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Surgency Characteristics Relating to Attention Deficit/Hyperactivity Disorder and Autism Spectrum Disorders In Boys With Fxs

Marjorie Lee Grefer
University of South Carolina - Columbia

SURGENCY CHARACTERISTICS RELATING TO ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDERS IN BOYS WITH FXS

by

Marjorie L. Grefer

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Jane E. Roberts, Director of Thesis

Kate Flory, Reader

Lacy Ford, Vice Provost and Dean of Graduate Studies

ABSTRACT

Children with fragile X syndrome (FXS) are at high risk for developing a range of behavioral disorders, including Attention Deficit/Hyperactivity Disorder (ADHD) and autism spectrum disorders (ASD). However, very few studies have investigated the comorbid profile of FXS and ADHD and the possible dissociation from the FXS and ASD profile. The present study examined the relationship of childhood temperament characteristics of the Surgency facet (activity level, impulsivity, approach, shyness, and smiling and laughter) and the severity of ADHD and ASD features at two measurement time points in childhood, preschool (ages 3-4) and at school entry (ages 5-6). The study consisted of males with FXS measured at each time point, as well as comparison of typically developing (TD) boys at the preschool measurement time point. Multiple regression analyses revealed that in boys with FXS, elevated activity level scores are associated with ADHD scores at preschool age and elevated shyness and decreased smiling and laughter is strongly associated with ADHD scores upon school entry. Impulsivity emerges as a strong indicator of elevated ADHD scores around school age, but even preschool impulsivity scores demonstrate some predictive value for higher ADHD scores later in school. Finally, no Surgency characteristic was significantly related to ASD scores at any age. Thus, the Surgency facet of temperament at these ages does not predict strong relationships of comorbid pathologies of ADHD and ASD in FXS, but may however serve as discriminative factor when studying these behavioral outcomes.

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CHAPTER 1

INTRODUCTION

Attention deficit/hyperactivity disorder (ADHD) is a behavioral disorder that first emerges in childhood and affects performance in the classroom, functional abilities at home, and development of peer relationships. It is a persistent pattern of inattention and/or hyperactivity/impulsivity that occurs across settings (American Psychological Association, 2000). ADHD affects nearly 10% of children throughout the United States (CDC, 2007). Children with genetic disorders, such as fragile X syndrome (FXS) are at a high risk for developing ADHD. Children with FXS often have many behavioral and cognitive concerns that arise amongst an array of developmentally abnormal features (Farzin et al., 2006). Many children with FXS are affected with irregular emotional and physiological reactivity, hyperactivity, impulsivity, inattention, and problematic patterns of emotional regulation (Hatton et al., 2003; Hatton et al., 2009; Roberts et al., 2009). These behavioral traits emerge early in development and may represent vulnerability for the manifestation of secondary conditions. The developmental trajectory of ADHD symptoms has been documented in typically developing populations, but has not been thoroughly examined in FXS. The recognition of this complex development of psychopathology is evident when investigated through a dynamic systems theoretical approach, which acknowledges a system of genetic, biological, and environmental components that interact in a transactional fashion over the course of time.

Fragile X syndrome is the most common heritable form of intellectual disability, affecting approximately 1 in 3600 males and 1 in 6000 females. The syndrome is caused by a trinucleotide (CGG) repeat expansion in the 5 untranslated region of the Fragile X Mental Retardation 1 (FMR1) gene on the X chromosome (Farzin et al., 2006). Children with FXS are extremely vulnerable to developing comorbid behavioral disorders such as anxiety (70%) and autism spectrum disorders (46%; Bailey, Raspa, & Holiday, 2008). The prevalence of ADHD symptoms in children with FXS is higher than rates found in individuals with other genetic conditions and in individuals with non- specific intellectual disability (Sullivan, Hatton, & Hammer, 2006). Specifically, nearly 84% of children with FXS have attention problems and 66% have problematic levels of hyperactivity (Bailey et al., 2008), which are core features of ADHD. Despite the knowledge about these high prevalence rates, very little research has actually examined the emergence of ADHD and its effect on cognitive and behavioral outcomes in FXS. Investigating the emergence and presentation of ADHD in FXS, and how this developmental relationship differs from common comorbidities in FXS, such as autism, will provide insight into the unique, early indicators of ADHD in the FXS population. Furthermore, recognition of the indicators of early emergence of ADHD symptoms will provide guidance in the consideration for early diagnostic procedures and intervention strategies for children with ADHD and FXS. The current study will investigate the concurrent and predicted relationships of the emergence of ADHD in young boys with FXS and its association with a specific set of temperament characteristics, those in the facet of Surgency, and comorbid conditions such as autism.

1.1 ADHD in FXS

Problems with attention and executive functioning are commonly observed in children with FXS, resulting in inhibitory control deficits (Bailey et al., 2008; Farzin et al., 2006; Hatton, Bailey, Hargett-Beck, Skinner, & Clark, 1999; Hatton et al., 2002; Sullivan et al., 2006). These deficits are associated with elevated levels of behaviors such as hyperactivity and impulsivity, and consequently disorders such as ADHD (Cornish, Sudhalter, & Turk, 2004; Scerif, Cornish, Wilding, Driver, & Karmiloff-Smith, 2007). When rated by parents and teachers, nearly 60% of boys with FXS were endorsed with enough symptoms to meet criteria for ADHD (Sullivan et al., 2006). While boys with FXS were more likely to meet for ADHD – inattentive type than the hyperactive type (Cornish et al., 2004; Sullivan et al., 2006), the high levels of hyperactivity and impulsivity warrant further investigation.

