The association between familial ASD diagnosis, autism symptomatology and developmental functioning in young children

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Abstract Few studies have directly compared individuals with and without a relative diagnosed with ASD on various domains. The present study aimed to examine the relationship between familial ASD diagnosis and the exhibition of ASD symptoms in young children with and without ASD diagnoses. Participants included 8353 children aged 17–37 months old and their families. They were divided into four groups based on individual and family diagnosis, then compared on autism symptomatology and developmental domains. No differences were found between ASD groups on overall scores and each of the factor domains, indicating no association between family ASD diagnosis and ASD symptomatology or developmental functioning. Disparate results were found for atypically developing groups with and without relatives diagnosed with ASD. Implications of these results are discussed.

Keywords Autism · Concordance · Familial risk · Autism symptomatology · Developmental functioning · Broad autism phenotype

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and the presence of restricted and repetitive behaviors and interests [1–3]. Symptom presentation and severity among individuals with ASD are heterogeneous, and the specific etiology of the disorder remains unknown [4–6]. Several risk factors related to ASD have been identified, with etiological studies suggesting a strong genetic role [7–13]; however, no single gene has been found to account for autism [6, 14]. Researchers have suggested that gene–environmental interactions may play a role, demonstrating that environmental factors influence the expression of vulnerable genes, while an individual’s response to environmental factors also varies as a result of genetic influences [8, 15, 16].

Family and twin studies have also provided evidence for the role of gene-environmental interactions in ASD. One twin study found that the environment shared by twins accounted for about 55% of the liability of autism while the genetic heritability only accounted for 37% [17]. Findings from several studies have also indicated that although there is a higher concordance rate between monozygotic twins compared with dizygotic twins, it is likely that ASD is caused by a combination of genetic and environmental factors [18–21]. As Folstein and Rutter stated, “it is not autism itself that is inherited but rather some genetic abnormality of language or sociability that interacts with other factors to produce autism” [22]. Moreover, relatives of affected individuals may also be found to carry genetic risk variants associated with ASD but be phenotypically unaffected [23]. Therefore, genetic risk factors may not be required nor sufficient to result in a diagnosis of ASD [23].

Significantly higher rates of ASD characteristics have also been found in first-degree relatives of individuals with ASD when compared to controls [24, 25]. For example, relatives of children with ASD have been shown to be at a higher risk for a range of social, language, and behavior abnormalities [15, 26, 27]. This finding has led to the introduction of the term broad autism phenotype (BAP), which refers to the subclinical impairment in core ASD symptoms
often found in relatives of individuals with ASD [28]. Characteristics of BAP are qualitatively similar to autism, but have milder effects on the individual’s functioning [29–31]. Studies on BAP have primarily focused on parents and the possible relationship of BAP with ASD symptom expression in their children [32–34].

In addition to BAP, research on autism in families with multiple individuals affected has also provided evidence for gene-environment interactions. One study found that children with an affected sibling have an increased risk of developing autism by 22 times compared to children without a family history [35]. Siblings in multiplex families have generally been found to be more similar on measures of verbal and nonverbal IQ and adaptive functioning than unrelated children with ASD, providing evidence for genetic effects on skill domains [36]. In contrast, other researchers have found that individuals in multiplex families exhibit differences in both symptomatology and severity from each other [37, 38]. For example, in a study relating symptom severity with birth order in children with ASD, differences in IQ scores and ASD severity were most significant when siblings were less than 2 years apart in age [39]. Although studies comparing relatives with autism have been conducted, there is currently limited research directly comparing individuals with and without family members with ASD. Previous research by Kozlowski and colleagues found significant differences in ASD symptomatology present only between children with and without ASD, regardless of having a relative also diagnosed with autism [40]. The study concluded that there was no association between family diagnosis and an individual’s ASD symptom severity. The aim of the present study was to build upon Kozlowski and colleagues’ findings utilizing a larger sample and participants who were diagnosed with ASD based on the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) [41] criteria. The current study aimed to examine the relationship between familial autism diagnosis and the presentation of autism symptomatology in young children with and without ASD. Developmental domains were also analyzed to examine the relationship between having a relative with autism and deficits in developmental functioning (i.e., adaptive behavior, personal–social, communication, motor, and cognitive skills) in children with and without ASD.

