AN EXAMINATION OF AUTISM SYMPTOMATOLOGY IN YOUNG CHILDREN
WITH FAMILY HISTORY OF AUTISM SPECTRUM DISORDER

A Thesis

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by

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Abstract

Multiple genetic and environmental factors have roles in the etiology of autism spectrum disorder (ASD). Thus, researchers have become increasingly interested in studying family members of individuals with ASD in order to examine possible risk factors and to identify early markers of the disorder. While family history of ASD may put an individual at risk for developing autism, there is limited research examining how the degree of relationship to the affected individual may be related to an individual’s presenting ASD symptomatology. Because closer familial relationships (i.e., first-degree relatives) have more shared genetic material and tend to have increased common environment than more distal relationships (i.e., second- or third-degree relatives), the present study aimed to examine if there was an association between degree of relationship and autism symptomatology in young children with a family history of ASD. Participants included 470 young children ($M = 25.64$ months, $SD = 5.07$) recruited through a statewide early intervention program who were diagnosed with ASD or identified as atypically developing with a family history of ASD. Regression analyses were conducted to investigate the relationships between group (e.g., ASD and atypically developing), degree of relationship (e.g., first-degree and second- or third-degree), and the interaction between group and degree of relationship and ASD symptomatology. Implications and clinical utility of these results are discussed.
Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by pervasive impairments in social interaction and communication, and the presence of restricted and stereotyped behaviors and interests (American Psychiatric Association [APA], 2013) that has become an increasingly popular area of research in the last few decades (Matson & Kozlowski, 2011; Matson & LoVullo, 2009). Research on these core deficits has been extensively investigated (Bertoglio & Hendren, 2009; Bodfish, Symons, Parker, & Lewis, 2000; Volkmar & Pelphrey, 2014; Wang & Zhong, 2012; Worley & Matson, 2012; Zander & Bölte, 2015).

Additionally, there is increasing research on families of individuals with ASD (Constantino, Zhang, Frazier, Abbacchi, & Law, 2014; Geschwind, 2011; Risch et al., 2014; Rutter, 2000). Prospective studies of siblings of children with ASD allow for identification of potential early markers for atypical development (Ozonoff et al., 2011). In addition to siblings, research on other relatives has increased. Researchers have studied the subclinical impairment of autism symptoms in relatives, which has provided evidence for the effect of gene and environment interactions playing a causal role in ASD (Bernier, Gerdts, Munson, Dawson, & Estes, 2012a; Gerdts & Bernier, 2011; Piven, Palmer, Jacobi, Childress, & Arndt, 1997; Risch et al., 2014). Interest in studying individuals with family history of ASD has grown in part because of the potential for further research on atypical development.

The current study was designed to explore the relationship between having a family member diagnosed with ASD and autism symptomatology in young children. Children with a family history of ASD were included in the study and further separated
into groups based on individual diagnosis (e.g., ASD or atypically developing). To further explore the relationship between family history and autism symptomatology, degree of relationship (e.g., first-degree and second- or third-degree relationships) was examined to study potential differences between groups.

**Diagnostic Criteria for Autism Spectrum Disorder**

The foundation for the condition we now know as autism is attributed to Leo Kanner and his publication of “Autistic Disturbances of Affective Context” in 1943. In this paper, Kanner described affected children as having communication deficits, severe socialization impairments, and a desire to maintain sameness. The basis of this condition was described as an “extreme autistic aloneness” or an inherent inability to relate to others, characterized by behaviors such as minimal eye contact, preference of objects rather than people, and not showing affection. In 1944, Kanner termed this set of symptoms as “infantile autism,” in which autism referred to the individual’s failure to form relationships with the external world (Kanner, 1944). Kanner stated that this social functioning deficit arises during infancy and results from an innate inability to relate with others.

Despite the early work of Kanner, autism was not included as a diagnosis into the *Diagnostic and Statistical Manual of Mental Disorders* until 1980, and several changes to the diagnostic criteria have subsequently been made over the course of the last 30 years. The APA released the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* in May 2013 (*DSM-5*; APA, 2013). The *DSM-5* collapsed previous autism subcategories of Autistic Disorder, Asperger’s Disorder, and PDD-NOS into one diagnosis of “Autism Spectrum Disorder” and included severity levels to indicate the
amount of support required by the individual. For a diagnosis of ASD, an individual must present with all three items of the Social Communication domain and at least two symptoms of the RRB domain. The Social Communication domain includes: (a) impairments in social-emotional reciprocity, (b) deficits in nonverbal communication, and (c) significant difficulties in developing and maintaining relationships. The domain of RRB includes: (a) stereotyped, repetitive motor movements, use of objects, or language; (b) strict adherence to routines; (c) abnormal and highly restricted interests; and (d) sensory sensitivities (i.e., hypo- or hyper-sensitivity) to stimuli or unusual interest in sensory aspects of the environment. Symptoms must be present in the early developmental period “but may not become fully manifest until social demands exceed limited capacities” (APA, 2013). These behaviors refer to individuals who may have less impairment of symptoms prior to inclusion in more demanding social environments, such as enrollment in school or similar settings.