With regards to attention, it has been shown that children with FXS attend less well to stimuli than their mental-age matched typically developing counterparts. More specifically, they experience greater difficulty attending to auditory than visual stimuli. Additionally, boys with FXS do not appear to benefit from a multimodal approach to the presentation of information as typically developing boys do (Secirf, Longhi, Cole, Kermiloff-Smith, Cornish, 2012). This atypical processing of information in boys with FXS is predictive of later problematic behaviors in school (Scerif et al., 2012). When these attentional deficits are studied longitudinally, both auditory and visual modalities yield stable results of behavioral difficulties in areas such as hyperactivity, inattention, and possible autistic symptomatology (Cornish, Cole, Longhi, Karmiloff-Smith, & Scerif, 2012).

1.2 Developmental Progression and Etiology of ADHD

Evidence suggests multiple mechanisms for the development of ADHD including, genetic, environmental, and various biological processes such as physiological arousal (Hankin, Abela, Auerback, McWhinnie, & Skitch, 2005). Also evidence suggests the ability for these mechanisms to predict the early emergence of ADHD. While DSM-IV diagnostic criteria states symptoms need to be present before the age of seven (American Psychiatric Association, 2013), the literature demonstrates that the preschool developmental stage (3-5 years of age) appears to be a critical time to detect these early emerging symptoms of ADHD due to increased demands of attention and behavioral regulation (Berger & Neyo, 2011; Thorell & Wahlstedt, 2006; Guy, Rogers, & Cornish, 2012). Children who are rated as overactive or impulsive in early childhood often encounter lower achievement in academics, poor social relationships, and multiple behavioral problems that affect their daily functioning skills. Early detection is important for treatment to reduce symptoms and optimize outcomes in all populations.

Etiological determination of ADHD is complex with the bulk of evidence suggesting a strong genetic component with heritability estimates of 60-80% (Hunter, Epstein, Tinker, Abramowitz, & Sherman, 2012). Broadly, genetics can provide great insight into the presentation and prevalence of the disorder, as well as the persistence of symptoms over time (Hankin et al., 2005). Multiple genes have been hypothesized to be responsible for the increased vulnerability of ADHD. These genes include the dopamine transporter gene (DAT1), dopamine D4 receptor gene (DRD4), dopamine beta-hydroxylase (DBH), and Fragile X Mental Retardation gene (FMR1). Genetic contributors are associated with impulsive and novelty seeking behaviors (Smith, Barkley & Shapiro, 2007, p. 75).

Another reliable early indicator of the later emergence of ADHD lies within a child's cognitive abilities. The Executive Functioning (EF) construct is a constellation of cognitive processes involved in selecting, initiating, and executing desired cognitive, behavioral, or emotional goals (Berger & Neyo, 2011; Schroeder & Kelley, 2009). Deficiencies in EF abilities are common in individuals with ADHD. Thus, breaking down EF into finite, separate processes and investigating them in younger children have provided information about their current functioning as well as longitudinal development of ADHD. Deficits in inhibition and attention are consistently linked with higher rates of ADHD in preschool-age children (Berger & Neyo, 2011; Thorell & Wahlstedt, 2006; Shoemaker, et al., 2012). For example, deficiencies in specific EF processes, such interference control (blocking out distracting stimuli) and response inhibition, were indicators of ADHD features observed in preschool and longitudinally in later childhood (Brocki, Nyberg, Thorell, & Bohlin, 2007). Interestingly, individual differences, such as cognitive development or language abilities (Guy et al., 2012), appear to be most influential on regulation performance around age 3, and then in the future, children give more consistent performances at age 5 regardless of individual differences. This emphasizes the importance of the rapid developmental period of preschool and its influence on the course of an individual's development across the lifespan (Guy et al., 2012).

These deficits in cognitive abilities have a direct relationship to behavioral components, such as hyperactivity and impulsivity, which affect broader deficits in emotional regulation (Barkley, 1997; Musser, Galloway-Long, Frick, & Nigg, 2013). Children with deficits in emotional regulation often cannot effectively communicate their feelings or modulate their reactions to stimuli, resulting in problematic response styles (Hatton et al., 1999; Cornish et al., 2012; Hankin, et al., 2005). Children with emotional dysregulation demonstrate challenging problems with behavioral inhibition, leading to an increase of impulsive behaviors, aggressive acts, and intensive negative reactions to periods of disappointment (Wheeler-Maedgen & Carlson, 2000). Poor organization and planning of daily activities often create dysfunction in familial settings, leading to parental stress and negative parent-child interactions (Graziano, McNamara, Geffken, & Reid, 2011). These early consequences of emotional dysregulation not only lead to increased vulnerability of ADHD later in childhood, but other serious problematic behaviors commonly associated with ADHD later in the lifespan, such as substance abuse, defiance, and conduct problems (Anastopoulos et al., 2010; Graziano, et al., 2011; Sobanski et al. 2010).

In summary, genetics, cognitions, and behavioral components interact to produce the observed manifestation of ADHD in the general population, as well as in children with FXS. It is crucial to emphasize the interplay of cognitive abilities (i.e., EF) and emotional regulation skills. This relationship contributes to the unique presentation of features associated with ADHD. These may include environmental contributions such as family dynamics, stressful life events, or poor peer relations (Herbert, Harvey, Roberts, Wichowski, & Lugo-Candelas, 2013; LaForett, et al., 2008; Tandon, et al., 2011). Childhood temperament characteristics are often indicators of emotional regulation styles. Specifically those in the facet of Surgency demonstrate how emotional regulation processes relate to cognitive abilities (e.g., attention, inhibition) to produce observed temperament characteristics that are key features to ADHD, such as activity level, impulsivity, and social approach.