Method

Participants

The study sample included 8,353 children aged 17–37 months (M = 26.14, SD = 4.99). Participants were selected from a pre-existing database that continues to expand with ongoing data collection. Specifically, the participants were part of a larger sample of children who received services through the Louisiana’s EarlySteps program, which provides early intervention services to children from birth to 36 months old with developmental delays or a medical condition that may result in developmental delay. Participants were excluded if their parent or caregiver neglected to provide information on their demographic form indicating if a biological family member had been diagnosed with ASD or if there were any missing or incorrectly coded data. The sample consisted of 69.6 % males (n = 5,796) and 30.3 % females (n = 2,531). Of the total participants, 37.3 % were African American (n = 3,115), 51.3 % were Caucasian (n = 4,281), and 8.6 % were of other ethnicities (n = 720), which included Hispanic, Asian, and Multiracial children. Of the 8,353 children, 1,107 were diagnosed with ASD (13.2 %) and 7,246 were classified as atypically developing (86.8 %). The children were assigned diagnoses of ASD or atypically developing based on methodology including diagnostic criteria of the DSM-5, scores on the Baby and Infant Screen for Children with ASD Traits (BISCUIT) [42], and developmental scores on the Battelle Developmental Inventory, Second Edition (BDI-2) [43]. These diagnoses were made by a licensed clinical psychologist with over 30 years experience in the field of developmental disabilities. The children who did not meet criteria for ASD were placed in the atypically developing groups and had diagnoses such as general developmental delay, premature birth, hearing impairment, cerebral palsy, speech delay, and various genetic syndromes (e.g., Down syndrome, Sotos syndrome, Fragile X, and DiGeorge syndrome). Demographic characteristics for the study participants are found in Table 1.

Regarding familial diagnosis of ASD, 540 participants’ parent or caregiver reported that a family member had been diagnosed with ASD. Of those children, 32.4 % had a sibling with ASD [brother: n = 131 (24.3 %), sister: n = 40 (7.4 %), and gender of sibling not specified: n = 4 (.7 %)]. Parents reported to have ASD in 2.8 % of the sample [father: n = 13 (2.4 %) and mother: n = 2 (.4 %)]. The most frequent relative reported to have ASD was a cousin [gender not specified; n = 240 (44.4 %)]. Additional family members diagnosed included uncle (n = 76; 14.1 %), aunt (n = 26; 4.8 %), grandfather (n = 2; .4 %), grandmother (n = 1; .2 %), nephew (n = 4; .7 %), and niece (n = 1; .2 %). Participants were subsequently divided into four groups based on individual diagnosis and family history of ASD (FH): ASD/FH, ASD/noFH, Atypical/FH, and Atypical/noFH.

Measures

The BISCUIT is a three-part assessment battery specifically designed to evaluate young children for ASD symptoms,
comorbidity, and challenging behaviors. The measure has been validated for children aged 17–37 months and holds an overall correct classification rate of .89 and internal reliability of .97 [44–46]. The BISCUIT Part 1 contains 62 items and assesses the presence of ASD symptoms. The evaluator reads each item to the parent or caregiver, who is instructed to rate the child as 0 = “not different; no impairment,” 1 = “somewhat different; mild impairment,” or 2 = “very different; severe impairment” in comparison to other children his or her age. Scores at or above 17 indicate that the child is at-risk for an ASD. The BISCUIT Part 1 is also divided into three factor domains reflecting deficits associated with ASD. The domains include social interaction, restricted and repetitive behaviors (RRB), and communication [44]. For the purposes of the current study, BISCUIT Part 1 scores were used as a measure of ASD symptomology.