**Autism Spectrum Disorder in Families**

Historically, the role of families in the etiology of ASD was thought to be primarily environmental and due to parenting. It was believed that ASD results from “refrigerator mothers” who lacked warmth and emotional support (Bettelheim, 1967). However, currently researchers have indicated that family factors in ASD are primarily due to high genetic contributions. Estimates of concordance rates of autism in families are higher than in the general population, ranging from 2 to 10% (Constantino, Zhang, Frazier, Abbacchi, & Law, 2014; Newschaffer et al., 2007; Risch et al., 2014). Twin studies have shown that monozygotic twins have even higher rates of up to 90%, compared to 10 to 30% concordance in dizygotic twins (Sebat et al., 2007). Ritvo et al.
(1989) found that when a family has one child with ASD, the risk of having another child developing the disorder was 8%. This risk increased to 35% when two children in the family were already diagnosed with ASD. A more recent study of sibling concordance rates has shown higher estimates of approximately 20% (Ozonoff et al., 2011).

In addition to increased risk, researchers have found significantly higher rates of ASD characteristics in first-degree relatives of individuals with ASD compared to controls. This finding has led to research on broad autism phenotype (BAP) (Gerdts & Bernier, 2011; Klusek, Losh, & Martin, 2014). BAP is defined as the subclinical impairment in ASD associated characteristics among relatives of individuals with ASD (Bernier et al., 2012a; De la Marche et al., 2012; Messinger et al., 2013). Traits associated with BAP include social-emotional impairments (e.g., difficulties with initiating and maintaining relationships, lack of affection), aloof personality traits (i.e., lower scores on measures of extraversion and agreeableness), and highly focused and unusual interests (Bailey, Palferman, Heavey, & Le Couteur, 1998). Although individuals with BAP have sub-threshold impairments in autism-associated domains, they may still experience significant challenges that warrant supports (Pruett, 2014). However, overall BAP tends to occur in low rates in simplex families (Davidson et al., 2014; Losh, Childress, Lam, & Piven, 2008).

Researchers have also found higher rates of cognitive and language delays in families of individuals with ASD (Folstein & Rutter, 1988). Additional studies of siblings of children with ASD have found that they are at increased risk for various social, language, and behavior impairments (Hallett et al., 2013; London & Etzel, 2000; Micali, Chakrabarti, & Fombonne, 2004; Miller et al., 2015). In addition to impairments
in autism symptoms, researchers have suggested that relatives of individuals with ASD may also exhibit face processing atypicalities (Adolphs, Spezio, Parlier, & Piven, 2008; Fiorentini, Gray, Rhodes, Jeffery, & Pellicano, 2012; Wilson, Freeman, Brock, Burton, & Palermo, 2010), problems with phonological processing (Schmidt et al., 2008), and abnormal patterns of gaze fixation (Dalton, Nacewicz, Alexander, & Davidson, 2007). Taken together, researchers have shown that relatives of individuals with ASD display not only impairments in ASD symptoms, but also broader developmental delays and associated deficits.

Research on multiplex families (i.e., more than one child diagnosed with ASD) has also provided insight into BAP. Multiplex families have been found to have a higher risk of having a second- or third-degree relative with the “lesser variant” of autism (i.e., Pervasive Development Disorder-Not Otherwise Specified) than simplex families, suggesting that there may be genetic loading in multiplex families (Szatmari et al., 2000). Studies have also indicated that ASD symptoms are more prevalent in multiplex families (Gerdts, Bernier, Dawson, & Estes, 2013; Szatmari et al., 2000; Virkud, Todd, Abbacchi, Zhang, & Constantino, 2009). For example, parents in multiplex families have been found to exhibit more BAP traits than parents in simplex families (Losh et al., 2008). These findings suggest that there may be different modes of inheritance for simplex autism compared to multiplex autism (Virkud et al., 2009); however, additional research is needed.

Studies on multiplex families have also examined differences between affected siblings. A study by Goin-Kochel and colleagues (2008) found that siblings in multiplex families have more similar verbal and nonverbal IQ and adaptive functioning scores than
unrelated children with ASD, which suggests a genetic component in skill domains.

Other studies have shown that individuals in families in multiplex families have differences in both symptomatology and severity (Reichenberg, Smith, Schmeidler, & Silverman, 2007; Robinson et al., 2014). For example, Martin and Horriat (2012) found greater differences in IQ scores and ASD severity when siblings were less than two years apart in age, compared to other age differences.

At present, there is limited research on examining the association between degree of relationship in family history and autism symptoms. A study by Pickles and colleagues (Pickles et al., 2000) found that ASD severity was related to familial loading for probands with speech, but found no variation in loading among nonverbal probands. This suggests that first-degree relatives of a verbal individual with ASD may experience more ASD impairments than more distal relationships. Additionally, male first-degree relatives may have higher risk of ASD, BAP impairments, and speech delays (Eriksson, Westerlund, Anderlid, Gillberg, & Fernell, 2012).

The role of genetics and family history is undeniably complex. Given the range of impairments found in families affected by ASD, it has been suggested that autism itself is not inherited; rather, what may be inherited is a genetic predisposition for communication or social impairments that interacts with environmental factors to result in ASD (Folstein & Rutter, 1988).
Purpose

A study by Kozlowski and colleagues (2012) analyzed ASD and atypically developing children, and separated them into groups based on family history of ASD. A significant difference was found between ASD and atypically developing children with a family history of the disorder; however, no significant differences were found within ASD and atypically developing groups based on family history. In contrast to findings by Kozlowski and colleagues, a study by Estabillo and colleagues (2016) indicated that there may be differences between atypically developing groups based on family history of ASD. A family history of ASD may play a role in autism symptomatology for atypically developing children. Children with a family history of the disorder were found to have higher endorsement of ASD symptoms than children without family history.

