parietal, but not midfrontal asymmetry, $r(30) = .28$, at F3/F4, ns ; $r(30) = .62$ at P3/P4, $p < .01$. These associations were unchanged after controlling for time interval, $r(30) = .29$ at F3/F4, ns ; $r(30) = .69$ at P3/P4, $p < .01$.

To examine the effect of age on the reliability of midfrontal and parietal asymmetry in children and adolescents with and without HFA, zero-order Pearson correlations for midfrontal and parietal asymmetry at Time 1 and Time 2 were computed separately for each age group (see Figures 4 and 5 for midfrontal asymmetry scatter plots for each age group). Results indicated significant test-retest reliability of midfrontal and parietal asymmetry within the Young group, $r(33) = .50$ at F3/F4, $p < .01$; $r(33) = .65$ at P3/P4, $p < .01$. These associations were unchanged after controlling for time interval, $r(33) = .52$ at F3/F4, $p < .01$; $r(33) = .66$ at P3/P4, $p < .01$. Within the Old group, results indicated significant test-retest reliability for parietal, but not midfrontal asymmetry, $r(32) =$

.27, at F3/F4, *ns*; $r(32) = .58$ at P3/P4, $p < .01$. These associations were unchanged after controlling for time interval, $r(32) = .26$ at F3/F4, *ns*; $r(32) = .59$ at P3/P4, $p < .01$.

Analyses Examining Associations of EEG Asymmetry, Age, and Social-Emotional Symptoms

Given the specific hypotheses related to the moderating effect of age on the associations between EEG asymmetry and outcome variables, age was used as an independent factor in all primary analyses. Therefore, preliminary diagnostic and age subgroup matching analyses were conducted to examine differences in chronological age, estimated Verbal Comprehension Index (VCI) and Perceptual Reasoning Index (PRI), and gender ratio between the diagnostic and age subgroups (HFA Young vs. HFA Old vs. CON Young vs. CON Old). As discussed in the “Preliminary Analyses” section, age groups were defined using a sample based median split at 163 months (Young $M = 135.30$ (17.54); Old $M = 182.34$ (10.92)). Table 3 presents the diagnostic and age group data on group matching variables (i.e., age in months, VCI and PRI).

Results of a 2 (Diagnostic groups: HFA vs. CON) X 2 (Age groups: Young vs. Old) MANOVA on chronological age, VCI, and PRI indicated a significant main effect of age group, Wilks’ Lambda = .27, $F(3, 91) = 80.93$, $p < .01$. Main effects of diagnostic group were discussed in the “Preliminary Analyses” section. Follow-up univariate analyses indicated the expected age group differences on age in months, $F(3, 91) = 241.81$, $p < .01$. Although the overall interaction of diagnostic and age groups was not significant, univariate analyses indicated a significant interaction on age, $F(3, 91) = 4.29$, $p < .05$. Post hoc analyses indicated that children in the HFA-Young sample were significantly younger ($M=155$ months, $SD=30$ months) than children in the CON-Young

sample (M=165 months, 24 months), $t(44) = -1.96, p = .056$. The effects of age will be examined in all future analyses. Additionally, results of a Chi Square examining the comparability of gender ratio between the diagnostic and age subgroups indicated no significant differences between groups, $X^2(1, 95) = 6.71, ns$. Therefore, gender was not included as a covariate in the analyses.

Within- HFA Group Analyses

Following methods outlined in Pradella (2006), anterior asymmetry subgroups for Left Frontal Asymmetry (LFA) and Right Frontal Asymmetry (RFA) were established by examining the midfrontal EEG alpha asymmetry index (i.e., F3/F4). All positive values were classified as LFA and all negative values were classified as RFA. EEG asymmetry scores with a value of 0.0 were classified as LFA. Additionally, parent report of hyperactivity symptoms (i.e., BASC-2 PRS Hyperactivity Scale) was used as a covariate in all within group analyses given the previously reported significant correlation between hyperactivity symptoms and midfrontal asymmetry in the HFA group.

EEG Asymmetry and Relation to Developmental Course of Symptom Impairment

In order to examine the association between midfrontal asymmetry and parent report of developmental course and symptom onset, two separate analyses were computed using Chi Square (i.e., only for ADI-R item #86) and group mean comparison methods, determined by the categorical vs. continuous nature of the ADI-R item involved. Table 4 presents asymmetry group means and standard deviations for four

items of the ADI-R concerning developmental course and symptom onset. Table 5 presents categorical data on ADI-R item #86.

Results of a Chi Square analysis examining the association between asymmetry group and ADI-R item # 86, “Age When Abnormality First Evident,” indicated significant differences on asymmetry group, $X^2(51) = 3.75, p = .05$. Examination of the ADI-R item X asymmetry group cross tabulation indicated that the RFA group consisted of significantly more subjects who were coded as exhibiting behaviors strongly indicative of autism by the age of three (20 RFA/11 LFA), while the LFA group consisted of more subjects exhibiting behavior indicative of atypicality, but not clearly autism by age three (11 LFA/6 RFA). To examine asymmetry group differences on the continuous ADI-R items (#’s 2, 9, 10, and 87), an independent samples *t*-test was computed. Although results did not yield significant asymmetry group differences, examination of the group means indicated patterns consistent with hypothesized relations of asymmetry group and developmental course of symptom impairment. Specifically, parents of HFA children with RFA reported earlier age of onset (#2) when compared to HFA children with LFA. Likewise, examiner’s judgment of age of onset (#87) was earlier for HFA children with RFA when compared to their LFA counterparts. Age of first words and phrases (item #’s 9 and 10) indicated that parents of children with RFA reported slightly earlier age of language acquisition when compared to LFA children.

EEG Asymmetry and Parent Report of Symptoms of Social Communication Impairment

To address the hypothesis that LFA children will display fewer symptoms of impairment on parent report measures of social communication, two MANCOVA’s were

computed. First, a 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANCOVA covarying for hyperactivity symptoms was computed on the SCQ Total Score, ASSQ Total Score, and SRS Total Score. Table 6 presents means and standard deviations for parent report measures of social communication symptoms for age and asymmetry groups. Results indicated a significant main effect of hyperactivity symptoms, Wilks' Lambda = .82, $F(3, 47) = 3.25, p < .05$. No significant multivariate effects of asymmetry group, age group, or the interaction of asymmetry and age group were observed. Follow-up univariate analyses indicated significant effects of hyperactivity symptoms on the ASSQ Total Score, $F(3, 47) = 9.24, p < .01$, and the SRS Total Score, $F(3, 47) = 6.37, p < .05$. Additionally, although the main effect of asymmetry group was not significant, univariate effects were examined given their relevance to specified hypotheses in this study. These results showed a marginally significant difference between LFA and RFA groups on SCQ Total Score, $F(3, 47) = 3.58, p = .065$. Examination of group means indicated that parents of children with RFA reported significantly greater levels of social communication impairment on the SCQ Total Score when compared to parent report of children with LFA.

A second, 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANCOVA covarying for hyperactivity symptoms was computed on two composite scales of the CCC-2, the General Communication Composite (GCC) and Social Interaction Deviance Composite (SIDC). Results indicated a significant main effect of hyperactivity symptoms, Wilks' Lambda = .76, $F(3, 47) = 7.15, p < .01$, and asymmetry group on parent report of social communication symptoms, Wilks' Lambda = .86, $F(3, 47) = 3.67, p < .05$. No significant effect of age group or the interaction of

asymmetry and age group was observed. Follow-up univariate analyses indicated a significant effect of hyperactivity symptoms on only the GCC, $F(3, 47) = 10.59, p < .01$. Additionally, univariate analyses indicated significant differences between LFA and RFA groups on both the GCC, $F(3, 47) = 6.83, p = .01$, and the SIDC, $F(3, 47) = 4.41, p < .05$. Interestingly, examination of group means on the CCC-2's GCC and SIDC indicates that consistent with the SCQ findings, parents of HFA children with LFA report higher levels of general communicative skills; however, they also report greater impairment in the social interaction domain (pragmatics of language).

A follow up MANCOVA was computed on individual subscales of the SCQ to determine if there were domain specific effects by asymmetry and age groups. See Table 6 for asymmetry and age group means and standard deviations of parent report measures of social communication symptoms. A 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANCOVA covarying for hyperactivity symptoms was computed on the Repetitive Behaviors Domain, Communication Domain, and the Social Interaction Domain subscale scores. Results indicated a significant main effect of hyperactivity symptoms on social communication symptoms, Wilks' Lambda = .82, $F(3, 47) = 3.21, p < .05$. Additionally, the interaction of asymmetry and age group was not significant. Follow-up univariate analyses indicated significant effects of hyperactivity symptoms on the SCQ Communication Domain, $F(3, 47) = 7.92, p < .01$. Additionally, although the main effect of asymmetry group was not significant, univariate effects were examined given their relevance to specified hypotheses in this study. These results indicated a significant effect of asymmetry group on the SCQ Social Interaction Domain $F(3, 47) = 4.59, p < .05$. Examination of asymmetry group means on the SCQ Social

Interaction Domain indicated that, contrary to the CCC-2 SIDC, parents of children with RFA reported higher levels of impairment when compared to children with LFA.

EEG Asymmetry and Direct Observation of Social Symptoms

In order to extend findings based on parent report, the effect of asymmetry group and age group on direct observation measures of social communication impairment was also examined. Two MANCOVA's were computed on data from the ADOS and Q-DOS. Table 7 presents asymmetry and age group means and standard deviations for direct observation measures of social communication skills. First, a 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANCOVA covarying for hyperactivity symptoms was computed on the ADOS Communication Domain Total Score, the ADOS Reciprocal Social Interaction Domain Total Score, and the ADOS Repetitive Behaviors and Stereotyped Patterns Domain Total Score. Results indicated no significant effects. An identical 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANCOVA covarying for hyperactivity symptoms was computed on the Q-DOS proportion of social and nonsocial eye contact, proportion of social and nonsocial smiles, and overall sociability composite. Results indicated no significant effects.

Between Group Analyses

MANOVA for EEG Asymmetry Variables

To examine the effect of diagnostic group and age on midfrontal and parietal EEG asymmetry, a 2 (Diagnostic groups: HFA vs. CON) X 2 (Age groups: Young vs. Old) MANOVA was conducted on the midfrontal and parietal asymmetry indices (i.e., F3/F4

and P3/P4). Results indicated no significant effect of diagnostic group, age, or the interaction of diagnostic and age groups.