The BDI-2 is a developmental assessment measure for young children up to age 8 [43]. The measure includes interviews with the parent/caregiver, structured activities administered by the evaluator, and observation of the child. The five domains tested are adaptive, personal-social, communication, motor, and cognitive skills. The BDI-2 contains 450 items that are rated in comparison to age norms and scored by the evaluator as 2 = “the child’s response meets the developmental milestone,” 1 = “the child’s skills are emerging,” or 0 = “the child did not attempt the task or the child’s response was inadequate to score.” Psychometric studies found test–retest reliability to be greater than .90 and internal consistency coefficients between .98 and .99 for all domain scores [43]. The sums of subdomain scaled scores were analyzed in the present study.

**Procedure**

The study was approved by the Louisiana Office for Citizens with Developmental Disabilities and the Louisiana State University Institutional Review Board prior to initiation of data collection. The BISCUIT was administered as part of the EarlySteps assessment protocol by trained evaluators specializing in psychology, social work, speech-language pathology, special education, occupational therapy, or physical therapy. All evaluators attended training on the BISCUIT, which included information on ASD and practice administration of the battery. Evaluations were conducted in the participant’s home and included administration of the BISCUIT and BDI-2.

During assessments, evaluators recorded parent responses on the BISCUIT demographic form and then the measure. Demographic information included name, date of birth, gender, ethnicity, birth weight, and current height and weight. Additional questions included parental concerns regarding their child’s development, age of the child at first concern, age of the child at developmental milestones (e.g., when began to crawl, walk, talk, use sentences), and diagnosis history. Lastly, information was obtained regarding if a family member had been diagnosed with ASD and their relationship to the child.

**Statistical analysis**

Chi square analyses were run to examine potential differences in demographic factors and to determine if the groups significantly differed in relatives diagnosed with ASD. An analysis of variance (ANOVA) was then conducted with group as the independent variable (IV) and total BISCUIT Part 1 score as the dependent variable (DV). Follow up analyses were conducted to examine differences in the prevalence of relatives with ASD between groups more extensively. A multivariate analysis of variance (MANOVA) was then run with group as the IV and the three BISCUIT factor domains as the DVs. Post hoc tests were run to determine the effect of group on each of the factor domains. Another MANOVA was performed with group as the IV and the five BDI-2 domains as the composite DVs. Post hoc tests were subsequently conducted to determine the effect of group on developmental functioning.

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<th>Table 1 Demographic characteristics by group</th>
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Results

A priori analyses were conducted to determine if the groups differed on demographic information. Significant differences were found between group and gender, $\chi^2(3) = 25.01, p < .01$. This difference is expected, given the higher prevalence of ASD in males than females [47]. An ANOVA was then conducted to determine if the groups differed in age. A significant difference was found between groups, $F(3, 8326) = 12.84, p < .01$, partial $\eta^2 = .005$. Although this difference was found, given the very small effect size, further analyses were still conducted to compare groups. A significant difference was found between groups on ethnicity, $\chi^2(6) = 15.96, p < .01$. This finding is also expected, given the relatively smaller sample of other races in this sample. These demographics, however, are representative of the racial demographics of the location of this study [48].

To determine the percentage of children with a relative diagnosed with ASD, family ASD was coded and examined by group. A higher percentage of children with ASD were found to have a relative with ASD (12.4 %) compared to children without ASD (5.6 %). This difference was found to be significant, $\chi^2(1) = 73.97, p < .01$.

An ANOVA was conducted to determine if total BISCUIT-Part 1 scores differed across groups. Levene’s test revealed a significant difference in variances between groups; therefore, Welch’s $F$-test was used for analysis [49]. There was a significant difference between groups on total BISCUIT-Part 1 scores, Welch’s $F(3, 477.18) = 1262.16, p < .01$, partial $\eta^2 = .47$. Given the differences between group sizes, Games-Howell post hoc procedures were conducted. Post hoc tests resulted in significant differences between the Atypical/noFH ($M = 14.37$, $SD = 12.74$) and all other groups ($p < .01$), as well as significant differences between the Atypical/FH ($M = 18.28$, $SD = 15.75$) and all other groups ($p < .01$). No significant difference was found between the ASD/noFH ($M = 54.11$, $SD = 21.50$) and ASD/FH group ($M = 55.36$, $SD = 19.63$), $p > .05$.

