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ORIGINAL ARTICLE

Gastrointestinal Issues in Infants and Children with Autism and Developmental Delays

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Abstract Controversy exists regarding whether gastrointestinal (GI) issues play a role in the symptomatology of autism spectrum disorder (ASD). While some studies have found GI problems to be more prevalent in individuals with ASD, others have reported no such difference. Studies looking at the relationship between GI issues and ASD symptom severity have also had mixed results. The current study examined 112 participants between the age of 17 to 37 months. Participants comprised four groups of 28 children: an ASD and no GI issues group, an ASD with GI problems group, an atypical development and no GI issues group, and an atypical development with GI issues group. The results of the current study suggest that although the prevalence of GI symptoms was higher in participants with ASD than those without, this difference was not significant. The study also found that GI issues were not related to ASD symptom severity or developmental functioning.

Keywords Autism · Gastrointestinal issues · Autism symptom severity · Developmental functioning

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by social and communication deficits, as well as restricted, repetitive behaviors and interests (American Psychiatric Association 2013; Matson et al. 2012; Tidmarsh and Volkmar 2003; Worley and Matson 2012). Many children with ASD also have one or more comorbid medical conditions (e.g., cerebral palsy, fragile X syndrome, tuberous sclerosis, Down syndrome, epilepsy; (Bauman 2010; Fombonne et al. 1997; Gillberg and Coleman 1996). Among the most frequently reported are gastrointestinal (GI)

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problems (e.g., constipation, gastroesophageal reflux, gastroenteritis; (Black et al. 2002; Hsiao 2014; Molloy and Manning-Courtney 2003). These co-occurring conditions are important to consider as they may influence the presentation and severity of symptoms, as well as overall development. They also may have significant implications for treatment goals and the professional groups who will be involved in treatment decisions (Matson et al. 2009a).

Researchers have reported prevalence rates of GI issues among children with ASD ranging from 9 to 61% (Black et al. 2002; Ibrahim et al. 2009; Mazefsky et al. 2014; Mazurek et al. 2012; Molloy and Manning-Courtney 2003). While some researchers have found that GI issues are more prevalent among individuals with ASD (Chaidez et al. 2013; McElhanon et al. 2014), others posit that they occur at similar rates in the general population (Black et al. 2002). In regard to young children, Bresnahan et al. (2015) found that children who received an ASD diagnosis were at increased risk for GI symptoms in the first three years of life as compared to typically developing children. Specifically, parents of young children with ASD were more likely to have reported constipation and food allergy/intolerance between 6 and 18 months, and from 18 to 36 months were more likely to have these symptoms as well as diarrhea. The findings of this study indicates that increased GI symptoms in this population may be present even at very young ages.

Studies on the effect of GI issues on children with ASD have also yielded mixed results. Some researchers hypothesized that the discomfort brought by GI problems may contribute to elevated rates of behavioral problems. Chaidez et al. (2013) found that irritability, social withdrawal, stereotypy, and hyperactivity were correlated with GI problems in children with ASD. Similarly, findings from Mazurek et al. (2012) suggested that GI problems were related to higher rates of anxiety and sensory over-responsivity. However, other researchers have refuted the connection between GI problems and problem behaviors. For instance, some studies have found that GI problems were not related to maladaptive behaviors (Pusponegoro et al. 2015), internalizing problems, externalizing problems, or affective problems (Mazefsky et al. 2014).

Few studies have assessed the relationship between GI problems, ASD symptom severity, and adaptive functioning. Similar to the research findings on the prevalence of GI issues and their relationship to behavioral problems, there is a lack of consensus regarding the association between GI issues and ASD symptom severity. While Mazefsky et al. (2014) found that ASD symptom severity, as measured by the Social Responsiveness Scale, was not significantly different in children with and without the presence of GI problems, this may be related to the fact that only children with high-functioning ASD were included in this study. Conversely, in a study by Wang et al. (2011), the authors reported a positive correlation between ASD symptom severity and odds of having GI problems. In this study, individuals were classified as having "full autism," "almost autism," or "spectrum," and unaffected siblings were considered a control group. Individuals in the "full autism" and "almost autism" groups had significantly more GI problems (e.g., constipation, diarrhea) than the unaffected sibling group; however, significant differences were not found between the "spectrum" group and the unaffected group.

Two previous studies have found that the presence of GI issues was not related to adaptive skills of children with ASD, as measured by the Vineland Adaptive Behavior

Scales (Mazefsky et al. 2014; Nikolov et al. 2009). An important note is that both of these studies included children ages 7–18 and 5–17 with average ages of 12.75 and 8, respectively. Therefore, these findings are most generalizable to school-aged children and adolescents. No studies have been found to have investigated the relationship between GI symptoms and adaptive or intellectual functioning in young children.