1.3 Temperament: Surgency

Traditionally, early temperament research has focused on reactivity, regulation, and arousal in young children (Posner & Rothbart, 2000). In typically developing child populations, early temperament traits may be associated with the emergence of externalizing behaviors such as ADHD (Nigg, Goldsmith, & Sachek, 2004; Rothbart & Bates, 2006;). Children with ADHD consistently are rated with lower levels of emotional stability and approach, as well as higher levels of negative reactivity (De Pauw & Mervielde, 2011; Nigg, 2006). Temperament is a reliable method for understanding the development of characteristics and behaviors in children, given that it has consistently been found to be stable from infancy through preschool and early childhood in typically developing populations (Casalin, Luyten, Vliegen, & Meurs, 2011; Putnam, Rothbart, and Gartstein, 2008).

Childhood temperament has been defined as constitutionally based individual differences in reactivity and regulation (Rothbart, 1981). Under Rothbart's model, temperament is comprised of three core facets: Negative Affect, Effortful Control, and Surgency. The Surgency facet includes impulsivity, activity level, smiling and laughter, shyness and social approach (Rothbart, Ahadi, Hershey, & Fisher, 2001). Impulsivity is characterized by the speed of initiation of response to a stimulus. Activity level includes the rate and extent of gross motor movement. Smiling and laughter is the observed positive affect in response to changes in stimulus intensity, rate, complexity, and incongruity. Shyness is the slow or inhibited response, or observed discomfort, in social situations. Finally, approach is described as the excitement in the anticipation of pleasant activities.

Children with high Surgency ratings are more likely to act out in impulsive or disruptive manners (Gartstein et al., 2012). Previous literature reviews have found that the Surgency facets of activity level and social approach predict higher levels of ADHD symptoms (Nigg et al., 2004, Nigg, 2006; Casalin, et al., 2011). These traits manifest in challenging behaviors associated with ADHD such as dampened abilities in anger control and non-compliance (De Pauw & Mervielde, 2011). Also, children with ADHD were rated one standard deviation higher on the Children's Behavior Questionnaire (Rothbart et al., 2001) scale of activity level when compared to the average rating of the general population. Additionally, activity level relates to how intensely a child exhibits other traits such as impulsivity, shyness, and approach (De Pauw & Mervielde, 2011). Surgency's relationship to activity level (indicating hyperactivity), the stability of impulsivity, and social approach indicates the potential and value of studying the relationship between early temperament characteristics and the emergence of ADHD. This relationship has not been thoroughly examined in FXS as a possible explanation for the elevated ratings of ADHD features observed in the literature (Bailey et al., 2001; Bailey et al., 2008; Sullivan et al., 2006).

1.4 ADHD and Surgency in FXS

There have been multiple investigations into the temperament profiles of children with FXS. Studies have consistently found that children with FXS are rated as more active, less adaptable, less approachable. Interestingly, children with FXS also exhibit less anger, intensity and sadness than non-FXS populations (Bailey et al., 2000; Hatton et al., 1999; Roberts, Boccia, Bailey, Hatton, & Skinner, 2006; Shanahan, Roberts, Hatton, Reznick, & Goldsmith, 2008). Recently, the domains of Negative Affect, Effortful Control, and Surgency seen in typically developing population have also been shown to represent temperament in children with FXS (Roberts, et al., 2012). Previous findings of increased impulsivity (Bailey et al., 2008; Farzin et al., 2006; Sullivan et al., 2006), hyperactivity (Bailey et al., 2008; Roberts et al., 2006; Sullivan et al., 2006), and lower inhibition (Berger & Neyo, 2011; Cornish et al., 2012; Guy et al., 2012; Thorell & Wahlstedt, 2006; Shoemaker, et al., 2012) suggest that the behavioral profiles seen in boys with FXS resemble patterns of atypical levels of Surgency characteristics. Surgency has not been examined as an early predictor of ADHD in FXS, as has been done in typically developing children (Nigg et al., 2004; Rothbart & Bates, 2006). Knowledge about innate individual differences such as temperament is informative about the development of problematic behaviors observed in FXS. Identification of these early temperament profiles can serve as possible predictive factors of later ADHD features. If identified early, these temperament styles may be addressed through intervention and training and thus potentially reduce the severity of ADHD behaviors.

1.5 ADHD and Autism in FXS

The prevalence rate for autism spectrum disorders (ASD) has seen a rapid increase in recent years in both FXS and non-FXS populations. The prevalence of autism in boys with FXS is approximately 46% (Bailey et al., 2008), though nearly 90% of children with FXS display symptoms of autistic behaviors (Bailey et al., 2008; Kaufmann et al., 2004). Given that boys with FXS experience high instances of multiple problematic behavior outcomes (e.g. ADHD, autism, anxiety, etc.), it is necessary to probe for specific indicators of either coexisting ADHD and ASD symptoms or for differential profiles of either ADHD or ASD. Children with comorbid autism and FXS often have significant cognitive deficits, exhibit scarce adaptive skills, and more severe problem behaviors (Bailey et al., 2001; Kau et al., 2004; Kaufman et al., 2004; Rogers, Wehner, & Hagerman, 2001). Also, common cognitive deficits such as inattention and inhibition control contribute to the manifestation of both ADHD and ASD in FXS (Cornish et al., 2012; Guy et al., 2012).

There has been little research conducted examining ADHD and ASD simultaneously in FXS. In one study where ASD was examined secondarily to ADHD in FXS populations, 16 out of the study's 63 boys (25%) with FXS were at or above the threshold for meeting criteria both ADHD and ASD (Sullivan et al., 2006). The same study found that 29% boys only met criteria for ADHD and 46% did not meet the criteria threshold for either. This demonstrates some overlap in symptoms in FXS populations, however there is still a significant portion of the FXS population exhibiting a unique presentation of symptoms, resulting in a differentiated profile of either ADHD or ASD. Clearly, the literature has demonstrated associations between ADHD features and autistic behaviors in children with FXS. However, there have been no direct comparisons of early indicators, such as temperament, and the development of ADHD and ASD in FXS.