EEG Asymmetry and Anxiety

To examine the relation between diagnostic, asymmetry, and age groups on symptoms of emotional impairment, including anxiety, three MANOVA's were computed. First, a 2 (Diagnostic groups: HFA vs. CON) X 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANOVA was computed on child report data of anxiety/dysphoria (BASC-2 SRP Anxiety Scale, Depression Scale, Social Stress Scale, and Interpersonal Relations Scale; LOI Total score; and MASC Total Score). Table 8 presents diagnostic, age, and asymmetry group means and standard deviations for self-report measures of emotional impairment. Results indicated an expected main effect of diagnostic group where HFA children reported more anxiety symptoms than children in the CON sample, Wilks' Lambda = .63, $F(7, 87) = 9.93$, $p < .01$. No main effect of asymmetry group or age group was observed. Additionally, the interactions of asymmetry, age, and diagnostic groups were not significant. Follow-up univariate analyses indicated significant differences between diagnostic groups on all self-report measures, $p < .01$. Additionally, although the main effect of age group was not significant, univariate effects were examined given that age effects were of interest in this study. These results indicated significant differences between age groups on the LOI Total Score, $F(7, 87) = 7.09$, $p < .01$, such that younger children across both diagnostic groups reported significantly more obsessive-compulsive symptoms when compared to older children.

A second, 2 (Diagnostic groups: HFA vs. CON) X 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANOVA was computed on child report data of anxiety specific to social situations, (SASC-R Fear of Negative Evaluation (FNE), SASC-R Social Avoidance and Distress-Specific to new situations (SAD-N), SASC-R Generalized Social Avoidance and Distress (SAD-G), and the SASC-R Total Score). See Table 8 for diagnostic, age, and asymmetry group means and standard deviations for self-report measures of social anxiety. Results again indicated an expected main effect of diagnostic group where HFA children reported more social anxiety symptoms than children in the CON sample, Wilks' Lambda = .77, $F(7, 87) = 8.49$ $p < .01$. No main effect of asymmetry group or age group was observed. Additionally, the interactions of asymmetry, age, and diagnostic groups were not significant. Follow-up univariate analyses indicated significant differences between diagnostic groups on all self-report measures of social anxiety, $p < .01$. Additionally, although the main effect of asymmetry group was not significant, univariate effects were examined given their relevance to specified hypotheses in this study. These results indicated a trend toward a significant difference between LFA and RFA groups on the SASC-R (SAD-G), $F(7, 87) = 3.00$, $p = .087$. Examination of group means on the SASC-R (SAD-G) indicates children with RFA reported more social anxiety symptoms than children with LFA across both HFA and CON samples.

A third, 2 (Diagnostic groups: HFA vs. CON) X 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANOVA was computed on parent report data of social-emotional symptoms (SASC-R Social Anxiety Total Score and BASC-2 PRS Anxiety, Depression, Social Stress, and Interpersonal Relations). Table 9 presents

diagnostic, age, and asymmetry group means and standard deviations for parent-report measures of social-emotional impairment. Results again indicated an expected main effect of diagnostic group where parents of HFA children reported more social-emotional symptoms than parents of children in the CON sample, Wilks' Lambda = .71, $F(7, 87) = 11.85$, $p < .01$. No main effect of asymmetry group or age group was observed. Additionally, the interactions of asymmetry, age, and diagnostic groups were not significant. Follow-up univariate analyses indicated significant differences between diagnostic groups on all parent-report measures of social-emotional impairment, $p < .01$. Additionally, although the multivariate interaction between diagnostic and asymmetry groups was not significant, univariate effects were examined given their relevance to specified hypotheses in this study. These results indicated a marginally significant interaction between diagnostic and asymmetry groups on the BASC-PRS Anxiety Subscale, $F(7, 87) = 3.39$, $p = .069$.

Post hoc comparisons indicated that there were greater differences in parent report of anxiety symptoms between diagnostic groups among children with RFA as compared to children with LFA. Specifically, RFA-HFA children were rated by their parents as experiencing more anxiety symptoms compared to RFA-CON children, $t(43) = 4.77$, $p < .01$, and LFA-HFA children were rated higher on anxiety symptoms compared to LFA-CON children, $t(51) = 1.96$, $p = .056$. However, there was no effect of asymmetry group within the HFA and CON groups

EEG Asymmetry and Anxiety: Evaluation of the Cognitive Processing Components of Anxiety

To examine the relation of diagnostic group, asymmetry group, and age with cognitive processing subtypes of anxiety symptoms, two MANOVA's were computed on measures of anxious apprehension and anxious arousal respectively. Given the literature on the differential association of these anxiety subtypes to EEG asymmetry, midfrontal asymmetry was used in the anxious apprehension analysis and parietal asymmetry was used in the anxious arousal analysis. Posterior asymmetry subgroups were defined using the same parameters as was discussed for the anterior subgroups (i.e., all positive values including 0.0 were classified as Left Posterior Asymmetry (LPA) and all negative values were classified as Right Posterior Asymmetry (RPA). Tables 10 and 11 present diagnostic, age, and asymmetry group means and standard deviations for self-reported anxious apprehension and arousal anxiety symptoms for the corresponding asymmetry subgroup (i.e., anterior asymmetry subgroups used for anxious apprehension symptoms (Table 10) and posterior asymmetry subgroups used for anxious arousal symptoms (Table 11)).

First, a 2 (Diagnostic Groups: HFA vs. CON) X 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANOVA was computed on child report of anxiety symptoms associated with anxious apprehension (MASC Perfectionism Scale, MASC Anxious Coping Scale, and the MASC Harm Avoidance Subdomain Total Score). No main effect of diagnostic, asymmetry, or age groups were observed. Results indicated only the interaction of asymmetry and age groups trended toward significance (Wilks' Lambda = .93, $F(7, 87) = 2.28$, $p = .09$). Follow-up univariate analyses indicated a significant interaction of asymmetry and age groups on two measure of anxious

apprehension: the MASC Anxious Coping Scale, $F(7, 87) = 6.28, p = .01$, and the MASC Harm Avoidance Domain Total Score, $F(7, 87) = 6.79, p = .01$. Post hoc comparisons indicated that younger RFA children reported significantly more symptoms of anxious apprehension than younger LFA children, (Anxious Coping Scale: $t(44) = 2.40, p < .05$; Harm Avoidance Domain Scale: $t(44) = 2.40, p < .05$) and older RFA children, (Anxious Coping Scale: $t(43) = 2.63, p < .05$; Harm Avoidance Domain Scale: $t(43) = 2.63, p = .01$). However, there was no effect of asymmetry group among children in the older age group.

Secondly, a 2 (Diagnostic Groups: HFA vs. CON) X 2 (Asymmetry groups: LPA vs. RPA) X 2 (Age groups: Young vs. Old) MANOVA was computed on child report of anxiety symptoms associated with autonomic arousal (MASC Tense Restless Scale, MASC Somatic Autonomic Scale, and the MASC Physical Symptoms Subdomain Total Score). Results indicated a main effect of age group where younger children reported more symptoms of anxious arousal when compared to older children, Wilks' Lambda = .90, $F(7, 87) = 3.21, p < .05$. No main effect of diagnostic or asymmetry group was observed. Results also indicated a significant interaction of diagnostic and asymmetry group, Wilks' Lambda = .91, $F(7, 87) = 2.73, p < .05$. Follow-up univariate analyses indicated a significant effect of age group on two anxious arousal scales, such that younger children reported more anxious arousal symptoms than older children, MASC Tense Restless Scale, $F(7, 87) = 8.50, p < .01$; MASC Physical Symptoms Domain Total Score, $F(7, 87) = 5.28, p < .05$. Results also showed a significant interaction of diagnostic and asymmetry group on the MASC Somatic Autonomic Scale, $F(7, 87) = 5.89, p < .05$. Post hoc comparisons indicated that HFA children with LPA reported

significantly more anxious arousal symptoms when compared to CON children with LPA, $t(64) = 3.80, p < .01$. However, there was no effect of diagnostic group among children with RPA, or an effect of asymmetry group among HFA and CON children.

EEG Asymmetry and Anger/Emotional Expression

To examine the relation between diagnostic group, asymmetry group, and age on symptoms of anger and emotional expression, a 2 (Diagnostic groups: HFA vs. CON) X 2 (Asymmetry groups: LFA vs. RFA) X 2 (Age groups: Young vs. Old) MANOVA was conducted on the PAES-III Anger In, Anger Out, and Anger Control Scales; the EESC Expressive Reluctance and Poor Awareness Scales; and the BASC-2 PRS Aggression Scale. Table 12 presents diagnostic, age, and asymmetry group means and standard deviations for self- and parent-reported anger/emotional expression symptoms.

Results indicated an expected main effect of diagnostic group where HFA children reported more anger/emotional expression symptoms than children in the CON sample, Wilks' Lambda = .79, $F(7, 87) = 3.67, p < .01$. No main effect of asymmetry group or age group was observed. Only the interaction of diagnostic and asymmetry groups was significant, Wilks' Lambda = .86, $F(7, 87) = 2.22, p < .05$. Follow-up univariate analyses indicated significant differences between diagnostic groups on three measures of anger/emotional expression, $p < .05$ for all measures (i.e., EESC Poor Awareness, EESC Expressive Reluctance, and BASC-2 PRS Aggression Scale). Additionally, although the main effect of age group was not significant, univariate effects were examined given that age effects were of interest in this study. These results indicated a significant difference between age groups on the EESC Poor Awareness

Scale, $F(7, 87) = 4.68, p < .05$, such that younger children reported greater symptoms of poor emotional awareness when compared to older children. Results also indicated a significant interaction of diagnostic and asymmetry groups on the PAES Anger Control scale, $F(7, 87) = 6.30, p = .01$. Post hoc comparisons indicated that HFA children with LFA reported more anger control symptoms when compared to HFA children with RFA, $t(49) = -2.41, p < .05$. However, there was no effect of asymmetry group among CON children or diagnostic group effect among children with RFA or LFA asymmetry.

Results also indicated a significant interaction of diagnostic and age groups on the EESC Expressive Reluctance Scale, $F(7, 87) = 4.93, p < .05$. Post hoc comparisons indicated that younger children in the CON group reported more symptoms of expressive reluctance when compared to older CON children, $t(42) = 2.04, p < .05$, and older HFA children reported more symptoms when compared to older CON children, $t(47) = 3.58, p < .01$. However, there was no effect of age group within HFA children or diagnostic group effect among younger children.