As a follow-up, the current study aimed to further examine the relationship between family history of ASD and autism symptomatology in young children by specifying the degree of relationship. The goal of this study was to identify if the degree of relationship was associated with autism symptom severity and symptomatology in young children. This study will enhance the understanding of the role of family history of ASD on deficits experienced by young children who are diagnosed with autism or are atypically developing. Findings from this study contribute to the growing literature on relatives of individuals with ASD.

The atypically developing children were of particular interest in this study. Although there is growing research on BAP in first-degree relatives of affected individuals, there is limited research examining BAP in more distal relationships. It is unknown if there are differences in ASD severity and symptomatology in atypically
developing children based on degree of relationship to affected individuals. Given the importance of early intervention on the prognosis of developmental delays, findings from this study may demonstrate that family history of ASD is not only a risk factor for developing the disorder, but degree of relationship may have differential effects on ASD severity and core symptoms of the disorder.

Based on previous literature, hypotheses were formulated with regard to the results of this study:

Hypothesis 1. Researchers indicated significant differences between ASD and atypically developing groups with family history of ASD (Estabillo et al., 2016; Kozlowski et al., 2012). Therefore, it was hypothesized that there would be significant differences between ASD and Atypical groups on ASD severity, Communication, Socialization, and RRB scores due to diagnosis. Because the measure assesses autism symptomatology in young children, diagnostic group will predict scores such that the ASD group will have higher scores than the Atypical group on each dependent variable.

Hypothesis 2. It was hypothesized that there would be an association between degree of relationship and ASD severity, Communication, Socialization, and RRB scores for children with ASD. Previous literature suggests that multiplex families (i.e., first-degree relationships) exhibit greater BAP traits than simplex families; therefore, it was hypothesized that children with ASD who have a first-degree relative also diagnosed with the disorder would have higher scores on each of the dependent variables.

Hypothesis 3. In contrast, it was hypothesized that there would be no significant difference between Atypical groups on ASD severity, Communication, Socialization, and RRB scores based on degree of relationship. Given the very limited research on how
degree of relationship may be associated with symptomatology in atypically developing children, it was unknown if degree of relationship would be a factor for atypically developing children. As such, the current study posited a null hypothesis that there would be no difference between atypical groups based on degree of relationship.
Methods

Participants

The participants for the current study were selected from a pre-existing database that continues to expand with ongoing data collection. All participants in the sample were recruited through the EarlySteps program, which is Louisiana’s Early Intervention System under the Individuals with Disabilities Education Act, Part C. In EarlySteps, children under 36 months of age who have developmental delays (i.e., a diagnosis of ASD or global developmental delay) or a medical condition likely to result in developmental delays (e.g., genetic disorders, premature birth, cerebral palsy, and epilepsy) qualify to receive services. Participants for the current study were enrolled in EarlySteps between February 2008 and October 2015.

Participants in this sample were between the ages of 17 to 37 months old, which is the age range validated for the BISCUIT. ASD diagnoses were made by a licensed clinical psychologist with over 30 years of experience with children with developmental disabilities. Diagnoses were made based on an algorithm consisting of DSM-5 criteria, developmental profiles from the Batelle Developmental Inventory-2 (BDI-2), BISCUIT-Part 1 scores, and clinical judgment. Children in the atypically developing group had various developmental delays including general developmental delay, cerebral palsy, speech delay, hearing impairments, and various genetic syndromes (e.g., Down syndrome, Fragile X syndrome, DiGeorge syndrome).

Of the total 9,340 children in the database, participants for the current study included 470 children ($M = 25.64$ months, $SD = 5.07$). Only participants who indicated a first-degree (i.e., biological parent or sibling), second-degree (i.e., grandparent, uncle,
aunt, nephew, niece, half-sibling), or third-degree relative (i.e., cousin) as having a diagnosis of ASD were included in the sample. Of the children with ASD, 188 parents indicated that they had another family member with ASD. Of the children identified as atypically developing, 592 had a family history of ASD. Due to unequal group sizes, participants were randomly selected from the atypical group such that the group size was no more than 1.5 times larger than the ASD+FH group (Pituch, Whittaker, & Stevens, 2013). This approach resulted with 188 children in the ASD+FH group and 282 children in the Atypical+FH group. Degree of relationship was subsequently split into two groups (e.g., first-degree and second- or third-degree). In the Atypical+FH group, 213 participants had second- or third-degree relatives with ASD and 69 had a first-degree relative with ASD. In the ASD+FH group, 134 participants had second- or third-degree relatives with ASD and 54 had a first-degree relative with ASD. Demographics for the study participants are shown in Table 1.