1.6 The Current Study

The purpose of the current study is to measure the emergence of ADHD and its co-occurrence with autism in young boys with FXS through examining their relationship to the temperament characteristics in Surgency at two critical developmental time points, preschool (ages 3-4) and school entry (ages 5-6). There is no research investigating the relationship between Surgency and behavioral disorders (ADHD, ASD) in the FXS population. Further, there is a lack of research investigating the emergence of ADHD symptom severity in FXS at the critical ages of childhood development, before and at school entry. The complexity in the development of comorbid psychopathology requires a theoretical approach that recognizes a dynamic system of multiple components. These components, such as genetics, biological factors, and cognitive abilities, interact with one another over the course of time. Our primary interest was the prediction of Surgency characteristics to ADHD symptoms and if these characteristics also predicted autism in boys with FXS. Second, we were interested in how the relationship between Surgency characteristics and ADHD and autism symptoms observed during preschool may differ between typically developing boys and boys with FXS. The current study therefore asked the following questions:

(1) What is the relationship between Surgency characteristics and ADHD severity, measured at both preschool and school age in boys with FXS?

We hypothesized that higher levels of Surgency characteristics of activity level, impulsivity, and smiling and laughter in boys with FXS will be associated with higher ADHD raw scores at each assessment time point. Further, we hypothesize that lower levels of shyness and social approach will be associated with higher ADHD raw scores in boys with FXS.

(2) Do Surgency characteristics measured at preschool age predict ADHD or ASD features measured at school age in boys with FXS?

We hypothesize that Surgency characteristics of activity level and impulsivity reported in preschool will be significant indicators of later ADHD scores reported at school entry. Further, since social impairment is common in ASD, we hypothesize that decreases in smiling and laughter and social approach, and increases of shyness, reported in preschool will yield higher ASD scores reported at school entry.

(3) Does the relationship between Surgency characteristics and ADHD severity differ between boys with FXS and typically developing (TD) boys at preschool?

We hypothesize that both boys with FXS and TD boys with higher levels of activity level and impulsivity will yield significantly higher ratings of ADHD scores. However, we expect boys with FXS to have higher ratings of Surgency characteristics and ADHD and ASD features than TD boys. We also hypothesize that decreased levels of social approach and smiling and laughter, and an increase in shyness, will result in significantly higher ASD scores in both boys with FXS and TD boys.

CHAPTER 2

METHODS

2.1 Participants

Participants were recruited to participate in a project including longitudinal studies of the development of FXS at the University of North Carolina at Chapel Hill. The aim of the larger project was concerned with investigating the cognitive, behavioral, and psychological trajectories of children with FXS. Data for the current sample were pulled from two studies associated with previously mentioned project in order to address the longitudinal research questions of the study. The first study included boys with FXS who were seen every twelve months for an assessment (n=20). The second study included boys with FXS and typically developing boys seen every eighteen months for assessment (FXS n= 13; TD n= 17). Participants' data were pulled from the relevant assessment ages, between ages 3 to 4 for the initial assessment ("preschool age") and then again between ages 5 to 6 for the subsequent assessment ("school entry"). Subjects were used from both samples to increase the power of the potential findings in the analyses.

This sample consisted of 33 boys with FXS and a control group of 17 typically developing boys. FXS status was confirmed through obtaining genetic testing records. Typical development was characterized as no evidence or suspicion of a developmental or intellectual disability. The control group was only included at the initial assessment because they were not followed longitudinally. The two groups were matched on chronological age. The FXS group at the time of the “preschool” assessment had an average age of 41.09 months (range: 36-59 months; SD= 6.50). The boys in the control group had an average age of 45.53 months (range: 38-53 months; SD= 4.26). At the subsequent “school entry” assessment, the FXS group had an average age of 64.79 months (range: 60-83 months; SD= 4.46).

2.2 Measures

Attention-deficit/hyperactivity disorder (ADHD). The Child Behavior Checklist (CBCL; 1.5-5, 6-18; Achenbach, 1991; Achenbach & Rescorla, 2001) was completed by participants’ mothers at the initial and subsequent assessment points. The CBCL is a widely used 118 item parent rating scale used to assess the internalizing and externalizing symptoms of children. Items are answered using a 3-point Likert scale of “not true (0)”, “somewhat or sometimes true (1)”, and “very true (2).” It is broken down into individual symptom-specific scales, composite scores (internalizing, externalizing, and total problems) and also provides scales based on criteria from the Diagnostic and Statistical Manual (DSM-IV). For the DSM-based scales, there are raw scores as well as t-scores indicating severity. Overall, the CBCL was normed on a large, representative sample of children and adolescents, yielding high rates of reliability (r= 0.95; Nakamura, Ebesutani, Bernstein, & Chorpita, 2009). The ADHD scale of the CBCL has shown consistent reliability, discriminative validity, and convergent validity. Further, inter-rater reliability yielded similarly high consistency (r= 0.96; Nakamura et al., 2009). For the present study, the raw scores scale of DSM-ADHD was used to assess parent’s endorsements of ADHD symptoms. The DSM-ADHD scale had high test-retest reliability (r= 0.93; Nakamura et al., 2009). The CBCL has also successfully been used previously with children with FXS (Bargagna, Canepa, & Tinelli, 2002; Hatton, et al., 2002; Hatton, et al., 2006; Farzin, et al., 2006). The ADHD raw scores were used as a dependent variable across all analyses.