CHAPTER 5: DISCUSSION

Summary of Study Goals

The goals of this study were to replicate and extend previous findings (Sutton et al., 2005; Burnette, 2005) on the relation of EEG asymmetry to autism syndrome-specific symptoms and comorbid psychopathology in populations of children with and without high functioning autism (HFA). Additionally, this study elaborated on previous self- and parent-reported findings of social impairment and comorbid social-emotional symptoms by including in vivo assessment of social interaction via the ADOS (Lord et al., 2000) and Q-DOS. Unique to this examination of EEG asymmetry in a population of HFA and non-HFA children and adolescents was the short-term longitudinal study design, allowing for two occasions of psychophysiological measurement. In this way, reliability of the measure itself could be examined, ultimately aiding in the valid interpretation of the results.

Reliability of EEG Asymmetry

Our previous research has suggested that measures of EEG asymmetry may be a useful marker of phenotypic variability in HFA children (Burnette, 2005; Sutton et al., 2005). However, before the validity of this type of measurement can be clearly evaluated, it is first important to understand its psychometric characteristics. In this regard, estimates of the stability or test-retest reliability of individual differences in EEG asymmetry among HFA children are especially important as measures with low reliability can impede or confound the ability to detect individual differences, and in this way, affect the validity of study results. Therefore, a central aim of this study was to provide the first

data on the test- retest reliability of EEG asymmetry in older children (135.30 months or 11.3 years) and adolescents (182.34 months or 15.2 years) both with and without HFA. Results of our short-term longitudinal study over an approximate 11-week time interval revealed moderate test-retest reliability for both midfrontal and parietal asymmetry across the entire sample (correlations of .39 and .60 respectively). However, analyses examining the stability of EEG asymmetry patterns *within* diagnostic and age groups varied by region, such that reliability at parietal sites was in the moderate range and relatively consistent across diagnostic and age groups (correlations ranged from .58 to .66), while reliability at midfrontal sites was more variable. Specifically, children in the HFA group and the Young group displayed significant test-retest reliability in the moderate range (correlations of .43 and .50 respectively), while children in the CON group and the Old group displayed low test-retest reliability (correlations of .28 and .27 respectively).

These findings add to previous related research. Studies with adults have reported fairly consistent findings of moderate test-retest reliability, similar to those observed for the HFA sample in this study, across varying time intervals (Sutton & Davidson, 1997; Tomarken et al., 1992; Vuga et al., 2006). Research with infants and young children has been equivocal with some studies reporting significant strong stability correlations over a 2.5 year interval from infancy to age 3 (Jones et al., 1997), while others have reported low to moderate stability across a 1 month interval and poor stability across 5 months (Fox et al., 1992). Vuga, Fox, Cohn, Kovacs, and George (2008) recently investigated the stability of EEG asymmetry over a one year time interval in typically developing children and children at-risk for depression ranging in age from 3 to 9 years (i.e., preschool age, 3-5 and school age, 6-9 years). Data indicated moderate test-retest reliability of midfrontal

asymmetry scores for preschool age children (correlations ranged from .31 to .48), and low to moderate test-retest reliability for school age children (correlations ranged from .18 to .45). Taken together, these findings support a state-trait model of EEG asymmetry, where asymmetry provides a reliable index of trait like BAS and BIS predispositions in children, including children affected by HFA. However, data in this study and elsewhere suggest that state factors, such as age and/or neurodevelopmental status, affect the stability of EEG asymmetry.

Age has been observed to impact cortical activity estimates (i.e., EEG alpha power and asymmetry) and the association of EEG asymmetry and social-emotional variables in several studies of children and adolescents with and without clinical diagnoses (Baving et al., 2002; Forbes et al., 2006; Pradella, 2006; Vuga et al., 2008). Results from the current study, along with the findings from past research examining the stability of EEG asymmetry across child development, indicate that reliability of anterior EEG asymmetry appears to vary as a function of age. It is interesting and important to acknowledge that posterior asymmetry estimates were stronger and more consistent when compared to anterior asymmetry estimates in this study. This observation provides insight into the underlying mechanisms involved in the accurate measurement of anterior asymmetry. One possibility for this variability is that ongoing neurodevelopmental shifts in the prefrontal cortex, which occur in disproportionately greater amounts during certain periods of development (i.e., puberty), impact the precision with which anterior EEG asymmetry can be measured.

Pradella (2006) discussed the possibility of neurodevelopmental changes impacting the pattern and meaning of EEG asymmetry in childhood and adolescence.

Specifically, the development and maturation of the dorsolateral prefrontal cortex (DLPFC) and the orbital frontal cortex (OFC), two structures which have been implicated in source localization studies of EEG asymmetry, were considered (Pizzagalli et al., 2005). Given research indicating that maturation of the DLPFC and OFC continues through adolescence (Blakemore & Choudhury, 2006), it was suggested that the age-based differences in the association of EEG asymmetry to social-emotional symptoms observed in their study reflected aspects of that maturation process (Pradella, 2006). Additionally, the possible impact of pubertal hormonal shifts was considered given research showing differences in synaptic connections in the prefrontal cortex pre- and post- puberty (Blakemore & Choudhury, 2006). Specifically, studies indicated a proliferation of synapses in the prefrontal cortex pre-pubertal onset, which is followed by elimination and reorganization of synaptic connections after puberty resulting in a gradual decrease in synaptic density in the frontal lobes in adolescence (Huttenlocher, 1979; Bourgeois et al., 1994; Woo et al., 1997). In considering the neurodevelopmental sensitivity of the older child (averaged age 11.3 years) and adolescent (averaged age 15.2 years) in the context of ongoing development, this research offers a possible explanation for the observed variability in the stability of anterior EEG asymmetry.

In addition to age effects on anterior EEG asymmetry stability estimates, diagnostic group also affected test-retest reliability. One possibility for the HFA groups' greater test-retest reliability may be because extreme temperaments or clinical diagnoses affect the stability of EEG asymmetry. This idea has some support in the depression literature, where some studies have found EEG asymmetry to be a stable measure of a predisposition to depression and therefore, not affected by changes in symptom severity.

In a study of seasonal affective disorder, Allen et al (1993) found evidence of stability in that depressed patients demonstrated relative less left frontal activity than controls both when symptomatic and when remitted two weeks later. Allen, Urry, Hitt, and Coan (2004) reported similar findings in a sample of adult female depressed patients. Results indicated moderate test-retest reliability over 8- and 16-week intervals regardless of changes in clinical state. Interestingly, the inverse was found in a study examining the test-retest reliability in depressed and non-depressed adults undergoing pharmacotherapy (Debener et al., 2000). Results indicated that the groups differed in temporal stability, where test-retest reliability was significant for controls, but not depressed patients. Examination of the asymmetry scores across assessments indicated random, or non-systematic, variability across sessions, which the authors concluded may be, in and of itself, a trait marker for depression. Given the pronounced temperamental differences exhibited by some children with HFA when compared to a non-HFA control sample and the consideration of the longstanding difficulties associated with autism as characterized by a developmental disorder, the reliability of a hypothesized trait marker of a temperamental feature (approach vs. withdrawal) is understandable and somewhat expected. Conversely, the lack of stability exhibited in the comparison sample may be reflective of a more moderate temperamental style and/or affective symptom profile, which increases the likelihood of susceptibility to state-like factors.

A discussion of the state and trait properties of EEG asymmetry is needed to account for the fact that although research with adults has shown that between 40 and 50% of the variance of anterior asymmetry is due to individual differences on a latent trait, the remainder is associated with state-specific factors (Hagemann, 2004; Hagemann

et al., 2005). As reviewed, Coan and Allen (2003a) offer two potential sources of non-trait variance in anterior EEG asymmetry scores: 1) occasion-specific but reliable variations in frontal asymmetry that characterize the variation in resting EEG assessments across multiple sessions of measurement (variations that are characteristic of the individual), and 2) state-specific changes in frontal asymmetry that characterize the difference between two conditions or between baseline resting levels and some condition. Although state-specific factors (e.g., the novel testing environment) could account for a portion of the variance in state-specific changes in EEG asymmetry, these effects are presumably relatively low because all subjects were exposed to these random factors. Additionally, given that EEG asymmetry is a baseline measure, no explicit experimental manipulation or stimulus presentation is involved. This leaves the possibility that factors involved in diagnosis and age (as discussed above) affect the degree to which some subjects (i.e., CON children and Old children) are more susceptible to state factors, while others (i.e., HFA children and Young children) are more resistant to the influence of state factors. Indeed, the idea that there may be individual differences in the magnitude of occasion-fluctuations has been proposed (Coan & Allen, 2003a). In at least two studies assessing test-retest reliability in anterior asymmetry, investigators classified participant data as stable or not stable based on whether their standardized second session score was within one third of a standard deviation of their standardized first session score (Tomarken et al., 1992; Wheeler et al., 1993). Interestingly, variability in at least one of these studies was considerable (only 32% of the sample demonstrated stability) (Wheeler et al., 1993). Moreover, the magnitude of the correlations between EEG asymmetry and some dependent measures of positive and negative affect were conditional on this

classification of stability, where the correlation of asymmetry and a measure of negative affect was significant and in the expected direction for those subjects with stable EEG asymmetry ($r = -.47$), but not unstable ($r = -.02$) (Tomarken et al., 1992). These studies provide evidence of the documented variability in stability of EEG asymmetry and highlight the potential impact of unstable asymmetry data in muddying the waters of interpretation. The abovementioned potential factors (i.e., neurodevelopmental factors associated with chronological age and pubertal status, variations in temperament or clinical diagnosis, and individual differences in stability) offer potential sources that contribute to this variability. Additionally, these studies offer a possible explanation for why some of the hypothesized relations between EEG asymmetry and social-emotional symptoms (e.g., in the CON sample) were not significant in this study. Perhaps, in a larger sample, where stability groupings could be computed, the hypothesized associations would be significant.

Anterior Asymmetry Subgroups as an Indicator of Individual Difference within HFA Children

Evidence for the reliability of EEG asymmetry bolsters the hypothesis that this type of measure may be a useful marker of meaningful differences in the behavior of HFA children. To further evaluate this hypothesis, a primary goal of this study was to replicate and extend observations of the association between anterior EEG asymmetry and varying levels of social communication impairment among children with HFA. Previous findings indicated that parents reported greater symptom severity for RFA versus LFA children with HFA on measures such as the SCQ Total score and SCQ Social Interaction Domain score (Sutton et al., 2005; Burnette, 2005). Consistent with

these findings, the results of this study indicated marginally significant differences with parents of RFA children reporting higher levels of impairment than LFA children on the same SCQ measures.