Table 1. Demographic information for study participants separated by group

<table>
<thead>
<tr>
<th></th>
<th>Atypical+FH All (N = 282)</th>
<th>Atypical+FH 2nd or 3rd degree (N = 213)</th>
<th>Atypical+FH 1st degree (N = 69)</th>
<th>ASD+FH All (N = 188)</th>
<th>ASD+FH 2nd or 3rd degree (N = 134)</th>
<th>ASD+FH 1st degree (N = 54)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M (SD)</td>
<td>25.26 (5.22)</td>
<td>25.22 (5.20)</td>
<td>25.39 (5.31)</td>
<td>26.21 (4.81)</td>
<td>26.19 (4.84)</td>
<td>26.28 (4.78)</td>
</tr>
<tr>
<td><strong>Gender (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>66.3</td>
<td>66.7</td>
<td>65.2</td>
<td>69.7</td>
<td>69.4</td>
<td>70.4</td>
</tr>
<tr>
<td>Female</td>
<td>32.6</td>
<td>32.4</td>
<td>33.3</td>
<td>29.8</td>
<td>30.6</td>
<td>28.3</td>
</tr>
<tr>
<td><strong>Ethnicity (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>31.6</td>
<td>31.9</td>
<td>30.4</td>
<td>34.6</td>
<td>33.6</td>
<td>37.0</td>
</tr>
<tr>
<td>White</td>
<td>57.4</td>
<td>57.3</td>
<td>58.0</td>
<td>54.3</td>
<td>54.5</td>
<td>53.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.1</td>
<td>0</td>
<td>3.7</td>
</tr>
<tr>
<td>Other</td>
<td>6.7</td>
<td>6.6</td>
<td>7.2</td>
<td>8.5</td>
<td>10.4</td>
<td>3.7</td>
</tr>
</tbody>
</table>

Note. AA = African American.

**Measure**

The BISCUIT is a three-part assessment battery designed to evaluate children 17 to 37 months of age for ASD symptoms, comorbidity, and challenging behaviors.
The measure has been validated for children 17-37 months of age. It has an overall correct classification rate of .89 and internal reliability of .97 (Matson, Wilkins, Sevin, et al., 2009; Matson, Wilkins, Sharp, et al., 2009). When distinguishing between ASD and atypically developing children, sensitivity rates have been estimated to be 93.4 and specificity rates have been found to be 86.6 (Matson, Wilkins, Sharp, et al., 2009).

The BISCUIT-Part 1 focuses on assessment of autism symptomatology. The measure contains 62 items which are administered by an assessor to the child’s parent or caregiver. Each question is rated on a 3-point Likert scale in which the parent or caregiver compares the child to same aged peers. Items are rated such that 0 = “not different; no impairment,” 1 = “somewhat different; mild impairment,” and 2 = “very different, severe impairment.” Questions include “use of language to communicate,” “socializes with others his/her age,” and “abnormal preoccupation with parts of an object or objects.” Total scores may be interpreted as a measure of ASD severity. Scores between 0 and 16 indicate “No ASD/Atypical Development.” Scores between 17 and 38 categorize the child as in the “Possible ASD” range. A total score of 39 and above classifies the child as in the “Probable ASD” range. Factor analysis of the measure indicated the items to load onto three factors, which include communication, socialization, and RRB (Matson, Boisjoli, Hess, & Wilkins, 2010). These factors aligned with the previous DSM-IV-TR domains for an Autistic Disorder diagnosis. In the current study, Cronbach’s alphas were calculated such that for the total BISCUIT-Part 1 items \( \alpha = .97 \). For the subscales, Communication was calculated as \( \alpha = .86 \), Socialization was found to be \( \alpha = .96 \), and RRB was \( \alpha = .92 \).
Procedure

The current study was approved by the State of Louisiana’s Office of Citizens with Developmental Disabilities and the Louisiana State University Institutional Review Board prior to initiation of data collection. As part of the EarlySteps assessment protocol, the BISCUIT was administered by evaluators who specialize in psychology, social work, speech-language pathology, special education, occupational therapy, and physical therapy. Evaluators previously attended a daylong workshop training on the BISCUIT, which included information on ASD and administration of the full BISCUIT battery. EarlySteps evaluations were conducted in the participants’ homes and included administration of the BDI-2 and BISCUIT.

During the EarlySteps assessment, evaluators record parent responses on the BISCUIT demographic form and the measure. Demographic information included name, date of birth, gender, ethnicity, birth weight, and current height and weight. Additional questions included first concerns regarding the child’s development, age of the child at first concern, and age of the child at developmental milestones. The child’s diagnosis history and family history of ASD were also obtained. Regarding family history, caregivers were asked if the child had a relative diagnosed with ASD, the individual’s relationship to the child, age of the relative at diagnosis, date of the assessment, and diagnosis received.
Statistical Analyses

Power Analysis

To determine the sample size required for the study, a priori power analyses were conducted using G*Power 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007). For these analyses, alpha was set to .05, power at .80, and effect size of .15 (Hinkle, Wiersma, & Jurs, 2003). The effect size of .15 is considered to be medium for a multiple regression (Cohen, 2008). With these parameters, the proposed study required a minimum sample size of 77 participants.

Preliminary Analyses

All statistical analyses were performed using SPSS 24.0. Data included for analysis were participant information (e.g., gender, age, ethnicity, diagnosis, and if a relative is diagnosed with ASD) and BISCUIT-Part 1 items. Only individuals who indicated a family history (FH) of first-, second-, or third-degree relatives as having ASD were included (i.e., more distal relationships were excluded for analyses). Groups were subsequently coded as categorical variables, with participants classified as ASD+FH or Atypical+FH. Total BISCUIT-Part 1 scores and communication, socialization, and RRB subscales were calculated in SPSS as their own variables.

The predictor and outcome variables were coded as follows. The dependent variables of the study (e.g., BISCUIT-Part 1 total score, communication, socialization, RRB) are calculated scores and therefore were all measured as continuous variables. The independent variables of the study were Group (e.g., ASD+FH, Atypical+FH) and Degree of Relationship (e.g., first-degree, second- or third-degree), which are both categorical variables. These variables were dummy coded for analyses. For Group
analyses, Atypical+FH was coded as 0 (i.e., reference group) and ASD+FH was coded as 1. For the Degree of Relationship analyses, second- or third-degree was coded as 0 and first-degree was coded as 1. The interaction between Group and Degree of Relationship was then calculated as its own variable by multiplying the two variables.