Autistic Behavior. Indication of autistic behavior severity was measured using the Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1998) at each assessment point. This is an experimenter rating scale of autistic behaviors based on observations made during each assessment. It yields a high internal consistency rate (r= 0.94) and is highly correlated with clinical ratings of autism (DiLalla & Rogers, 1994; Eaves & Milner, 1993). The measure is comprised of 15 items that measure a range of autistic behaviors. There is robust support for the constructs of social communication/interaction, sensory abnormalities, and emotional regulation measured in CARS. Each item is rated on a scale from 1 (within normal limits) to 4 (severely abnormal), allowing for a total score between 15 and 60. Scores above 30 indicate a profile of autistic behavior ranging from mild to moderate to severe. Discriminative validity has been demonstrated in the scale's sensitivity in discriminating children with autism from children without autism (DiLalla & Rogers, 1994; Eaves & Milner, 1993). The CARS has been reliably used with children with FXS (e.g. Bailey et al., 2001; Hatton et al., 2002; Hatton et al., 2006). The total raw score scale was used as a dependent variable across all analyses.

At the initial preschool assessment, 36% (n= 12) of boys with FXS were above the CARS clinical cutoff score for ASD. The mean score was 27.2 (range: 16.5 – 36.0; SD= 5.27). At the subsequent school entry assessment, 33% (n= 11) of boys with FXS met criteria for an ASD. The mean score was 27.56 (range: 16.5 – 29.0; SD= 6.02). At the initial preschool assessment, no TD boys met criteria for an ASD. The mean score was 15.09 (range: 15.00 – 15.50; SD= 0.20).

Temperament: Surgency. The Children's Behavior Questionnaire (CBQ) by Rothbart, Ahadi, Hersey, and Fisher (2001) was completed by mothers at each assessment timepoint to assess the characteristics of Surgency in children. The CBQ is comprised of 195 items, loading onto 15 scales of children's temperament. These scales are activity level, anger/frustration, attentional focusing, discomfort, fear, high intensity pleasure, impulsivity, inhibitory control, low intensity pleasure, perceptual sensitivity, positive anticipation (approach), sadness, shyness, smiling/laughter, soothability. A principal factor analysis suggested that the 15 scales loaded onto three theoretical constructs of temperament: Negative Affectivity, Surgency (Extraversion), and Effortful Control (Rothbart, Ahadi, Hershey, and Fischer, 2001; Roberts, et al., under review). Each item is answered using a 7-point Likert scale ranging from "extremely untrue of my child" to "extremely true of my child." Internal consistency reliability ranged from 0.67 to 0.94, with a mean internal consistency score of 0.77 across the 15 scales (Rothbart, Ahadi, Hershey, and Fischer, 2001). A confirmatory factor analysis (CFA) was further conducted on the 15 scales and suggested the three-factor structure was the best fitting model for typically developing children (Rothbart, Ahadi, Hershey, and Fischer, 2001). These scales demonstrated adequate internal consistent reliability, given their strong factor loadings. The scales were completed by participants' mothers. The five Surgency characteristic subscales (activity level, impulsivity, approach, shyness, and smiling and laughter) were used as the independent variables across all analyses.

2.3 Procedure

Data Collection. Data was collected as part of a larger assessment battery. Two examiners went to the participants' home to conduct the assessments. Parent rating scales (CBQ, CBCL) were mailed home ahead of the scheduled assessment and then collected on the day of the assessment. Examiners completed the CARS post-assessment. At the initial time point (preschool), raw scores were obtained from both typically developing boys and boys with FXS for the CBQ, for the CBCL, and the CARS. At the subsequent point (school entry), raw scores from boys with FXS were obtained for Surgency domains using the CBQ, for the CBCL, and for the CARS.

CHAPTER 3

RESULTS

Means and standard deviations for parent-reported Surgency characteristics raw scores are presented in Table 3.1. The means and standard deviations of the raw scores of parent-reported ADHD and experimenter reported ASD are presented in Table 3.2. Multiple regression analysis was the model used throughout. Multiple regression was employed in order to examine differences seen in Surgency (activity level, impulsivity, social approach, shyness, and smiling/laughter) as differential predictors of ADHD and autism severity. During the initial preschool assessment, trends in the relationships of Surgency characteristics and concurrent ADHD and autism raw scores were examined in both the FXS and control groups. Trends in the relationships of Surgency characteristics ratings and concurrent ADHD and autism ratings in boys with FXS were examined at the school age assessment. Finally, multiple regression analyses were conducted to examine the predictability of Surgency ratings. Through examination of the data, all assumptions for multiple regression were met. Preliminary findings yielded that from the initial assessment (preschool) to the subsequent assessment (school age) in the FXS group, the ADHD rating's Pearson's correlations (r= .39, p= 0.05) and autistic behavior rating's Pearson's correlations (r= .68, p = 0.05) were significant. Further, it was found that in the FXS group, at both assessments, that ADHD ratings and ASD ratings were not correlated and independent of each other. ADHD and ASD ratings were found to be uncorrelated and independent in the TD group as well. Normality of residuals was found.

3.1 Preschool Surgency and Concurrent ADHD and ASD in FXS and TD

ADHD. Analyses were conducted examining the five Surgency characteristics as predictors of ADHD in the FXS preschool group. The model was statistically significant, $F(5, 25) = 2.50$, $p = 0.05$. The correlation coefficient was 0.58, indicating the Surgency characteristics accounted for 34% of the variance found in ADHD raw scores. Activity Level was significantly related to ratings of ADHD ($\beta = .53$, $p = 0.01$). No other Surgency characteristics significantly related to ADHD scores in the FXS group. In the control group of typically developing boys, the overall model was not significant, $F(5,11) = 1.5$, $p = 0.27$. Surgency scores in TD boys had no significant relationship to the ADHD raw scores. See Table 3.3 and Figure 3.1.

ASD. Analyses were conducted examining the five Surgency characteristics as predictors of the ASD raw score outcome variable in the FXS group. The model was not significant, $F(5,25) = 1.0$, $p = 0.42$. In the control group of typically developing boys, the model was also not significant, $F(5, 11) = 0.92$, $p = 0.50$. It was found that no Surgency characteristics significantly related to ASD raw scores. See Table 3.3 and Figure 3.2.