Perhaps even more informative were the new observations that HFA children with LFA were rated by their parents as demonstrating higher overall communicative competence (CCC-2 GCC), but greater impairment on scales of pragmatic or nonverbal communication (CCC-2 SIDC). Additionally, these data replicated the finding that anterior asymmetry subgroups differentiated HFA children based on retrospective parent report of developmental course and symptom onset. Significant findings from this study are in line with data reported in Burnette (2005), albeit on a different ADI-R item (i.e., “Age when Abnormality First Evident”), and indicate that negative asymmetry scores (i.e., RFA) are associated with early and more confident recognition of atypical (and stereotypically autistic) development, while positive asymmetry scores (i.e., LFA) are associated with early, but less unambiguously autistic impairment. Contrary to our expectations, direct observation measures of social communication impairment (i.e., ADOS and Q-DOS) demonstrated little sensitivity to individual differences on social approach and avoidance continuums within children with HFA.

The seemingly contradictory findings with the SIDC of the CCC-2 and the SCQ’s Social Interaction Domain are elucidated when considering the particular items comprising each scale. Careful review of the items included in the SCQ Social Interaction Domain indicates that a large majority of the items query social interaction behaviors and symptoms between the ages of 4 and 5 as opposed to current (i.e., 12 past items vs. 3 current). In contrast, the CCC-2 examines only current communication skills and deficits,

and therefore provides a more accurate description of HFA children's current verbal and nonverbal communicative profile. In light of these item format differences, the observation that HFA children with RFA are more impaired in social interaction (largely determined based on behaviors rated between ages 4 and 5), is consistent with the current ADI-R findings suggesting RFA children exhibit early and more unambiguously autistic symptoms and behaviors by the age of three when compared to children with LFA.

Ultimately, these findings support the overall argument of identifiable and meaningful motivationally-based subgroups within HFA children, as defined by their relative standing on measures of anterior asymmetry. With consideration of the nuanced differences between the two measures of parent-reported social interaction symptoms, along with the collection of findings from this analysis of individual differences within children with HFA, a hypothesized timeline of symptom onset and developmental course can be offered. Specifically, biases to approach vs. withdrawal-related behaviors are meaningful at very early ages given their specified association to early identification of both level and quality of impairment, where withdrawal-oriented children are being identified by their parents as exhibiting more unambiguously autistic behaviors by age three. Conversely, HFA children predisposed to approach-related behaviors are being identified as impaired, although the quality of their symptoms are not unambiguously autistic before the age of three. Given the limitations of our current study our timeline leaps ahead to pre-adolescence/adolescence where these speculated patterns from childhood are further elaborated by information from parent report of current social communication impairment. Here, data support the continued observation of greater overall parent-reported diagnostic symptom impairment in children with withdrawal-

oriented biases when compared to approach-related biases. Additionally, approach-oriented children and adolescents are exhibiting less impairment in the area of general communicative competence; however, they are rated by their parents as exhibiting more symptoms of social interaction deviance (i.e., pragmatic and nonverbal components of communication). The following interpretation is offered in an attempt to account for this constructed timeline. Presumably over the course of development, HFA children with approach-related biases (LFA) receive or initiate more overall verbal and nonverbal stimulation from their social environment. This added stimulation functions to strengthen their fundamental communication skills as these children are more likely to both initiate social interactions and discourse based on their motivational profile, but also receive more social stimulation simply by virtue of being more approach-oriented (resulting in greater competency in general communication). However, this approach motivation comes at a price, as their increased opportunities for interaction are met with their pronounced social communication difficulties associated with the diagnosis, resulting in more apparent atypicalities in the social use of language (e.g., lack of social reciprocity and poor nonverbal skills) (Mundy et al., 2007).

Speculation as to the underlying mechanism affecting parental perception of symptom severity involves individual differences in motivational predispositions to approach vs. avoidance behaviors. One idea here is that biases to approach vs. avoidance behaviors serve to mask or amplify underlying autism symptom deficits. Presumably, a young child (below the age of three) that is more active and approach-oriented, but still exhibiting social communication atypicalities (e.g., verbal atypicalities, or repetitive or highly routinized behaviors or interests) could easily be overlooked or viewed as highly

active, but non-autistic. While the socially reticent or avoidant/withdrawn young child who is less responsive and socially engaging fits the more classic profile of children with autism, and therefore his/her symptoms are more readily identifiable to parents and clinicians. One can extend these assumptions to older children and adolescents and consider the potentially confounding effect motivational styles to approach vs. avoid may have on expression and accurate identification of autism syndrome-specific symptoms.

A recently published prospective study of siblings of children with autism between the ages of 6 and 36 months provides some support for this idea (Bryson et al., 2007). Researchers assessed infants every 6 months in an effort to identify early indicators of the disorder. Areas assessed included cognitive functioning, temperament, and behavior profiles. Results of the data on the nine at-risk children who all went on to develop autism or an ASD indicated the presence of two subgroups. The early onset group (met ADOS criteria for autism at 18 months) demonstrated a severe and early regression in cognitive functioning between 12 and 24 months, and a behavioral profile (in all but one child) marked by a difficulty to socially engage (i.e., showing less and typically only fleeting eye contact), no or very little social smiling, little interest in or pleasure in interacting with others, minimal interest or exploration of toys, heightened visual fixation, and repetitive and/or atypical behaviors. Temperamental profiles of these children were characterized by irritability, intolerance of intrusions, proneness to distress/negative affect, difficulties with self- or other-regulation state, and difficulties with being comforted by others. The later onset group (diagnosed by 36 months) demonstrated average and stable IQ, and a more variable behavioral and temperamental profile. Behaviors for these children were described as similar to that of the early onset

group, but apparent later (18 months vs. 12 months), and also included hyperactivity (“high and unfocused motor activity”), poor sustained attention, relatively greater interest and pleasure in social interactions with others (but without social initiations as evidenced by little social referencing and virtually no sharing of interests), relatively more responsiveness to others, and self-initiated social communication was rare (although instrumental requests were present). Temperamental features were also somewhat mixed and included a relative absence of the features described in the early onset group, but also included tantrums (associated with language delays), seriousness in demeanor (directing little positive affect to others), content being alone, and resistance to and irritation by others’ intrusions (Bryson et al., 2007). The more variable behavioral and temperamental profile exhibited by the later onset children is more reflective of an approach-related bias. Whether this bias interfered with the researcher’s ability to make an earlier diagnosis or that the symptoms simply emerged later in these children is difficult to ascertain. Of great interest, will be future work from this lab examining the cognitive, behavioral, and temperamental profiles of those at-risk children that did not go on to develop a diagnosis.

Data on objective measures of social interaction competence (i.e., ADOS and Q-DOS) lacked sensitivity to individual differences in social communication impairment. Several reasons for this lack of sensitivity are proposed. First, the ADOS is an instrument that was developed to assess qualitative differences in impairment between autistic and non-autistic individuals on the three autism-specific domains. As such, the codes provide comprehensive descriptions of different types of social communication impairment that subsume both impairments associated with withdrawal or avoidance behaviors and those associated with approach behaviors. Additionally, the coding system (0 to 2) restricts the

range of variance that would be needed to identify individual differences within autistic groups. The Q-DOS was developed to circumvent these expected limitations of the ADOS in identifying clinical subtypes; however, the quantitative coding system was not comprehensive in its measurement of prosocial behaviors. For example, although eye contact and smiles were rated on two dimensions (social vs. nonsocial), duration of eye contact was not included which prevented the ability to distinguish between sustained vs. fleeting eye contact. Further development of this measure to include both frequency of eye contacts/smiles and duration is necessary as it promises to be a valuable tool for capturing these nuanced, but very meaningful, qualitative differences in social behavior. Implications for accurate assessment of social interaction style within the context of autism are most readily identifiable for work in development of intervention techniques and individualized treatment.

The implications of these data are far-reaching as anterior EEG asymmetry has been shown in now three independent studies to reflect stable and meaningful differences within children with HFA (Sutton et al., 2005; Burnette, 2005). In this way, this psychophysiological measure of approach vs. avoidance predispositions may aid in the psychometric identification of clinically observed differences in the phenotypic expression of autism. Additionally, the data replicating the association between anterior asymmetry and developmental course and symptom onset, not only aid in constructing a developmental picture of child factors affecting accurate early identification and diagnosis, but also offer a promising tool for concurrent assessment of these characteristics given the predictive utility of the measure of asymmetry in children as young as 10 months.

EEG Asymmetry and Comorbid Social-Emotional Symptoms

Data from this study failed to support the previous research showing a significant association between comorbid social-emotional symptoms and left anterior asymmetry within children with HFA (Sutton et al., 2005; Burnette, 2005). Indeed, trends in these data suggested the inverse of past research as HFA children with RFA and their parents reported greater impairment on two separate measures of anxiety (i.e., SASC-R SAD-G and BASC-2 PRS Anxiety scale). Associations of increased anxiety symptoms and RFA were echoed in the self-report of CON children; however, parent data indicated that LFA-CON children experienced more impairment in anxiety when compared to RFA.

The discrepant findings reported here further complicate the understanding of the relation of anterior asymmetry and social-emotional status in children with HFA. One possibility for these inconsistencies is that they are merely a reflection of the considerable heterogeneity in symptom expression observed in populations of children with HFA. Review of the HFA anterior asymmetry subgroup means from the two previous studies showing significant associations between LFA and social-emotional symptoms provides some support for this idea (Sutton et al., 2005; Burnette, 2005). Examination of anterior subgroup mean differences indicates comparable levels of impairment for children in the LFA group, but discrepant impairment levels in the RFA group. Specifically, RFA-HFA children from this study self-reported relatively higher levels of impairment compared to RFA children from past studies. Additionally, it is important to note that the current study's observation of the associations of RFA and anxiety/dysphoria symptoms in HFA children are far from robust (p ranged .07 to .09) and were only evident on 1 of 9 self-report scales and 1 of 3 parent report scales examined. Further, given the lack of

convergent findings from parent report data and the documented low validity of parent report of children's internalizing symptoms (Kolko & Kazdin, 1993), the parent report findings of increased LFA and increased social-emotional symptoms in the CON sample are questionable.