An additional ANOVA was conducted to test total ASD symptomatology by relative type. To do so, the ASD/FH group was sub-coded to indicate if the relative with an ASD diagnosis was a first-degree relative (i.e., parent or sibling; $n = 54$) versus second- or third-degree relative (i.e., grandparent, uncle, aunt, nephew, niece, cousin; $n = 83$). Levene’s test was not found to be significant, $p > .05$. No significant difference in BISCUIT-Part 1 scores was found between relative types, $F(1, 135) = .52, p > .05$, partial $\eta^2 = .004$.

A MANOVA was performed to determine if the groups significantly differed on the three factors of the BISCUIT-Part 1 (i.e., social interaction, RRB, communication). Box’s test was found to be significant; however, as stated by Tabachnick and Fidell (2007), larger sample sizes produce greater variances and covariances, and as a result probability values tend to be conservative; therefore, significant findings may be trusted in this case [50]. Additionally, given the sample of atypically developing children, normality in scores may not be tenable. Using Pillai’s trace, there was a significant effect of group on scores on three factors of the BISCUIT-Part 1, $V = .502$, $F(9, 23553) = 525.49, p < .01$, partial $\eta^2 = .17$.

The significant effect of group in the MANOVA was followed up with ANOVAs for each factor of the BISCUIT-Part 1. A significant difference between groups was found on each of the three factors: Social interaction factor, Welch’s $F(3, 463) = 1004.98, p < .01$, partial $\eta^2 = .45$; RRB, Welch’s $F(3, 465.07) = 844.16, p < .01$, partial $\eta^2 = .45$; and Communication, Welch’s $F(3, 500.34) = 530.95, p < .01$, partial $\eta^2 = .12$. Games-Howell post hoc tests were conducted to examine pairwise comparisons between groups. No differences were found between the ASD groups on any of the BISCUIT-Part 1 factors ($p > .05$). Significant differences were found between the Atypical/noFH group and both ASD groups on each of the three factors ($p < .01$). Similarly, significant differences were found between the Atypical/FH group and both ASD groups on each of the BISCUIT-Part 1 factors ($p < .01$). In comparing the Atypical/noFH and Atypical/FH groups, significant differences were found on the Social Interaction and RRB factors ($p < .01$), but not on the Communication factor ($p > .05$). Results are shown in Table 2.

To determine if the groups significantly differ on the BDI-2 developmental domains, a MANOVA was conducted with the five domains as a composite DV. Box’s test was again found to be significant, but as previously stated, the resulting probability values tend to be conservative when utilizing larger samples sizes. Using Pillai’s trace, there was a significant effect of group on BDI-2 domain scores, $V = .10$, $F(15, 21516) = 50.52$, partial $\eta^2 = .034$.

Follow up ANOVAs were conducted for each of the BDI-2 developmental domains. A significant difference between groups was found on each of the five domains: Adaptive Behavior, Welch’s $F(3, 452.11) = 162.71, p < .01$, partial $\eta^2 = .04$; Personal-Social, Welch’s $F(3, 468.11) = 317.70, p < .01$, partial $\eta^2 = .07$; Communication, Welch’s $F(3, 455.22) = 233.55, p < .01$, partial $\eta^2 = .07$; Motor, Welch’s $F(3, 449) = 64.20, p < .01$, partial $\eta^2 = .03$; and Cognitive, Welch’s $F(3, 450.66) = 153.77, p < .01$, partial $\eta^2 = .06$.

Additional Games-Howell post hoc tests revealed differences between groups on each of the BDI-2 domains. First, no differences were found between the ASD groups on any of the five BDI-2 domains ($p > .05$). In comparing Atypical and ASD groups, both Atypical groups were found to
be significantly different from each of the ASD groups in all domains except Motor ($p < .01$). On the Motor domain, only the ASD/noFH group differed from the Atypical groups. The same pattern of significant differences was found between the Atypical/noFH and Atypical/FH groups on the Personal-Social, Communication, and Cognitive domains ($p < .01$). These results are shown in Table 3.