3.2 School Age Surgency and Concurrent ADHD and ASD in FXS

ADHD. Analyses were conducted examining the five Surgency characteristics as predictors of the ADHD raw score outcome variable. The model was statistically significant, $F(5, 26) = 6.19$, $p = 0.01$. The correlation coefficient was 0.74, indicating that the Surgency characteristics accounted for 55% of the variance found in ADHD raw scores. Higher impulsivity ($\beta = .87$, $p = 0.01$) and shyness ($\beta = .67$, $p = 0.01$) were associated with elevated ADHD scores. The remaining Surgency scores did not yield a significant relationship with ADHD scores. See Table 3.4.

ASD. Analysis was conducted examining the five Surgency characteristics as predictors of the ASD raw score outcome variable. The model was not significant, $F(5,26) = 1.10$, $p = 0.39$. See Table 3.4.

3.3 Preschool Surgency Predicting School Age ADHD and ASD in FXS

ADHD. Analyses were conducted examining the five Surgency characteristics reported in preschool as predictors of the ADHD raw score outcome variable reported at school entry. The model was statistically significant, $F(5, 25) = 4.00$, $p = 0.01$. The correlation coefficient was 0.67, indicating that the Surgency characteristics accounted for 45% of the variance seen in ADHD scores. Higher impulsivity ($\beta = 0.56$, $p = 0.02$) and lower smiling and laughter ($\beta = -0.45$, $p = 0.03$) in preschool were related to higher ADHD scores at school age. See Table 3.5.

ASD. Analyses were conducted examining the five Surgency characteristics reported in preschool as predictors of the ASD raw score outcome variable reported at school entry. The model was not significant, $F(5,25) = 0.53$, $p = 0.75$. See Table 3.5.

Table 3.1. Surgency Characteristic Raw Scores for FXS and TD Boys

	Preschool		School Age
Surgency Characteristics (CBQ)	FXS (n=33)	TD (n=17)	FXS (n= 33)
Activity Level			
M	5.15	5.21	5.38
SD	0.88	0.70	0.83
Approach			
M	4.78	5.34	5.09
SD	0.92	0.79	0.84
Impulsivity			
M	4.55	4.55	4.67
SD	0.85	0.76	0.90
Shyness			
M	4.62	3.33	4.49
SD	1.23	1.30	1.33
Smiling & Laughter			
M	5.54	5.83	5.64
SD	0.79	0.71	0.80

Table 3.2. ADHD and ASD Raw Scores for FXS and TD Boys

	Preschool		School Age
ADHD (CBCL)	FXS (n=33)	TD (n=17)	FXS (n= 33)
M	4.52	4.24	8.09
SD	2.23	2.51	1.93
ASD (CARS)			
M	27.20	15.09	27.60
SD	5.19	0.19	5.93

Table 3.3. Regression Results for FXS and TD Boys at Preschool

	ADHD				ASD			
	Coefficient	SE	t	*p*	Coefficient	SE	t	*p*
FXS (n=33)								
Activity Level	1.35	0.50	2.70	0.01	-1.97	1.33	-1.48	0.15
Approach	-0.19	0.50	-0.37	0.72	-1.38	1.33	-1.04	0.31
Impulsivity	0.21	0.70	.30	0.77	.517	1.85	0.28	0.78
Shyness	0.28	0.43	.65	0.52	-.327	1.15	-0.29	0.78
Smiling & Laughter	0.12	0.60	.21	0.84	-.827	1.60	-0.52	0.61
TD (n=17)								
Activity Level	0.47	1.44	0.33	0.75	0.12	0.12	0.99	0.35
Approach	-0.17	1.20	-0.14	0.89	-0.09	0.10	-0.95	0.37
Impulsivity	2.27	1.47	1.55	0.15	-0.10	0.12	-0.80	0.44
Shyness	0.79	0.75	1.06	0.31	-0.11	0.06	-1.76	0.11
Smiling & Laughter	0.83	1.18	0.70	0.50	-0.03	0.10	-0.34	0.74