EEG Asymmetry, Anxiety Subtypes, and Age

Results from analyses examining subtypes of anxiety failed to elucidate the apparent complexity in the association of anterior asymmetry and social-emotional symptoms in children with HFA. The relation of left frontal asymmetry and increased anxious apprehension symptoms was only apparent for children in the Old sample. Specifically, only adolescents (mean age = 15.2 years) exhibited the hypothesized association of LFA and increased anxious apprehension symptoms, while younger children (mean age = 11.3 years) displayed the inverse association of RFA and increased symptoms (i.e., MASC Perfectionism, Anxious Coping, and Harm Avoidance Total Score). It is possible that these apparent age effects are related to self-report validity and the accurate reflection of endorsed anxiety symptoms and experienced anxiety symptoms as a function of age. Additionally, findings from analyses with posterior asymmetry indicated that only children in the CON sample displayed the hypothesized association of RPA and increased anxious arousal, while HFA children displayed the inverse association of LPA and increased arousal symptoms (i.e., MASC Somatic Autonomic Scale). This pattern of findings appears to reflect past research (Sutton et al., 2005; Burnette, 2005) only in posterior, rather than anterior regions. The interpretation of these results is unclear; however, Heller et al. (2003)'s model suggests that comorbid

symptoms of depression can confound the association of RPA and anxious arousal symptoms. Heller et al. (1995) demonstrated this idea by showing that symptoms of anxiety (marked by high arousal) and depression (marked by low arousal) are distinguished by opposing patterns of right posterior asymmetry (i.e., anxiety is associated with increased activity and depression is associated with decreased activity). Given that children in the HFA sample reported more depressive symptoms than children in the CON sample, it is possible that depressive symptoms confounded the relation between RPA and anxious arousal. It will be important to control for comorbid symptoms of depression in future analyses to test the validity of this proposed interpretation.

Additionally, results from these analyses added new and interesting information about the expression of anxiety at different developmental ages. Specifically, age effects were observed on measures of anxious arousal and obsessive compulsive symptoms where younger children (regardless of diagnostic group) reported greater impairment when compared to older children (i.e., MASC Tense Restless, MASC Physical Symptoms Total Score, and LOI). These data are reflective of normative developmental phenomena related to the differential expression of anxiety symptoms where younger children tend to report more arousal related anxiety symptoms, while adolescents report more social criticism related anxiety symptoms (Weems & Costa, 2004).

EEG Asymmetry, Age, and Anger/Emotional Expression

Data on anger and emotional expression also revealed interesting patterns about developmental trends and expression of symptoms. Results on anger and emotional expression showed an age effect where younger children in both the HFA and CON

samples reported more symptoms of poor awareness of emotional expression when compared to older children. Results also showed an interaction of diagnostic and age groups on expressive reluctance where older HFA children and younger CON children report more symptoms of expressive reluctance when compared to younger HFA and older CON children. Again, the interpretation of the age-related findings involves consideration of developmental trends in awareness and expression of emotion. Certainly, the observation of younger children reporting poorer cognitive awareness of emotions is documented in the literature (Bretherton, Fritz, Zahn-Waxler, & Ridgeway, 1986; Altshuler & Ruble, 1989). Additionally, the similar response pattern observed between older HFA children and younger CON children indicating their increased experience of expressive reluctance may be reflective of their generalized developmental delay in social emotional cognition (i.e., perspective taking skills).

Findings also showed an interaction of diagnostic and asymmetry group such that HFA children with LFA reported more symptoms of controlled anger, while CON children demonstrated the inverse association of RFA and increased symptoms. These data are contrary to the literature on the association of anger to LFA and previous findings in children with HFA, which showed a significant association between RFA and controlled anger symptoms (Burnette, 2005). As reviewed above, comparison of sample means from Burnette (2005) indicates a slight increase in expression of symptoms in the LFA group and a slight decrease in expression of symptoms in the RFA group. Once again, these inconsistent findings may be most reflective of the considerable variability in autism and comorbid symptom expression in children with HFA.

Study Limitations and Future Directions

One major limitation of this study was that diagnostic groups were poorly matched, as children in the HFA sample were significantly younger, more male, and displayed lower verbal cognitive functioning compared to children in the CON sample. These sample inequalities make interpretation of the between-group findings less clear and in need of replication for greater confidence in results. Future studies will require samples that are well-matched on these important variables.

Given the specific hypotheses regarding the moderating effect of age on the association of EEG asymmetry to social symptoms, and the considerable heterogeneity observed among children with HFA, future analyses will require larger sample sizes of children of varying ages with elevations on autistic and non-autistic specific symptoms (i.e., hyperactivity). In this study, age was arbitrarily divided at the median in order to divide groups into equal and meaningful age subgroups. However, a more comprehensive investigation of age effects would involve recruiting a large sample with a broad age range and examining the effect of age as a continuous variable. Additionally, results from this study indicated an association of hyperactivity symptoms to EEG asymmetry (only in the HFA group) and parent report of children's social communication impairment. Due to study goals, hyperactivity symptoms were used as a covariate in order to examine the relation of core autism symptoms and EEG asymmetry without the effects of comorbid symptoms. Given the substantial overlap of ADHD symptoms in children with autism, and the potential for comorbid symptoms to confound parental perception of impairment, future work should recruit larger sample sizes of HFA and non-HFA children with elevations on ADHD symptoms in order to analyze the effects of comorbid hyperactivity.

Four areas of potential interest are offered for future work investigating the nature of the effect of hyperactivity symptoms on the relation between anterior asymmetry subgroups and social communication impairment: 1) the impact of hyperactivity symptoms on cortical activity and anterior asymmetry, 2) the impact of hyperactivity symptoms on parental perception of autism-specific symptoms, 3) the impact of hyperactivity symptoms on children's self-report of attention, social-emotional, and obsessive-compulsive symptoms, and 4) the interactions of these potential factors.

In addition to larger samples, younger samples (toddler to preschool age) are needed in order to comprehensively examine the hypothesis that motivational biases to approach vs. withdrawal related behaviors differentially affect symptom onset, course, and presentation, and therefore age of identification, in children with HFA. Future work in this area is needed to evaluate the hypothesis that withdrawal-oriented children exhibit behaviors more stereotypically autistic and are therefore, identified by parents and clinicians at younger ages. The converse hypothesis that approach-oriented children exhibit additional behaviors, not necessarily consistent with autism (e.g., hyperactivity and social approach), which function to mask the underlying autism syndrome and delay accurate identification of the disorder, must also be evaluated. Additionally, assessment of younger children will allow for the examination of current symptoms of social communication impairment using direct observation measures such as the ADOS and/or the Q-DOS. Further, concurrent assessment of symptoms will extend the current findings of the relation of motivational bias and symptom onset based on retrospective parent report.

Direct observation measures of social communication impairment failed to provide meaningful information on individual differences within children and adolescents with HFA. Extending direct observation measures to include the examination of more naturally occurring social skills and deficits via a structured peer interaction may provide a more ecologically valid representation of the qualitative differences in HFA children's social competencies and deficits. Additionally, modification of the Q-DOS to include frequency and duration of spontaneous and responsive eye contact and smiles will provide a more accurate and therefore useful measure of observable individual differences in social interaction behaviors and/or qualitative styles to social interaction among children with HFA.

Additionally, a much needed extension of these findings is the evaluation of the role of individual differences in motivational bias, as measured by anterior EEG asymmetry, in treatment responsiveness. Specifically, a potential future study paradigm might resemble the Sherer and Schreibman (2005) study which categorized children into treatment responders vs. non-responders based on their behavioral profiles. In addition to behavioral measures, the addition of pre-intervention EEG asymmetry assessment would add to the theoretical understanding of the psychophysiological systems (i.e., BIS/BAS) that may underlie the observable differences in behavior. A series of intervention studies specifically examining motivational predictors of response to intervention would move the research and clinical field forward in offering more individually-tailored treatments based on a "goodness-of-fit" between a child's individual temperamental traits and the theoretical requisites of the intervention technique (i.e., behavioral (DTT) vs. child-centered (PRT)).

In addition, inclusion of a specific measure of behavioral inhibition and behavioral activation would aid in validating the hypothesized relations between EEG asymmetry and motivational tendencies of approach and withdrawal. More specifically, inclusion of observational lab-based measures designed to more directly assess approach and avoidance tendencies (i.e., Balloon Analog Risk Task (BART)) would provide a more objective index of motivational tendencies and confirm data from behavioral measures using self/parent report. Likewise, inclusion of parent and self report measures of behavioral inhibition and activation tendencies will add to the effort to validate the construct measured by EEG asymmetry.

Replication of these findings will be necessary in order to rule out the possibility of sample-specific results. In addition, combining the findings of this study with neuro-imaging research would allow for a more direct examination of the proposed neuro-developmental changes associated with development and puberty. Additionally, given the current findings suggesting that age and/or neurodevelopmental status affects the stability of EEG asymmetry, future work using EEG asymmetry should employ the use of longitudinal methods in order to account for instability due to neurodevelopmental status or developmental changes related to age. Ultimately, the preliminary assessment of test-retest reliability in research investigating EEG asymmetry in populations of children and adolescents will allow for more accurate interpretation of the results.

Conclusion

This study contributes to the growing literature examining the impact of motivational predispositions, as indexed by anterior EEG asymmetry, on symptom onset,

course, and expression in children with high functioning autism. Data from this study provide support for the notion that EEG asymmetry is a reliable indicator of motivationally-based differences in behavior in HFA children. Further, this study demonstrates that anterior asymmetry subgroups are useful markers of phenotypic variability that are meaningfully related to the experience and expression of symptoms of core autism impairment (i.e., communication impairment). Implications from this research suggest that variability in motivational predispositions to approach vs. avoidance behavior may underlie the qualitative differences in communication impairment associated with the different diagnoses along the spectrum of autism (i.e., High Functioning Autism vs. Asperger Syndrome).

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APPENDIX A

Table 1: Diagnostic Group Data on Age and Cognitive Functioning

Measure	HFA Group		Control Group		t-value
	M	SD	M	SD	
	N = 51		N = 44		
Age in Months	154.87	30.21	165.00	23.64	-1.83 ^a
Verbal Comprehension Index	100.59	14.41	107.00	12.88	-2.27*
Perceptual Reasoning Index	101.63	16.67	101.43	15.09	.06

^a Adjusted degrees of freedom for violation of unequal variances assumption. VCI = WISC-IV Verbal Comprehension Index and PRI = WISC-IV Perceptual Reasoning Index, both from the Wechsler Intelligence Scale for Children – Fourth Edition.