Despite the low level of consensus, several treatments based on the assumed relationship between GI issues and ASD symptomatology have become popular. Studies have been conducted to evaluate the effectiveness of such treatments (e.g., gluten-free casein-free, ketogenic diet) and the results are typically inconclusive (Harris and Card 2012; Hyman et al. 2016; Johnson et al. 2011; Mari-Bauset et al. 2014; Mulloy et al. 2010; Zhang et al. 2013).

The aim of the current study was to investigate whether GI problems have a significant association with ASD symptom severity and developmental functioning in toddlers. As such, it builds on the previous research on the potential connection between GI issues and behavior problems and adds to the limited literature on young children. Overall ASD symptom severity and developmental functioning were examined among young children with ASD as well as those with atypical development without a diagnosis of ASD. Based on the existing literature, the hypothesis of the current study is that GI issues are not related to ASD severity or developmental functioning.

Method

Participants

A total sample of 5317 toddlers ages 17 to 37 months old (M = 25.25; SD = 4.62) was recruited. All participants were enrolled in EarlySteps, Louisiana's statewide early intervention program, via the Louisiana State Office for Citizens with Developmental Disabilities (OCDD). Children qualify for EarlySteps services if they are under the age of 36 months and have a developmental disability or a condition that identifies the child as at risk for developmental delay under the Individuals with Disabilities Education Act, Part C. There were four groups of participants: 1) children with ASD and comorbid GI problems (ASD + GI; n = 28); 2) children with ASD and without comorbid GI issues (ASD; n = 652); 3) children without ASD who had atypical development as well as GI problems (Atypical + GI; n = 136); and 4) children without ASD with atypical development and without GI problems (Atypical; n = 4501). The total sample was used to assess the prevalence GI issues. Follow-up analyses used a matched sample (n = 112); specifically, participants in the three largest groups were matched for age and gender to the smallest group (i.e., ASD + GI group), which resulted in four groups of 28 toddlers.

Of the matched groups subsample, 53.57% were male (n = 60) and 46.63% were female (n = 52). In regards to ethnicity, 44.64% of the matched groups subsample were African American (n = 50), 40.18% were Caucasian (n = 45), and 15.18% were of another or unspecified race (n = 17). A breakdown of demographic information can be found in Table 1.

Table 1 Demographic Information of Matched Groups Subsample (n = 112)

	Atypical (*n* = 28)	Atypical + GI (*n* = 28)	ASD (*n* = 28)	ASD + GI (*n* = 28)	Total (*n* = 112)
Age (in months), *M*(*SD*)	26.39(4.69)	26.36(4.70)	26.39(4.69)	26.39(4.69)	26.38(4.63)
Gender, no. (%)					
Male	15(53.57)	15(53.57)	15(53.57)	15(53.57)	60(53.57)
Female	13(46.43)	13(46.43)	13(46.43)	13(46.43)	52(46.43)
Race/Ethnicity, no. (%)					
Caucasian	10(35.71)	14(42.86)	11(39.29)	10(35.71)	45(40.18)
African American	13(46.43)	12(50.00)	12(42.86)	13(46.43)	50(44.64)
Other/Unspecified	5(17.86)	2(7.14)	5(17.86)	5(17.86)	17(15.18)

Measures

Baby and Infant Screen for Children with aUtIsm Traits- Part 1 (*BISCUIT- Part 1*).

The *BISCUIT* is an informant-report measure made up of three parts that assesses ASD symptomology, comorbid psychopathology, and challenging behaviors among children aged 17 to 37 months. It includes a demographic form that collects data on a range of factors such as medical and developmental history (e.g., medical problems, previous developmental disability diagnoses), including the presence or absence of GI issues. The *BISCUIT-Part 1* was used as a measure of autism symptomatology consists of 62 items related to three domains (i.e., Socialization/Nonverbal Communication; Repetitive Behavior/Restricted Interests; Communication; (Matson et al. 2010). For each item, informants provide ratings according to a 3-point Likert scale (0 = "not different; no impairment;" 1 = "somewhat different; mild impairment;" 2 = "very different; severe impairment") comparing their child to same-aged peers. Psychometrics of the *BISCUIT-Part 1* support its use as a sound measure with an internal reliability of .97 and an overall correct classification rate of .89 (Matson et al. 2009b). Convergent validity was demonstrated with the *Modified Checklist for Autism in Toddlers (M-CHAT)* and the Personal-Social domain of the *Battelle Developmental Inventory, Second Edition (BDI-2*), and divergent validity was demonstrated through small correlations with the *BDI-2*'s Adaptive and Motor domains (Matson et al. 2011).