Preliminary analyses were conducted to examine potential differences between groups on demographic information. Chi-square analyses were performed to determine if there were significant differences between groups on gender and ethnicity. Chi-square analysis indicated no significant difference between group on gender, $\chi^2(1) = .47, p > .05$. No significant difference was found between groups on ethnicity, $\chi^2(3) = 1.08, p > .05$. To examine differences between groups on age, an analysis of variance was conducted. The mean age for the ASD+FH group was 26.21 months ($SD = 4.81$), while the mean age for the Atypical+FH group was 25.26 months ($SD = 5.22$). Levene’s test did not indicate unequal variances between groups, $F(1, 468) = 3.10, p > .05$. The difference in age was found to be significant between groups, $F(1, 468) = 3.98, p = .047$. Thus, results from this study must be interpreted with caution as they may not generalize to the population.

**Data Analyses**

Multiple regression assumptions were also checked. First, all predictor variables were categorical and the outcome variables were continuous. Second, all predictors had variation in value. Multicollinearity was then examined through tolerance and variance inflation factors (VIF), as well as examination of correlations between predictor variables. Tolerance values of greater than .1, VIF values of less than 10, and correlation coefficients less than .9 show that the assumption of no multicollinearity is met (Field,
For each of the four regression models, tolerance, VIF, and correlation coefficients were within the suggested ranges, indicating that the no multicollinearity assumption was met for each model. To test the assumption of independent errors, the Durbin-Watson test statistic was computed. According to Field (2013), this statistic may vary between 0 and 4, with a value of 2 indicating that the residuals are uncorrelated. For each model, this statistic was within the suggested range. To test assumptions of linearity and homoscedascity, histograms and normal probability plots of the residuals for each of the model were examined. For each of the four models, the histograms indicated normal distributions. Normal probability plots also did not show large deviations from normality for any of the four models.

Multiple linear regression models were then created with the Enter method. This allowed the Group, Degree of Relationship, and interaction term to be entered simultaneously into the regression models. Multiple regression analyses allowed for examination of the predictive influence of the independent variables on each of the dependent variables (i.e., BISCUIT-Part 1 total score, Communication, Socialization, RRB). Subsequent analyses are referred to by model. Model 1 indicates analyses with the BISCUIT-Part 1 total score as the dependent variable, Model 2 refers to the regression model with the Communication subscale as the dependent variable, Model 3 is the regression model with the Socialization subscale as the dependent variable, and Model 4 indicates analyses with the RRB subscale as the dependent variable.
Results

To test if there was a significant difference between groups on degree of relationship, a chi-square test was conducted. No significant difference between Atypical+FH and ASD+FH groups was found, $\chi^2(1) = 1.06, p > .05$. This finding revealed that in this study, children with ASD do not tend to have more first-degree relatives also diagnosed with the disorder than atypically developing children.

Table 2. Results of the regression analyses for Group and Family Degree variables predicting BISCUIT-Part 1 total scores and subscales

<table>
<thead>
<tr>
<th>Variable</th>
<th>$R^2$</th>
<th>$B$</th>
<th>$SE B$</th>
<th>$\beta$</th>
<th>$t$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BISCUIT-Part 1 total score</td>
<td>.55</td>
<td>41.13</td>
<td>1.93</td>
<td>.78</td>
<td>21.30</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Group</td>
<td></td>
<td>41.13</td>
<td>1.93</td>
<td>.78</td>
<td>21.30</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Family Degree</td>
<td></td>
<td>4.14</td>
<td>2.43</td>
<td>.07</td>
<td>1.71</td>
<td>.09</td>
</tr>
<tr>
<td>Group x Family Degree</td>
<td></td>
<td>-7.73</td>
<td>3.72</td>
<td>-0.10</td>
<td>-2.08</td>
<td>.04</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Communication</td>
<td>.22</td>
<td>4.01</td>
<td>.41</td>
<td>.47</td>
<td>9.86</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Group</td>
<td></td>
<td>4.01</td>
<td>.41</td>
<td>.47</td>
<td>9.86</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Family Degree</td>
<td></td>
<td>.46</td>
<td>.51</td>
<td>.05</td>
<td>.91</td>
<td>.36</td>
</tr>
<tr>
<td>Group x Family Degree</td>
<td></td>
<td>-.16</td>
<td>.78</td>
<td>-.01</td>
<td>-.20</td>
<td>.84</td>
</tr>
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<td>Socialization</td>
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<td>.96</td>
<td>.77</td>
<td>20.91</td>
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<tr>
<td>Group</td>
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<td>20.12</td>
<td>.96</td>
<td>.77</td>
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</tr>
<tr>
<td>Family Degree</td>
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<td>1.21</td>
<td>.07</td>
<td>1.57</td>
<td>.12</td>
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<td>1.86</td>
<td>-.07</td>
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<td>.13</td>
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<tr>
<td><strong>Model 4</strong></td>
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<tr>
<td>RRB</td>
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<td>13.80</td>
<td>.77</td>
<td>.72</td>
<td>17.96</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Group</td>
<td></td>
<td>13.80</td>
<td>.77</td>
<td>.72</td>
<td>17.96</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Family Degree</td>
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<td>.97</td>
<td>.06</td>
<td>1.29</td>
<td>.20</td>
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<tr>
<td>Group x Family Degree</td>
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<td>1.48</td>
<td>-.12</td>
<td>-2.41</td>
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Note. Model 1: $F(3, 466) = 188.72, p < .001$. Model 2: $F(3, 466) = 44.25, p < .001$. Model 3: $F(3, 466) = 186.46, p < .001$. Model 4: $F(3, 466) = 129.34, p < .001$.