* $p < .05$

Table 2: Stability of EEG Asymmetry across Time

	Whole Group N = 65	Young Group N = 32	Old Group N = 33	HFA Group N = 35	CON Group N = 30
EEG Asymmetry					
Midfrontal	.39**	.50**	.27	.43**	.28
Parietal	.60**	.65**	.58**	.66**	.62**

* $p < .05$, ** $p < .01$

Table 3: Diagnostic and Age Group Data on Age and Cognitive Functioning

	HFA Group N = 51		Control Group N = 44	
	Young n = 28 (24 males)	Old n = 23 (20 males)	Young n = 18 (11 males)	Old n = 26 (17 males)
Age in Mths ^{a, b, d, e}	131.36 (17.12)	183.50 (12.39)	141.43 (16.84)	181.31 (9.57)
VCI ^{a, b, c}	100.61 (12.91)	100.57 (16.35)	109.50 (14.87)	105.27 (11.28)
PRI ^{a, b}	100.36 (16.48)	103.17 (17.14)	104.22 (14.73)	99.50 (15.31)

^a Significant multivariate Diagnostic Group effect. ^b Significant multivariate Age Group effect.
^c Significant univariate Diagnostic Group effect. ^d Significant univariate Age Group effect.
^e Significant univariate interaction of Diagnostic X Age Group. Age in Mths = Age in months.
VCI = WISC-IV Verbal Comprehension Index and PRI = WISC-IV Perceptual Reasoning Index, both from the Wechsler Intelligence Scale for Children – Fourth Edition.

Table 4: Within Group Analyses: Asymmetry Group Data on ADI-R Items

Continuous ADI Data	LFA Group N = 24		RFA Group N = 27	
	M	SD	M	SD
Age of 1 st Concern	30.21	19.95	26.19	15.25
Age of 1 st Words	23.96	14.38	22.41	10.71
Age of 1 st Phrases	37.54	15.58	35.93	13.92
Interviewer's Judgment of Onset of Developmental Abnormalities	24.21	10.59	23.33	8.63

Table 5: Within Group Analyses: Asymmetry Group Data on ADI-R Item #86

	LFA n = 24	RFA n = 27	X^2 value	<i>p</i> -value
ADI-R #86: "Age when Abnormality First Evident"				
No Abnormality Evident by age 3	1	0		
Development Probably Abnormal by age 3, but not of a Degree that is Incompatible with Normality	1	1		
Behaviors Strongly Indicative of Autism by age 3	11	6		
Behaviors Indicative of Atypicality, but not Clearly Autism by age 3	11	20		
Total	24	27	3.75*	.05

Table 6. Age and Asymmetry Group Data on Parent Report of Social Communication Impairment in the HFA Group

	LFA Group N = 24		RFA Group N = 27	
	Young	Old	Young	Old
Diagnostic Questionnaires				
Social Communication Questionnaire (SCQ)				
Total Score ^{a, c}	18.43 (6.49)	18.30 (5.14)	22.36 (6.51)	22.08 (5.77)
Communication Domain ^{a, b}	5.71 (2.13)	5.90 (2.03)	7.14 (2.54)	6.62 (2.26)
Social Interaction Domain ^{a, c}	6.64 (3.86)	5.40 (2.72)	7.36 (3.69)	9.15 (3.11)
Repetitive Behavior Domain ^a	4.57 (2.34)	5.50 (2.32)	5.93 (1.49)	4.69 (1.89)
Autism Spectrum Screening Questionnaire (ASSQ)				
Total Score ^{a, b, c}	22.50 (9.74)	28.00 (8.84)	31.07 (8.18)	27.38 (7.96)
Children's Communication Checklist – Second Edition (CCC-2)				
GCC ^{a, b, c}	40.21 (13.79)	37.50 (14.81)	24.29 (14.26)	29.23 (12.54)
SIDC ^{a, c}	-10.57 (8.12)	-14.10 (9.54)	-4.93 (8.00)	-9.08 (9.07)
Social Responsiveness Scale (SRS)				
Total Score ^{a, b}	77.93 (11.15)	77.90 (13.25)	84.07 (7.59)	79.08 (15.78)

^a Significant multivariate effect of covariate, parent report of hyperactivity symptoms.

^b Significant univariate effect of the covariate, parent report of hyperactivity symptoms.

^c Significant univariate Asymmetry Group effect.

Table 7: Age and Asymmetry Group Data on Direct Observation of Social Communication Impairment in the HFA Group

Direct Observation Measures	LFA Group N = 24		RFA Group N = 27	
	Young (n = 14)	Old (n = 10)	Young (n = 14)	Old (n = 13)
Autism Diagnostic Observation Schedule (ADOS)				
Communication Domain	3.79 (1.12)	4.30 (1.34)	4.07 (1.49)	3.69 (1.93)
Social Interaction Domain	8.43 (2.95)	8.00 (3.50)	8.29 (2.40)	7.38 (3.38)
Restricted Interests and Repetitive Behavior Domain	1.07 (.997)	0.80 (1.40)	0.86 (1.29)	0.77 (1.17)
Quantitative ADOS (Q-DOS)	(n = 10)	(n = 5)	(n = 9)	(n = 10)
Average Social Eye Contact	5.73 (4.52)	9.40 (4.59)	10.50 (6.81)	10.70 (10.27)
Average Non-Social Eye Contact	5.78 (5.78)	10.25 (6.02)	10.56 (4.32)	8.70 (8.36)
Average Social Smiles	1.03 (1.18)	2.90 (2.99)	2.89 (2.28)	2.48 (3.25)
Average Non-Social Smiles	2.85 (3.28)	2.15 (1.57)	2.61 (2.43)	2.53 (1.87)

* No significant multivariate or univariate effects.

Table 8. Diagnostic, Age and Anterior EEG Asymmetry Group Differences on the Self-Report of Emotional Impairment and Social Anxiety

	HFA Group N = 51				Control Group N = 44			
	LFA		RFA		LFA		RFA	
	Young	Old	Young	Old	Young	Old	Young	Old
Obsessive-Compulsive Symptoms (LOI)								
Total Score ^{a,b,c}	11.29 (5.61)	10.70 (7.89)	16.43 (11.28)	8.54 (7.97)	5.82 (4.58)	2.40 (1.99)	6.57 (6.24)	3.27 (2.16)
Social-Emotional Impairment (BASC-2 SRP)								
Anxiety ^{a,b}	54.00 (7.93)	55.10 (12.63)	55.00 (12.79)	49.62 (10.30)	44.00 (4.58)	46.00 (12.03)	47.57 (8.81)	46.64 (6.92)
Depression ^{a,b}	54.14 (10.53)	51.30 (12.35)	53.43 (11.51)	52.69 (8.41)	46.00 (4.52)	42.67 (3.24)	45.71 (4.61)	45.00 (7.10)
Interpersonal								
Relations ^{a,b}	45.64 (9.70)	42.30 (15.10)	47.64 (9.66)	45.85 (13.55)	53.64 (7.50)	54.53 (4.85)	54.14 (5.98)	56.00 (5.14)
Social Stress ^{a,b}	57.57 (10.92)	55.10 (18.85)	54.64 (10.05)	53.00 (12.82)	46.18 (6.93)	42.27 (5.79)	43.00 (8.51)	43.00 (4.96)
Social Anxiety (SASC-R)								
SAD-N ^{a,b}	16.36 (4.38)	16.90 (4.43)	18.50 (5.67)	20.38 (5.38)	14.09 (4.72)	14.27 (5.06)	14.71 (7.11)	14.73 (3.88)
SAD-G ^{a,b,d}	10.00 (2.83)	8.60 (3.13)	11.36 (3.48)	11.69 (4.17)	7.27 (2.90)	6.67 (2.63)	7.86 (4.06)	6.27 (1.95)
FNE ^{a,b}	18.50 (7.31)	21.30 (6.58)	24.64 (9.24)	21.92 (9.67)	18.64 (6.30)	15.13 (6.15)	17.86 (7.86)	14.73 (5.16)
Total Score ^{a,b}	44.86 (11.81)	46.80 (10.65)	54.50 (16.01)	54.00 (16.71)	40.00 (8.50)	36.07 (12.04)	40.43 (18.35)	35.73 (9.49)

^a Significant multivariate Diagnostic Group effect. ^b Significant univariate Diagnostic Group effects. ^c Significant univariate Age Group effect. ^d Trend toward a significant univariate Asymmetry Group effect. LOI = Leyton Obsessional Inventory for Children and Adolescents; BASC-2 SRP = Behavioral Assessment System for Children – Second Edition, Self-Report; SASC-R = Social Anxiety Scale for Children – Revised; SAD-N = Social Avoidance and Distress - Specific to New Situations Subscale; SAD-G = Generalized Social Avoidance and Distress Subscale; FNE = Fear of Negative Evaluation from Peers Subscale.

Table 9: Diagnostic, Age and Anterior EEG Asymmetry Group differences on the Parent-Report of Social-Emotional Impairment

	HFA Group N = 51				Control Group N = 44				
	LFA		RFA		LFA		RFA		
	Young	Old	Young	Old	Young	Old	Young	Old	
Social Anxiety (SASC-R)									
Total Score ^{a,b}	51.50 (15.23)	47.20 (16.58)	51.86 (13.30)	48.85 (14.87)	36.55 (13.60)	33.60 (12.65)	39.57 (12.95)	33.00 (8.60)	
Social-Emotional Impairment (BASC-2 PRS)									
BASC-2 Anxiety ^{a,b,c}	58.21 (12.86)	57.00 (11.26)	63.07 (11.19)	61.77 (13.33)	51.91 (18.03)	49.20 (11.57)	46.57 (16.65)	44.09 (8.46)	
BASC-2 Depression ^{a,b}	56.71 (15.37)	63.70 (16.34)	68.93 (13.01)	64.46 (13.47)	45.55 (16.40)	50.67 (9.21)	49.71 (12.71)	48.36 (7.61)	

^a Significant multivariate Diagnostic Group effect. ^b Significant univariate Diagnostic Group effects. ^c Trend toward a significant univariate interaction of Diagnostic X Asymmetry Groups. SASC-R= Social Anxiety Scale for Children – Revised, Parent Version; BASC-2 PRS = Behavioral Assessment System for Children – Second Edition, Parent-Report Scale.