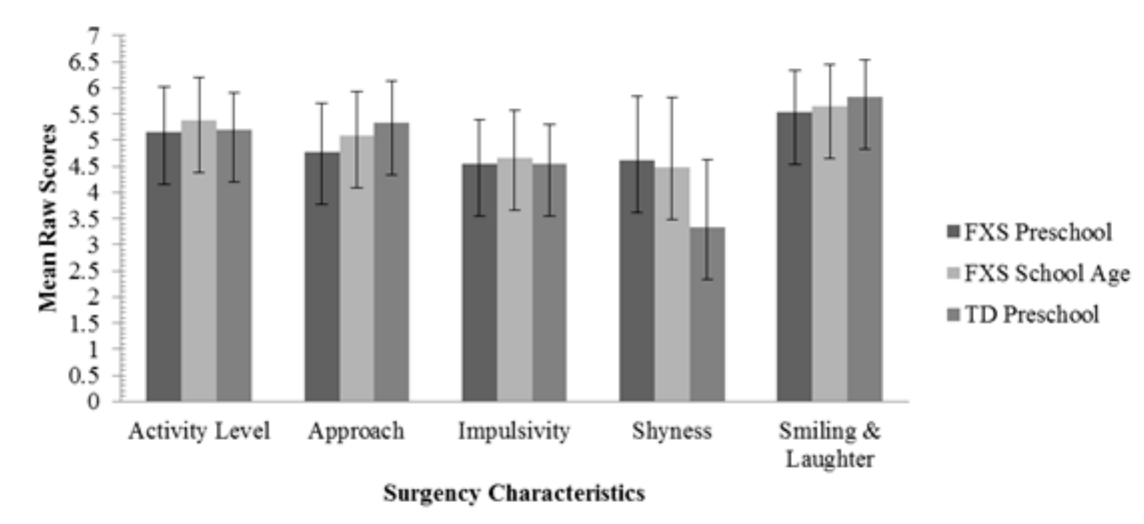

Figure 3.1. Surgency Characteristic Raw Scores for FXS and TD Boys

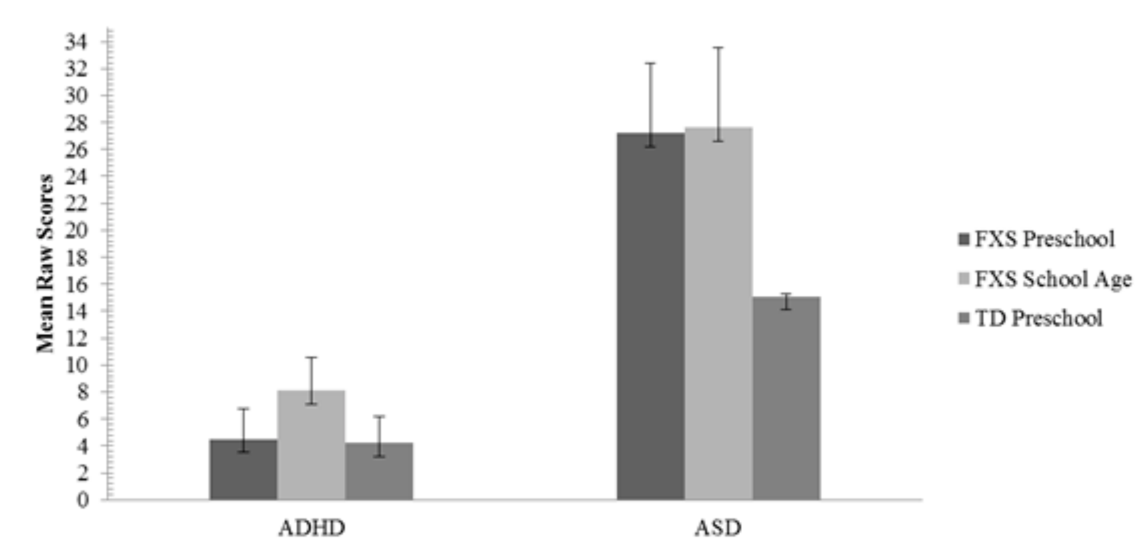

Figure 3.2. ADHD and ASD Raw Scores for FXS and TD Boys

Table 3.4. Regression Results for FXS Boys at School Age

	ADHD				ASD			
	Coefficient	SE	t	*p*	Coefficient	SE	t	*p*
FXS (n=33)								
Activity Level	-0.09	0.54	-0.167	0.09	-0.10	2.19	-0.05	0.96
Approach	0.01	0.37	0.03	0.98	-1.08	1.52	-0.71	0.48
Impulsivity	2.06	0.65	3.19	0.00	2.25	2.64	0.85	0.40
Shyness	.99	0.36	2.76	0.01	1.424	1.47	0.97	0.34
Smiling & Laughter	-0.15	0.39	-0.38	0.70	-1.23	1.60	-0.77	0.45

Table 3.5. Regression Results for Preschool Surgency Predicting School Age Raw Scores of ADHD/ASD in Boys with FXS

	ADHD				ASD			
	Coefficient	SE	t	*p*	Coefficient	SE	t	*p*
FXS (n=33)								
Activity Level	0.16	0.42	0.37	0.72	-0.83	1.59	-0.52	0.61
Approach	0.33	0.42	0.78	0.45	-0.49	1.59	-0.31	0.76
Impulsivity	1.42	0.59	2.41	0.02	1.45	2.21	0.66	0.52
Shyness	0.56	0.36	1.53	0.14	0.46	1.37	0.34	0.74
Smiling & Laughter	-1.14	0.51	-2.24	0.30	-1.88	1.91	-0.99	0.33

CHAPTER 4

DISCUSSION

The current study examined the early emergence of ADHD symptoms and their association with Surgency, as well as a possibly comorbidity between ADHD and autistic behaviors in boys with FXS. Data were collected from two time points, preschool and school entry, in an effort to gain insight about the emergence of these problematic behaviors and the predictive value of temperament. Detection of early markers indicative of future behavioral disorders allows for earlier identification and, subsequently, earlier intervention.

4.1 Preschool Surgency and Concurrent ADHD and in FXS and TD

This study demonstrates the potential value of detecting early emerging temperament facets to detect problem behavior in boys with FXS. Using characteristics of Surgency measured in preschool, we found that approach, impulsivity, shyness, and smiling and laughter were not related to preschool ratings of ADHD; however replicating previous studies that found salient hyperactive features in boys with FXS (Farzin et al, 2006; Sullivan et al, 2006), elevated activity level scores are associated with ADHD scores at preschool age. The relationship between activity level and ADHD scores is more salient in boys with FXS than in typically developing boys, who did not have any significant relationships found between activity level and ADHD scores. Furthermore, the relationship between activity level and ADHD was only significant at the preschool time point and not at school entry. Thus, while elevated activity is typically associated with this developmental state, the level of severity appears to denote a potential early marker for ADHD seen only in boys with FXS.

4.2 School Age Surgency and Concurrent ADHD in FXS

At the school entry time point, the Surgency characteristics of approach, activity level, and smiling and laughter were not associated with ADHD; however elevated levels of shyness and impulsivity were strongly associated with ADHD scores reported concurrently. An increase in shyness was not predicted and this might be due to the behaviors "shyness" is measuring on the CBQ, such as the inability to properly engage in social interactions. The inability to engage, or circumstances such as significant experiences with peer rejection, may result in a lack of motivation to partake in social interactions. Or, the impulsive nature seen in these boys may result in inappropriate responses to situation where one would expect pleasurable reactions. Commensurate with previous literature (Bailey et al., 2008; Sullivan et al., 2006), increased levels of impulsive behavior were related to higher levels of ADHD scores. The emergence of problematic impulsive behaviors become salient as tasks that require executive functioning and inhibition become more frequent in the typical school settings.