Results for each of the four models can be found in Table 2. For Model 1, which examined ASD symptom severity as the dependent variable, a regression model was created with BISCUIT-Part 1 total score as the outcome variable. Results of the regression indicate that the predictors significantly predicted BISCUIT-Part 1 total score,
\( F (3, 466) = 188.72, p < .001, R^2 = .55, \) adjusted \( R^2 = .55. \) Examination of the predictors shows that Group significantly predicted BISCUIT-Part 1 total score (\( B = 41.13, t (464) = 21.30, p < .001 \)). Family degree did not significantly predict BISCUIT-Part 1 total score (\( B = 4.14, t (464) = 1.71, p > .05 \)); however, the interaction between Group and Family Degree was found to significantly predict scores (\( B = -7.73, t (464) = -2.08, p < .05 \)).

Model 2 analyzed the Communication subscale as the dependent variable. The predictors in Model 2 were found to significantly predict Communication subscale score, \( F (3, 466) = 44.25, p < .001, R^2 = .22, \) adjusted \( R^2 = .22. \) Examination of the predictors shows that Group significantly predicted Communication subscale score (\( B = 4.01, t (464) = 9.86, p < .001 \)); however, neither Family degree (\( B = .46, t (464) = .91, p > .05 \)) nor the interaction between Group and Family Degree (\( B = -.16, t (464) = -.20, p < .05 \)) were found to significantly predict Communication subscale scores.

Model 3 examined the Socialization subscale score as the dependent variable. Results of the regression indicate that the predictors significantly predicted Socialization subscale score, \( F (3, 466) = 186.746, p < .001, R^2 = .55, \) adjusted \( R^2 = .54. \) Examination of the predictors shows that Group significantly predicted the Socialization subscale score (\( B = 20.12, t (464) = 20.91, p < .001 \)). Family degree (\( B = 1.90, t (464) = 1.57, p > .05 \)) and the interaction between Group and Family Degree (\( B = -2.83, t (464) = -1.53, p > .05 \)) did not significantly predict Socialization subscale score.

Results of the regression for Model 4, which examined RRB subscale score as the dependent variable, indicate that the independent variables significantly predicted RRB subscale score, \( F (3, 466) = 129.34, p < .001, R^2 = .45, \) adjusted \( R^2 = .45. \) Examination
of the predictors shows that Group significantly predicted RRB subscale score (B = 13.80, t (464) = 17.96, p < .001). Family degree did not significantly predict RRB subscale score (B = 1.24, t (464) = 1.29, p > .05); however, the interaction between Group and Family Degree was found to significantly predict scores (B = -3.56, t (464) = -2.41, p < .05).

To examine differences in scores within groups, several independent samples t-tests were conducted. Mean scores and standard deviations can be found in Table 3. BISCUIT-Part 1 total scores were not significantly different between ASD+FH groups based on degree of relationship, t (186) = 1.11, p > .05. No significant difference was found between Atypical+FH groups, t (280) = -1.92, p > .05. Independent samples t-tests also indicated no difference in Communication subscale scores between Atypical+FH groups, t (280) = -.83, p > .05, or ASD+FH groups, t (186) = -.62, p > .05. For the Socialization subscale, independent samples t-tests also indicated no difference between Atypical+FH groups, t (280) = -1.79, p > .05, or ASD+FH groups, t (186) = -.57, p > .05. Regarding the RRB subscale, analyses indicated no difference between Atypical+FH groups, t (280) = -1.59, p > .05, or ASD+FH groups, t (186) = 1.68, p > .05.

Table 3. Mean BISCUIT-Part 1 total and subscale scores separated by group

<table>
<thead>
<tr>
<th></th>
<th>Atypical+FH</th>
<th>ASD+FH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N = 282)</td>
<td>2nd or 3rd degree (N = 213)</td>
</tr>
<tr>
<td>BISCUIT-Part 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M (SD)</td>
<td>17.45 (15.66)</td>
<td>16.44 (14.21)</td>
</tr>
<tr>
<td>Communication</td>
<td>7.11 (4.03)</td>
<td>7.00 (4.01)</td>
</tr>
<tr>
<td>M (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Socialization</td>
<td>5.26 (7.73)</td>
<td>4.79 (7.15)</td>
</tr>
<tr>
<td>RRB</td>
<td>3.71 (5.68)</td>
<td>3.41 (5.14)</td>
</tr>
<tr>
<td>M (SD)</td>
<td></td>
<td></td>
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</tbody>
</table>
Discussion

Much of the research on families affected by ASD focuses on simplex and multiplex families (Gerdts et al., 2013; Losh et al., 2008), or is designed to study at-risk children (i.e., prospective studies of younger siblings of children with ASD) (Cornew, Dobkins, Akshoomoff, McCleery, & Carver, 2012; Landa & Garrett-Mayer, 2006; Sacrey et al., 2015; Zwaigenbaum et al., 2009). At present, there is limited research examining how the degree of relationship may be associated with ASD severity and symptom domains; therefore, the present study sought to examine how degree of relationship may be related to ASD symptomatology in young children with a family history of ASD.