Table 10. Diagnostic, Age and Anterior EEG Asymmetry Group Differences on Anxious Apprehension Symptoms

	HFA Group N = 51				Control Group N = 44			
	LFA		RFA		LFA		RFA	
	Young	Old	Young	Old	Young	Old	Young	Old
Anxious Apprehension Symptoms (MASC)								
Perfectionism	44.36 (10.70)	53.30 (13.11)	54.00 (9.30)	46.15 (11.13)	47.18 (11.66)	46.27 (7.62)	45.00 (13.44)	44.18 (9.33)
Anx Cop ^{a,b}	49.43 (11.13)	59.60 (12.36)	60.29 (9.68)	50.38 (11.36)	50.91 (11.68)	49.67 (9.80)	52.14 (7.88)	48.36 (10.58)
Harm Avd ^{a,b}	46.71 (10.31)	58.20 (13.09)	58.79 (6.92)	48.38 (11.42)	49.27 (13.13)	47.80 (8.52)	48.86 (11.96)	45.82 (10.95)

^a Significant univariate Diagnostic Group effect. ^b Significant univariate Asymmetry X Age Group interaction. Significant 3-way interactions are not reported due to insufficient sample sizes. MASC = Multidimensional Anxiety Scale for Children; Perfectionism = Perfectionism Scale; Anx Cop = Anxious Coping Scale; Harm Avd = Harm Avoidance Scale.

Table 11. Diagnostic, Age and Posterior EEG Asymmetry Group Differences on Anxious Arousal Symptoms

	HFA Group N = 51				Control Group N = 44			
	LPA		RPA		LPA		RPA	
	Young	Old	Young	Old	Young	Old	Young	Old
Anxious Arousal Symptoms (MASC)								
Tns Rstlss ^{a, b, d}	56.58 (11.33)	51.87(10.76)	57.67 (13.00)	47.63 (10.54)	50.00 (9.13)	47.89 (7.49)	54.60 (8.88)	45.14 (5.40)
Som Auto ^{a, b, c}	52.58 (11.26)	53.60 (12.33)	51.00 (6.06)	46.38 (5.78)	43.85 (6.50)	44.89 (5.85)	53.60 (11.33)	46.14 (8.47)
Phys Sxs ^{a, b, c, d}	55.21 (11.55)	53.00 (12.15)	54.67 (9.53)	46.75 (8.26)	46.69 (8.64)	46.00 (6.67)	54.60 (11.01)	45.14 (7.40)

^a Significant multivariate Age Group effect. ^b Significant multivariate Diagnostic X Asymmetry Group interaction. ^c Significant univariate Diagnostic Group effect. ^d Significant univariate Age Group effect. ^e Significant univariate Diagnostic X Asymmetry Group interaction. MASC = Multidimensional Anxiety Scale for Children; Tns Rstlss = Tense Restless Scale; Som Auto = Somatic Autonomic Scale; Phys Sxs = Physical Symptoms Total.

Table 12. Diagnostic, Age and Anterior EEG Asymmetry Group Differences on Anger and Emotional Expression Symptoms

	HFA Group N = 51				Control Group N = 44			
	LFA		RFA		LFA		RFA	
	Young	Old	Young	Old	Young	Old	Young	Old
Self Report of Anger Expression (PAES-III)								
Anger in ^{a,b}	10.21 (2.46)	9.50 (2.55)	9.00 (2.94)	10.08 (2.53)	8.91 (1.87)	8.47 (2.30)	10.86 (2.34)	9.64 (2.16)
Anger out ^{a,b}	9.43 (2.03)	8.90 (2.81)	9.93 (2.65)	9.15 (2.34)	8.45 (2.84)	8.20 (1.82)	8.14 (2.80)	8.91 (2.47)
Anger cntrl ^{a,b,e}	11.36 (1.74)	12.00 (1.41)	10.64 (1.69)	10.31 (1.89)	11.36 (2.01)	10.20 (1.61)	11.57 (1.72)	11.27 (1.79)
Parent Report of Anger Expression Symptoms (BASC-2 PRS)								
Aggression ^{a,b,c}	51.07 (8.37)	54.70 (11.41)	56.36 (11.17)	54.15 (13.51)	47.27 (5.29)	46.93 (5.71)	48.29 (9.91)	48.82 (6.91)
Self Report of Emotional Expression Symptoms (EESC)								
Pr Awrnss ^{a,b,c,d}	19.79 (6.29)	17.50 (4.35)	22.93 (7.41)	19.77 (6.52)	17.27 (5.75)	14.07 (2.31)	17.57 (6.75)	15.82 (4.94)
Exp Reluc ^{a,b,c,f}	18.71 (5.93)	22.90 (5.67)	22.00 (5.81)	22.46 (6.75)	20.73 (4.67)	16.47 (4.79)	19.57 (7.44)	17.73 (5.14)

^a Significant multivariate Diagnostic Group effect. ^b Significant multivariate Diagnostic X Asymmetry Group effect. ^c Significant univariate Diagnostic Group effect. ^d Significant univariate Age Group effect. ^e Significant univariate Diagnostic X Asymmetry Group interaction. ^f Significant univariate Diagnostic X Age Group interaction. PAES = Pediatric Anger Expression Scale – Third Edition; Anger Cntrl = Anger Control Subscale; BASC-2 PRS = Behavioral Assessment System for Children – Second Edition, Parent Report Scale; EESC = Emotional

APPENDIX B

Figure 1. Test-Retest Reliability of Midfrontal Asymmetry (Entire Group)

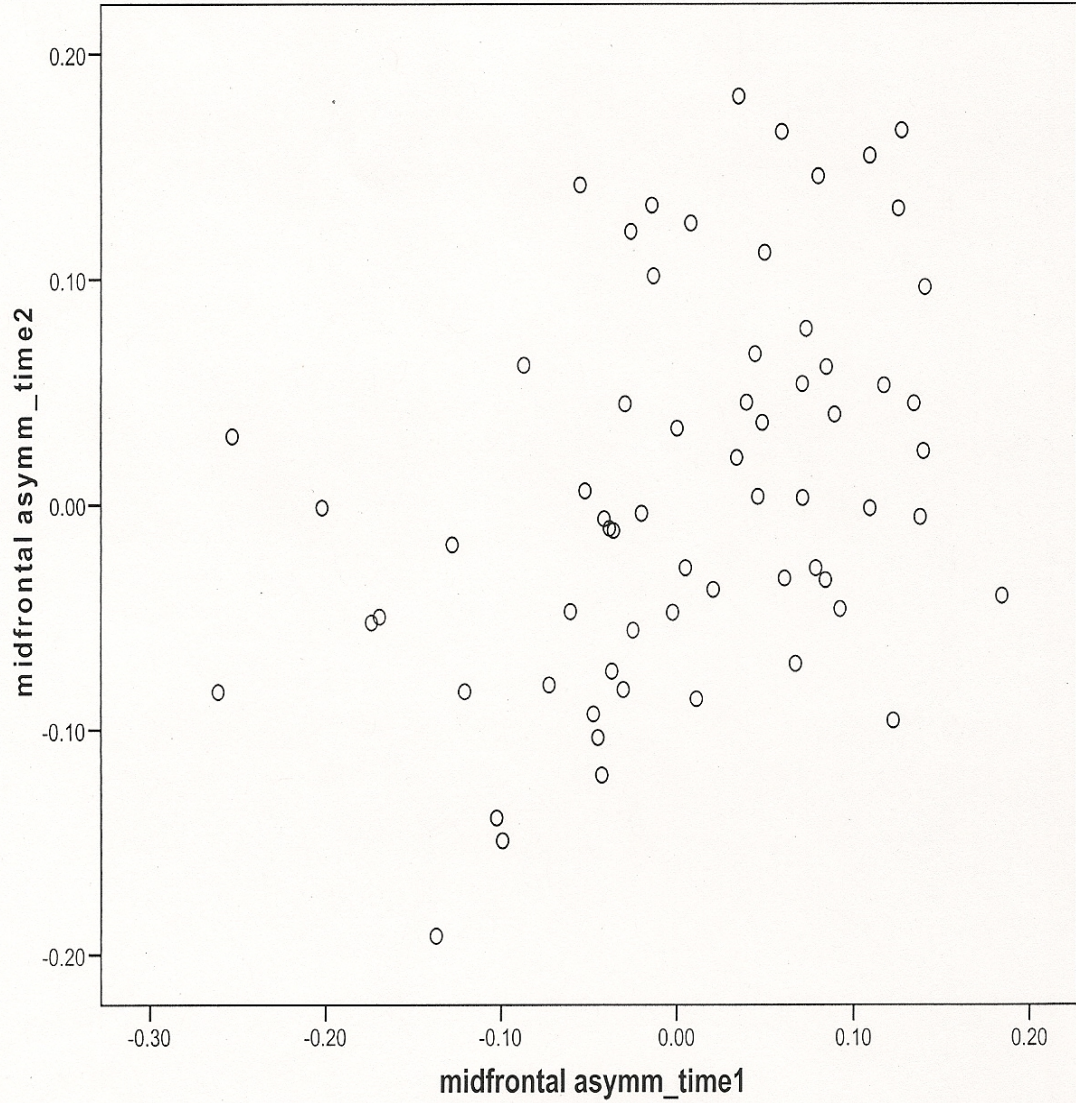


Figure 2. Test-Retest Reliability of Midfrontal Asymmetry (HFA group)