Battelle Developmental Inventory, Second Edition (*BDI-2*). The *BDI-2* is designed to assess the developmental skills of children from birth to 7 years 11 months old through both informant-report and structured observation. The *BDI-2* includes 450 items which make up five developmental domains: Adaptive, Personal-Social, Communication, Motor, and Cognitive (Bliss 2007). Each item is scored on a 3-point scale (0 = "no ability in the skill," 1 = "emerging ability," 2 = "ability at the skill") and the sums of item scores result in scores for each domain and a total developmental quotient (DQ). Total DQ and the domain scores have a mean of 100 and a standard deviation of 15. The *BDI-2* is psychometrically sound with test-retest reliability estimates of above .90 for total DQ and each domain. Internal consistency was calculated at .99 for total DQ. Evidence of validity was established through comparisons with several well-

established measures of child development including the *Bayley Scales of Infant Development, Second Edition (BSID-II)* and the *Preschool Language Scales* (*PLS-4*; Bliss 2007). For the current study, total DQ and scores from each of the five domains were used to assess developmental functioning.

Procedure

The *BISCUIT-Part 1* and the *BDI-2* were administered as part of a larger assessment battery that included parent interviews and child observations conducted in the child's home or daycare. The assessments were conducted by approximately 175 EarlySteps service providers who held an appropriate degree and certification or licensure in various fields such as occupational therapy, physical therapy, psychology, special education, social work, and speech-language pathology. They were proficient in evaluating and treating young children and underwent training in the administration of the measures used in this study.

Diagnostic labels of ASD for research purposes were assigned by a licensed clinical psychologist with over 30 years of experience in the field of intellectual and developmental disabilities in accordance with the *Diagnostic and Statistical Manual, Fifth Edition* (*DSM-5*), specifically by mapping data from *BISCUIT-Part 1* and *BDI-2* to the *DSM-5* diagnostic criteria. Information about the presence of GI issues was obtained through caregiver report on the demographic subsection of the *BISCUIT*.

Statistical Analyses

Statistical analyses were performed using SPSS Statistics (Version 21). To explore the relationship between GI issues and ASD symptom severity, an analysis of variance (ANOVA) was conducted with group (i.e., Atypical, Atypical + GI, ASD, and ASD + GI) as the independent variable (IV) and ASD symptom severity, calculated as the total *BISCUIT-Part* 1 score, as the dependent variable (DV). A second ANOVA was conducted to examine differences in developmental functioning, calculated as the total *BDI-2* score, between groups. Scheffé post hoc comparisons were conducted to further examine group differences following each ANOVA.

Further, to explore group differences across the five developmental domains of the *BDI-2*, a multivariate analysis of variance (MANOVA) was conducted with group as the IV and scores from the five developmental domains (i.e., Adaptive, Personal-Social, Communication, Motor, and Cognitive) as the DVs. Subsequent ANOVAs were conducted to examine developmental differences more closely with use of a Bonferonni correction (i.e., p of less than .01). Scheffé post-hoc tests followed the ANOVAs and were used to examine developmental domain differences across groups.

Results

Initial descriptive analyses using the total sample of 5317 children indicated that children with ASD had a higher rate of GI issues (4.1%) compared to children without ASD (2.9%). However, this difference was non-significant, χ^2 (1) = 2.78, $p > .05$.

The following analyses used the matched sample (n = 112). The first ANOVA showed significant group differences in ASD symptom severity, as measured by total *BISCUIT-Part 1* score, $F(3108) = 41.83$, $p < .00$. As expected, results from the Scheffé post hoc tests indicated that toddlers in the ASD groups (i.e., ASD and ASD + GI groups) differed significantly in ASD symptom severity from the Atypical groups (i.e., Atypical and Atypical + GI groups). However, the Atypical group did not significantly differ from the Atypical + GI group, and the ASD group did not significantly differ from the ASD + GI group in regards to ASD symptomology.

The second ANOVA indicated significant differences in overall developmental functioning, as measured by total *BDI-2* score, between groups, $F(3, 108) = 5.20$, $p < .01$. Following Scheffé post hoc tests, only one group difference was found. Toddlers in the ASD group significantly differed in developmental functioning from children in the Atypical group. Results are shown in Table 2.

A MANOVA was then conducted to further examine developmental functioning and determine if the groups differed in any of the five developmental domains of the *BDI-2*. Using Pillai's trace, there was a significant effect of group on the scores from the five developmental domains, $V = .31$, $F(3108) = 2.47$, $p < .00$. The significant effect of group in the MANOVA was followed up with ANOVAs for each developmental domain, and a Bonferroni adjusted significant level of .01 was applied (i.e., p of .05 divided by five domains). Univariate ANOVAs revealed significant effects of group on the adaptive domain, $F(3, 108) = 6.55$, $p < .01$; personal-social domain, $F(3, 108) = 7.16$, $p < .01$; communication domain, $F(3, 108) = 4.96$; $p < .01$; and cognitive domain, $F(3, 108) = 5.63$, $p < .01$. There was no significant group effect on the motor domain. Results are shown in Table 2.