When examining rates of first- and second- or third-degree relatives with ASD, no significant difference was found between ASD and atypically developing groups. This shows that although family history is a risk factor, children with ASD do not tend to have more first-degree relatives diagnosed with the disorder than atypically developing children.

The strongest predictor of BISCUIT-Part 1 total score and each of the subscale scores is diagnostic group, which supports Hypothesis 1. As the measure utilized in the study was specifically designed to assess ASD symptom severity and symptomatology in young children, properly discriminating between ASD and atypically developing groups is necessary. Examination of the regression models shows how group predicts scores when controlling for the other variables. For each of the models, having a diagnosis of ASD resulted in higher scores. In Model 1, children with ASD had scores 41.13 points higher than atypically developing children. This is important to note given that cut-off
scores on the BISCUIT-Part 1 classify children with scores above 39 as in the “Probable ASD” range. Thus, Model 1 indicates that children with ASD are categorized in the appropriate range when controlling for the other variables.

For each of the subscales, children with ASD also had more severe deficits. In Model 2, which examined predictability of Communication subscale scores, children with ASD score 4.01 points higher than atypically developing children. Given that speech/language delays and hearing impairment are common diagnoses in the atypically developing group, a smaller point difference between the groups may be expected. Although the difference was only 4.01 points, it was found to be significant in the model. For Model 3, group also best predicted Socialization subscale scores such that children with ASD score 20.12 points higher than atypically developing children. Additionally, in Model 4, children with ASD were found to score 13.80 points higher on the RRB subscale than atypically developing children. These differences indicate that although atypically developing children may experience deficits in these domains, the level of impairment is consistently greater in children with ASD.

Although changes to diagnostic criteria for ASD have led to controversy and long-term effects of these changes are still being researched, the deficits experienced by individuals with ASD are well studied (Lord & Bishop, 2015; Matson, Hattier, & Williams, 2012; Smith, Reichow, & Volkmar, 2015; Wing, Gould, & Gillberg, 2011). As a spectrum disorder, there is significant heterogeneity in severity and symptom expression among individuals with the disorder (Mitchell et al., 2006; Seltzer et al., 2003; Travis & Sigman, 1998; Wetherby, Watt, Morgan, & Shumway, 2007). This phenomenon may be particularly true for children at young ages, who may not fully
exhibit symptoms until they are older. This highlights the importance of the DSM-5’s criteria stating that symptoms may not fully manifest until social demands exceed one’s capacity. As individuals may be able to compensate for deficits, it is important to recognize early markers for ASD. In young children, these deficits may include failure to make appropriate eye contact, lack of initiation of social interactions, absence of joint attention, and deficits in pretend play skills (Howlin, 2006; Rutter, 1978). Given the overlapping symptoms (e.g., speech delay, lack of response to name) across developmental delays, deficits must be monitored should they result in ASD and thus warrant additional supports.

To examine the degree of relationship as a factor in ASD severity and subscale scores, results from this study did not indicate that degree of relationship itself significantly predicted scores. Thus, having a first-degree relative diagnosed with ASD did not result in higher severity or subscale scores than individuals with second- or third-degree relatives diagnosed. Given the heterogeneity of ASD, this result is expected. Multiple genetic and environmental factors contribute to the development of ASD, and this finding indicates that degree of relationship itself does not have a significant role.

Significant interactions were found in Models 1 and 4, such that children with ASD and first-degree relatives diagnosed with ASD were found to have lower BISCUIT-Part 1 and RRB subscale scores. As such, findings from this study do not support Hypothesis 2. This finding is surprising given that researchers have found that multiplex families exhibit greater ASD symptomatology (Bernier, Gerdts, Munson, Dawson, & Estes, 2012b; Gerdts et al., 2013; Taylor et al., 2015). In a study examining symptom domains, Szatmari and colleagues (2000) found that social impairments, but not
communication deficits or RRB were more common in relatives from multiplex families compared to simplex families. This indicates that first-degree relatives in multiplex families may exhibit greater social skills deficits; given the gene-environment interactions that result in ASD (London & Etzel, 2000), it is important to note that the greatest deficit in families with increased genetic loading for the disorder is social skills rather than communication deficits or RRB.

Findings from this study differ from similar research. The lower BISCUIT-Part 1 total scores and RRB subscale scores found in this study may be due to inclusion of parents and siblings within the first-degree group rather than only siblings. Additionally, these results may be attributed to sample characteristics rather than differences between groups. It is possible that for the children in this sample, they endorsed less ASD severity and RRB; however, without additional measures (e.g., diagnostic measures of severity) this is unclear. Future studies should be conducted to confirm these data. It is also important to consider that given the young age of the participants, symptoms may not yet fully manifest themselves. Thus, the severity of various impairments may not become apparent until social demands exceed the child’s current abilities.

In contrast to the ASD groups, the atypically developing children were not found to have significant differences on BISCUIT-Part 1 total scores or subscales when separated by degree of relationship. Prior to this study, it was unknown how degree of relationship would be associated with ASD severity and symptoms in atypically developing children; thus, the study posited a null hypothesis. Independent samples t-tests also revealed no significant differences in ASD severity of subscale scores between
atypical groups. Given that no difference was found on any scale for atypical groups, Hypothesis 3 was supported.