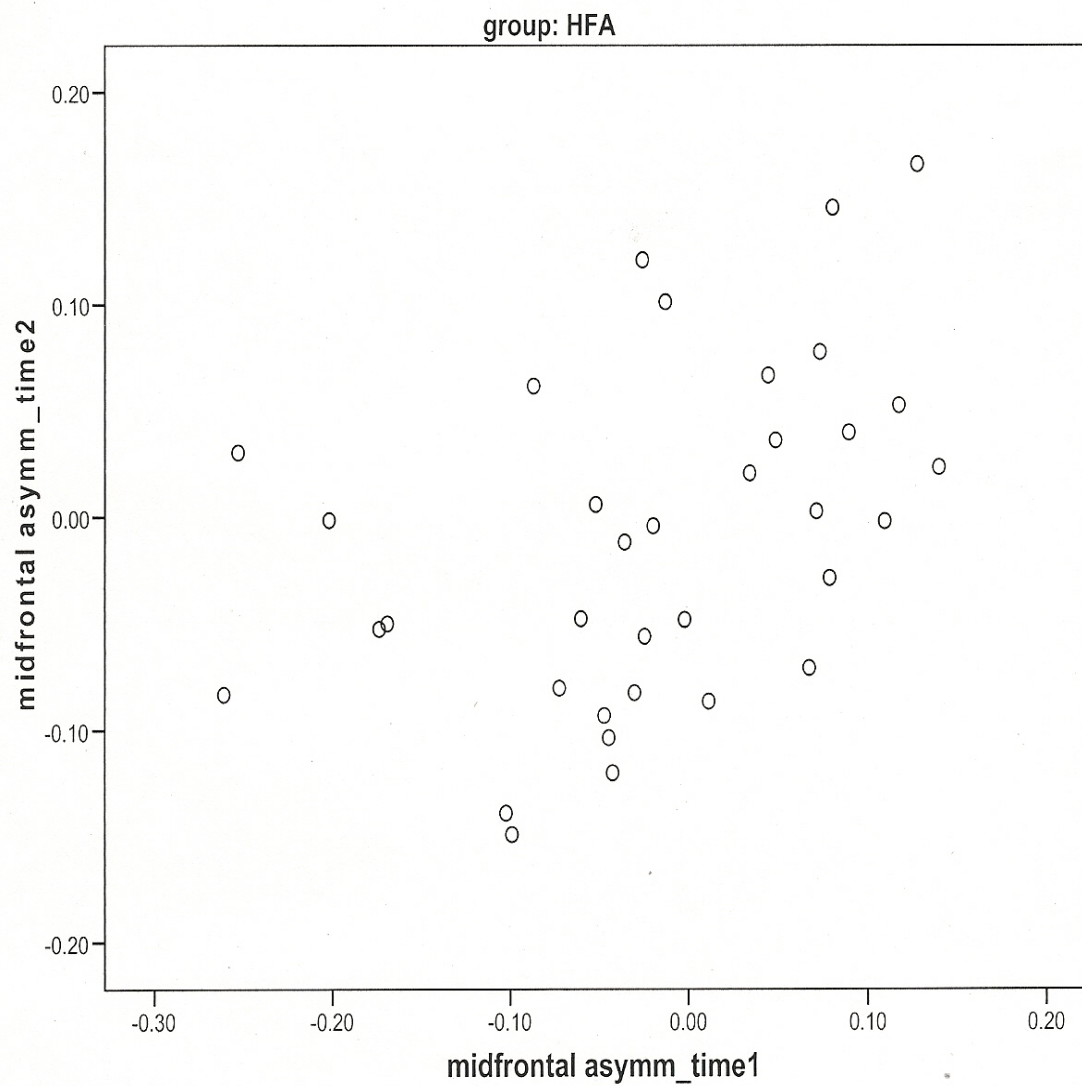


Figure 3. Test-Retest Reliability of Midfrontal Asymmetry (CON group)

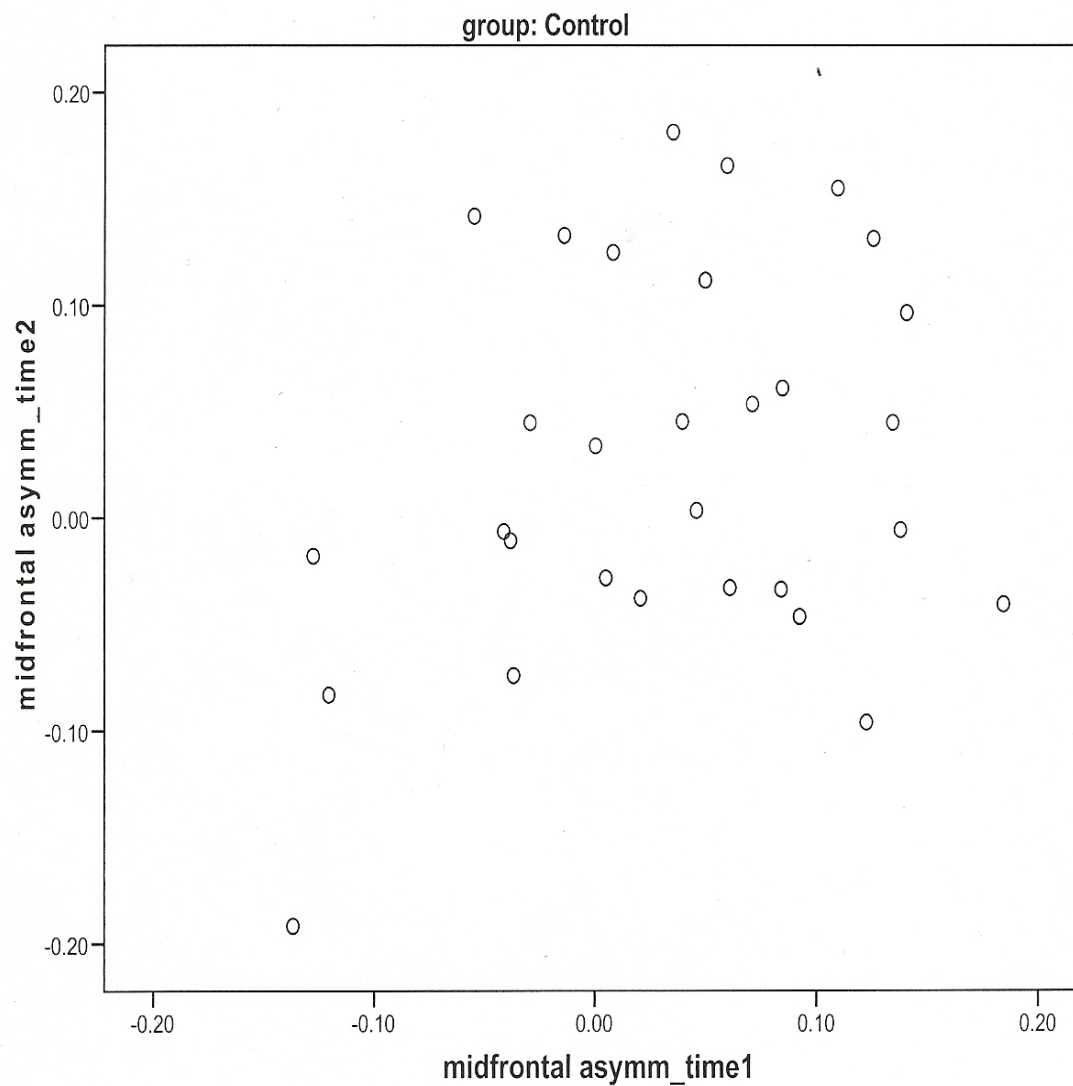


Figure 4. Test-Retest Reliability of Midfrontal Asymmetry (Young group)

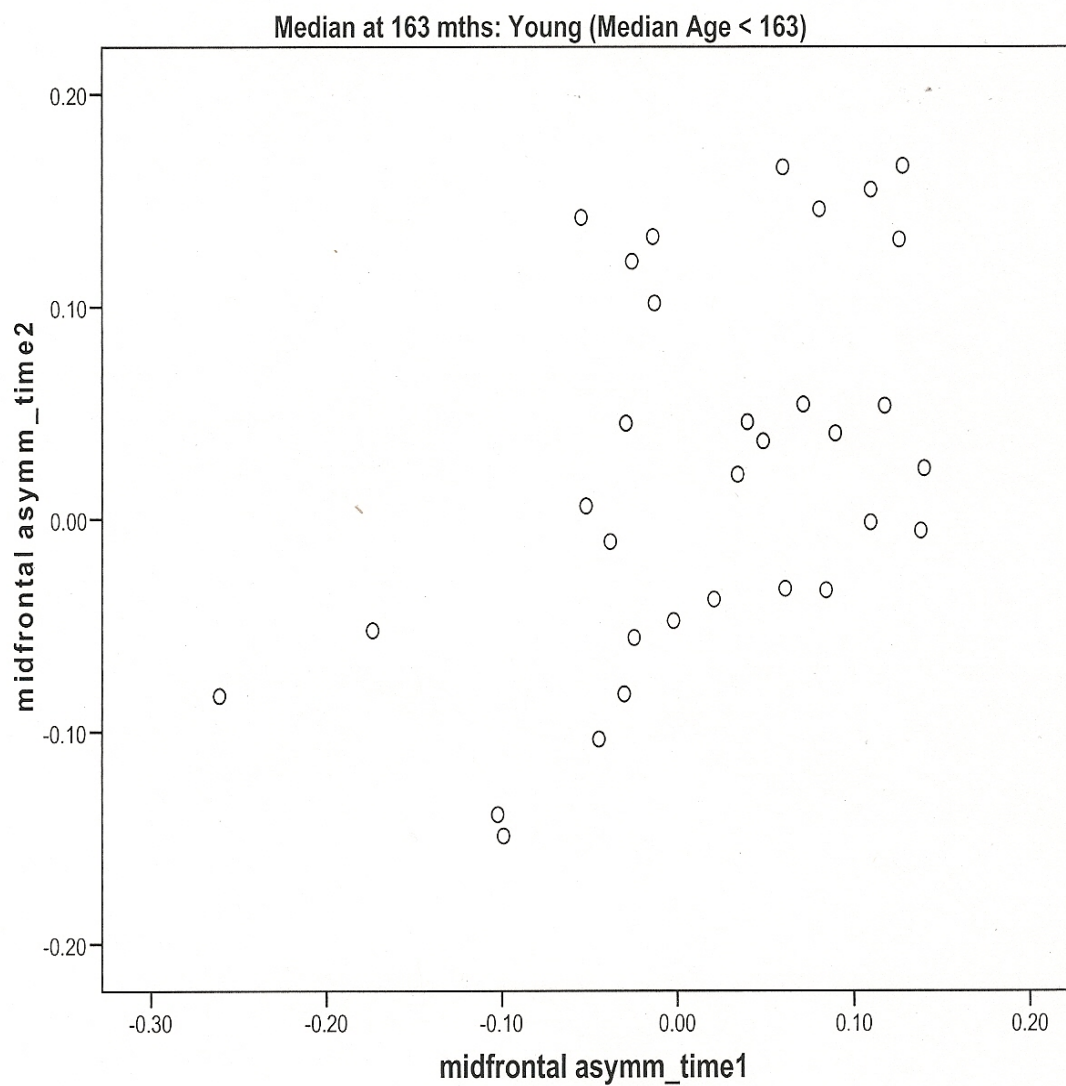


Figure 5. Test-Retest Reliability of Midfrontal Asymmetry (Old group)