**Discussion**

The high prevalence of ASD diagnoses within families supports current research on genetic influences on the development of ASD. Similar to previous findings, about 10% of children with ASD were found to have a relative also diagnosed with the disorder. When comparing to the prevalence in the general population, a somewhat high percentage of the atypically developing children had a relative diagnosed with ASD. This may provide evidence for the role of BAP in that atypically developing children with a family history may present with similar skills deficits as children with ASD. This finding may also support research on the shared etiologies for many neurodevelopmental disorders, which may result in elevated symptoms of overlapping features of other disorders such as intellectual disability or attention deficit hyperactivity disorder [51–56].

Previous research by Kozlowski et al. found that significant differences in ASD symptomatology were only present between children with and without ASD, independent of whether a family member was also diagnosed with ASD [40]. Similarly, this study did not find significant differences between ASD groups, indicating that having a relative with ASD may not impact total autism symptoms in children ultimately diagnosed with the disorder. In contrast to the previous study, the current study did find differences in total BISCUIT-Part 1 scores between atypically developing groups. The mean BISCUIT-Part 1 total score of atypically developing children with a family history of ASD met cut-off for being identified as “at-risk” for autism (i.e., mean score >17), while atypically developing children without a family history did not. This result supports BAP research showing greater ASD symptoms in family members of individuals with autism. While these children were not diagnosed with ASD, children who had a family history tended to present with higher ASD symptomatology. These results may assist in the differential diagnosis of developmentally delayed children. That is, atypically developing children with a family history of ASD may demonstrate ASD symptoms but not meet criteria for ASD.

This study was also designed to assess total ASD symptoms by relative type. To determine if there was an effect of relationship type within the ASD/FH group, no significant
difference was found. Given that relatives who are more closely related (i.e., parents and siblings) share more genetic material and typically the same environment than distal relations such as grandparents or cousins, higher total scores would be expected in individuals who had parents or siblings diagnosed with ASD; however, results did not show an association between relative type and ASD severity. This finding may be due to reporter bias, as caregivers with a family history of ASD may endorse more autism symptoms in their children regardless of relative degree, but the reason behind this finding is not clear. Therefore, more research should be conducted to confirm these data.

The current study also found differences from previous research in analysis of core symptoms on the BISCUIT-Part 1. Children with ASD presented with similar symptomatology to each other on each of the three factors, again independent of whether a family member was diagnosed with ASD. However, for atypically developing children, there may be an association between family history and their deficits in social interaction and RRBs. Although it is unknown whether this influence may be genetic or environmental, there does appear to be an influence of family history on these domains in atypically developing children. This result may be due to the presence of BAP in families with ASD and/or overlapping symptoms with other developmental disorders.

Significant differences were also found between groups on the BDI-2 developmental domains. The Atypical groups had higher developmental domain scores than the ASD groups on each of the subdomains. Although both atypically developing children and children with ASD may have difficulties in these areas, children with ASD were found to have greater deficits in skills. In examining the subdomains, family history of ASD was not found to impact the ASD groups but significant differences were found between the Atypical groups on the Personal-Social, Communication, and Cognitive domains. These domains, while not specific to ASD, are deficits that are the most related to the disorder on the BDI-2. These findings suggest that there may be an influence of family diagnosis of ASD on more general ASD-related domains. Such a pattern of behavior may also point to the higher rate of related developmental delays in children who have a family history of ASD.

The findings of the current study provide evidence of the role of BAP among young children with relatives diagnosed with ASD. However, this study does have limitations, which should be considered when interpreting the results. Most importantly is the reliance on parent report for a relative’s ASD diagnosis. Given the inability to confirm these diagnoses with record review, these reports may not be fully accurate. Additionally, having a family member diagnosed with ASD may lead parents or caregivers to report more ASD symptoms. Parents who are familiar with autism-associated behaviors may be more sensitive to atypical behaviors in their children. Future researchers should address these concerns to extend the findings of the current study.

Compliance with ethical standards
Conflict of interest None.

Disclosure Johnny L. Matson, Ph.D. is a co-author of the Baby and Infant Screen for Children with autism Traits (BISCUIT), which is owned and distributed through his wife, Deann Matson’s, company Disability Consultants, LLC.

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