Overall, these findings suggest that degree of relationship may not affect ASD severity or subscale scores for atypically developing children. Although ASD children with a first-degree relative also diagnosed were found to have lower BISCUIT-Part 1 total scores and RRB subscale scores, no significant difference was found on any dependent variable in this study for the atypically developing children. This suggests that having a first-degree relative with ASD is not associated with greater severity in total score, communication skills, socialization deficits, or RRB. However, there are clinical implications for the atypically developing group. Although no statistically significant difference in total scores was found, when considering the cut-off scores, the atypically developing children with a first-degree relative affected had a mean BISCUIT-Part 1 total score of 20.58, while the atypically developing children with a second- or third-degree relative affected had a mean score of 16.44. Though the scores were not found to be significantly different from each other, a score of 20.58 would place a child in the “Possible ASD” range, while a score of 16.44 would classify a child as in the “No ASD/Atypical Development” range. Scoring in the “Possible ASD” range would warrant further assessment for the child, resulting in more time needed for additional evaluation and resources utilized. Findings from the present study indicate that atypically developing children with a first-degree relative diagnosed with ASD may be referred for follow-up assessment, while an atypically developing child with a second- or third-degree relative with ASD may not.
Taken together, results from the current study suggest that degree of relationship plays a role in ASD symptomatology for young children with family history of the disorder. Given the differences in results from previous research and clinical implications of the study findings, additional research to confirm these data is warranted.

**Limitations and Future Directions**

Several limitations must be considered when interpreting these results. Most importantly is use of parent report to indicate family history of ASD. Because the current study was not able to verify diagnoses, either via direct assessment or chart review, this limits the study. In order to more clearly demonstrate effects of degree of relationship within ASD and atypically developing groups, future studies should confirm the relative’s diagnosis where possible. As the measure is a parent report, scores also may not appropriately reflect the child’s level of functioning. Given that all participants had a family history of ASD, parents may be more familiar with ASD symptoms. Having another individual with ASD in the family may provide a frame of reference for the parent to judge their own child’s deficits. Thus, the parent may rate the child as having greater or lesser impairment, depending on the functioning level of the affected relative.

Given the limited information collected from the relatives in the study, future research should gather more data on the relatives. It would be of interest to examine supplementary information such as ASD severity, IQ, and adaptive functioning of the affected relative. These additional variables may be factors of interest when examining the relationship between family history and ASD symptomatology.

Future research studies should also consider if there may be differences between genders. Although prior research has not found significant differences in ASD
prevalence among relatives of affected males compared to females (Goin-Kochel, Abbacchi, Constantino, & Autism Genetic Resource Exchange Consortium, 2007), there may be differences in ASD severity and/or symptomatology based on family history and gender. Because girls with ASD tend to have more severe symptoms, lower cognitive functioning, and behavioral difficulties than boys (Dworzynski, Ronald, Bolton, & Happé, 2012; Haney, 2015; Kirkovski, Enticott, & Fitzgerald, 2013; Rivet & Matson, 2011), examining how family history and degree of relationship may play a role in the development of ASD for girls is of interest to the field.

**Conclusion**

Studying family members of individuals with ASD allows researchers to identify early markers of the disorder. Research on affected families provides information on how autism may manifest in simplex compared to multiplex families. Much of the current research has focused on how family history results in higher risk for developing ASD; however, there is currently limited research examining how the degree of relationship may play a role in ASD severity and symptomatology. First-degree relatives have more shared genetic and environmental effects than second- or third-degree relatives; therefore, the present study examined the association between degree of relationship and autism symptomatology in young children with family history of ASD. Regression models indicated that the most predictive factor in determining ASD severity and subscale scores was the individual’s diagnosis. When examining how degree of relationship predicted scores, the degree of relationship itself was not found to be a significant predictor; however, the interaction between group and degree of relationship was significant in the ASD severity and RRB models. Contrary to prior research and the
study hypotheses, children with ASD and a first-degree relative also with the disorder had lower scores on the BISCUIT-Part 1 total and RRB subscale when controlling for other variables. Additional research is needed to examine these results. For atypically developing children, there was no significant association between degree of relationship and ASD severity or subscales. Thus, children who are atypically developing and have a first-degree relative affected with ASD do not exhibit greater ASD severity or symptoms than atypically developing children with second- or third-degree affected relatives. Despite the lack of significant difference between groups, the clinical implications of these findings are to continue to monitor early markers of autism in children with a family history of ASD. Both ASD and atypically developing groups met the cut-off score for being identified as “Possible ASD” on the BISCUIT-Part 1; thus, parents and clinicians should continue to monitor ASD symptoms in young children and assess for ASD should there be any concerns.
References


Vita

Jasper A. Estabillo is a doctoral student in the Clinical Psychology program at Louisiana State University, specializing in Child Psychology with particular emphasis in Autism and Developmental Disabilities. She received her undergraduate degree in Human Development and Psychology at the University of California, San Diego. During her time there, she worked in the Department of Psychology assisting with memory studies and research on young children with siblings with ASD. Prior to graduate school, she worked as a research coordinator at the University of California, San Diego Department of Psychiatry and the Autism Discovery Institute at Rady Children’s Hospital, San Diego on a genetic study aimed at relating de novo copy number variations to ASD and related neurodevelopmental disorders. Her previous clinical work includes behavior therapy as an Applied Behavior Analysis interventionist and social skills group facilitator for adolescents with high-functioning ASD. Currently, Jasper’s research and clinical interests focus on early identification and intervention of ASD and developmental disabilities.