4.3 Preschool Surgency Predicting School Age ADHD in FXS

Finally, the predictive value of Surgency characteristics and the emergence of ADHD features was examined. This was done with use of Surgency characteristics reported in preschool and their relationship to reported ADHD features at school ages. The Surgency characteristics reported in preschool of activity level, approach, and shyness were not predictive of ADHD scores reported at school entry. However, elevated preschool levels of preschool impulsivity and decreased preschool levels of smiling and laughter did predict higher levels of ADHD scores reported at school entry. Concerning the decrease in smiling and laughter findings, a child with FXS may be incapable sustaining attention to engage in interactions that would be rated as smiling and laughter on the CBQ. Previous research concerning the development of attention indicates that attending to stimuli and switching attentional focus between stimuli is difficult for children with FXS (Cornish et al., 2012; Scerif et al., 2012). If attention focusing is a problem for boys with FXS, the ability to attend to parents long enough to engage in to-and-fro interactions to elicit positive smiling and laughter ratings is not likely.

Impulsivity ratings had the strongest relationship to ADHD scores overall and were shown to be the greatest indicators of concurrent or future reports of ADHD. Impulsivity has demonstrated to be a key item in the early identification of ADHD in young boys with FXS. Problematic levels of impulsivity emerge early and these elevated levels sustain overtime. Identifying elevated impulsive traits early in childhood can lead to earlier awareness of the possible presence or future development of ADHD. Earlier identification will lead to implementation of various interventions targeted at decreasing impulsive behavior and the earlier these management skills are taught, the more likely children and families will be able to prevent undesirable consequences that result from impulsive behavior, such as poor school performance, ineffective emotional regulation strategies, and poor social relationships.

4.4 Surgency and Autistic Behaviors in FXS

Finally, in an attempt to understand comorbidity and specificity of the development of ADHD in young boys with FXS, ASD rating scores were examined. It was predicted that decreased ratings of approach and smiling and laughter and increased shyness would be indicative of higher ASD ratings. In the current study, no Surgency characteristics were significantly related to ASD scores at any age in FXS, and there was no significant relationship seen between Surgency characteristics and ASD scores in the typically developing boys in preschool. While previous research has shown a correlation of increased ADHD scores related to increased ASD scores (Farzin et al., 2006; Sullivan et al., 2006), the Surgency domain of temperament at these ages does not predict strong relationships of comorbid pathologies. However, the Surgency characteristics serve as discriminative factors when studying these behavioral outcomes. The Surgency characteristics provided insight into the differentiated development of ADHD and ASD and that characteristics such as activity level, impulsivity, and smiling and laughter are more indicative of present and future elevated concerns of the presence of ADHD, rather than ASD, in boys with FXS.

4.5 Limitations

There were three main limitations in the study. First, non-diagnostic measures were used to assess the outcome measures, the CARS and the CBCL. The scores are continuous in nature and more focused with reporting overall symptomology than diagnostic cutoffs. Throughout the study, ADHD and ASD are discussed in terms of “symptoms”, “features”, and “behaviors” to emphasize the point that our aim was to find associations between temperament scores in FXS and elevated symptomology of ADHD and ASD and the goal was not to see which participants met for cutoff. A second limitation was using parent reported measures for Surgency characteristics and ADHD ratings. As with any study reliant on parent reporting, there are possible problematic concerns when using parent rating scales. Parents own pathology (such as ADHD/ASD) can confound reports in how they view their child's behaviors. Also, another common issue of parent rating scales is the prevalence of under or over endorsing symptoms, and this concern is seen across research and clinical settings. Parents can have skewed points of view of what "typical" development looks like for children, resulting in biased answers in their reports. Furthermore, given the similarities between Surgency characteristics and ADHD features, it may be hard for parents to differentiate between temperament characteristics and behaviors associated with ADHD. Parents may be rating obsevations of their child as both a temperament characteristic and a problematic behavior. Greater specificity as to what qualifies an observation of a child as a Surgency characteristic and what is a behavior associated with ADHD would possibly increase the accuracy of reporting. Finally, a third limitation may be the sample size (N=33). Compared to temperament and behavioral disorders in typical populations, this is a small sample. However, given the low prevalence of FXS in the general population, sample sizes of 30 and up are considered adequate (Hatton, 2006; Farzin et al., 2006).

4.6 Future Directions and Conclusions

Concerning future directions, it would be beneficial to examine parent reported temperament in conjunction with experimental and physiological measures, such as variability seen in heart rate activity or cortisol levels. Physiological data provides another objective source of information on ADHD features such as hyperactivity, inhibition, and attention. Also, more longitudinal research should be conducted to examine the persistence of symptoms in the developmental trajectory of individuals. Even in the short time from preschool to school entry, there was an observed shift in the saliency of characteristics related to ADHD outcomes. Following participants throughout the remainder of childhood and adolescence would be informative to the presentation of ADHD features and how they may change with maturation.

The current study presents the first examination of Surgency characteristics as indicators of concurrent and predictive ADHD features in boys with FXS. The results of this study provide insight into the possible temperamental indicators associated with the early emergence of ADHD. Additionally, it was found that these Surgency characteristics were not related to comorbid autistic behaviors in these boys with FXS, suggesting Surgency characteristics are more informative for understanding the unique development of ADHD in FXS. Future studies should continue to investigate biological and environmental contributors to the early emergence of ADHD in individuals with FXS. The identification of early emergent features of ADHD can potentially contribute information for early intervention strategies for children with FXS, as well as the broader, non-FXS population.

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