Results from the Scheffé post hoc tests revealed that for the adaptive domain, there were significant differences between Atypical group and ASD + GI group ($p < .01$), Atypical + GI group and ASD + GI group ($p < .05$). For the personal-social domain, there were significant differences between Atypical group and ASD group ($p < .01$), Atypical group and ASD + GI group ($p < .05$), Atypical + GI group and ASD group ($p < .05$). For the communication domain, there were significant differences between Atypical group and ASD group ($p < .05$), Atypical group and ASD + GI group ($p < .05$). For the cognitive domain, there were significant differences between Atypical + GI group and ASD group ($p < .05$), Atypical + GI group and ASD + GI group ($p < .05$). Results are shown in Table 2.

Discussion

Frequent anecdotal reports of GI problems in children with ASD have led to investigations of the relationship between GI issues and ASD. However, researchers have not reached a consensus as to whether children with ASD are more prone to have GI problems (Black et al. 2002; Ibrahim et al. 2009; Mazefsky et al. 2014; Mazurek et al. 2012; Molloy and Manning-Courtney 2003). Studies regarding the effect of GI problems on problem behaviors and ASD symptom severity have also reported mixed results (Chaidez et al. 2013; Mazefsky et al. 2014; Mazurek et al. 2012; Pusponegoro et al. 2015). While these studies covered a range of ages, few studies have looked at toddlers. The current study aimed to further investigate the prevalence of GI problems,

Table 2 Mean Scores and Standard Deviations for BISCUIT-Part 1and BDI-2 (n = 112)

	Atypical (n = 28) $M(SD)$	Atypical + GI (n = 28) $M(SD)$	ASD (n = 28) $M(SD)$	ASD + GI (n = 28) $M(SD)$	Total (n = 112) $M(SD)$
BISCUIT-Part 1 Total	15.21 (8.62)$^{c.d.**}$	19.54 (14.41)$^{c.d. **}$	55.68 (25.96)$^{a.b.**}$	56.71 (19.95)$^{a.b.**}$	36.79 (26.68)**
BDI-2 Total	82.46 (17.98)$^{c.*}$	81.21 (15.57)	69.75 (14.23)$^{a.*}$	70.79 (14.26)	76.05 (16.44)**
BDI-2 Adaptive	85.43 (15.41)$^{d.**}$	84.79 (13.96)$^{d.*}$	74.86 (12.91)	72.07 (14.05)$^{a.**b.*}$	79.29 (15.13)**
BDI-2 Personal-Social	91.82 (15.34)$^{c.**d.*}$	89.07 (14.61)$^{c.*}$	77.14 (14.03)$^{a.**b.*}$	79.83 (12.96)$^{a.*}$	84.46 (15.13)**
BDI-2 Communication	79.04 (16.93)$^{c.d.*}$	75.75 (18.37)	66.68 (14.62)$^{a.*}$	65.71 (12.24)^{a*}	71.79 (16.53)**
BDI-2 Motor	93.86 (16.26)	92.11 (16.99)	87.50 (17.89)	89.79 (21.49)	90.81 (18.18)
BDI-2 Cognitive	80.25 (16.37)	81.79 (19.49)$^{c.d.*}$	70.61 (11.49)$^{b.*}$	70.21 (13.12)$^{b.*}$	75.71 (14.57)**

*p values significant at $p < .05$

**p values significant at $p < .01$

[a] Significantly different from Atypical group

[b] Significantly different from Atypical + GI group

[c] Significantly different from ASD group

[d] Significantly different from ASD + GI group

and GI issues' relationships with ASD symptom severity and developmental functioning in young children under the age of 3 years.

In the current study children with ASD were not found to be more prone to develop GI problems than children without ASD. Although children with ASD had higher prevalence of GI problems (4.1%) than those without ASD (2.9%), this difference was not significant. While significant group differences were found in ASD symptom severity and overall developmental functioning, these differences were found to be accounted for by the presence or absence of ASD rather than GI problems. This is consistent with previous studies that reported no associations between the presence of GI problems and ASD symptom severity (Chandler et al. 2013; Nikolov et al. 2009) and adaptive skills (Mazefsky et al. 2014; Nikolov et al. 2009; Postorino et al. 2015).

A consistent pattern was found across all *BDI-2* domains: differences between ASD and ASD + GI groups remained small and nonsignificant for all five developmental functioning domains, suggesting that children with ASD and comorbid GI issues do not have more impaired functioning than children with ASD but no GI issues. Different patterns were found across the five developmental domains in relation to the groups with children with atypical development. Four of the domains (i.e., adaptive, personal-social functioning, communication, and cognitive) exhibited significant group differences. In regard to the adaptive domain, the comorbid ASD and GI problems group, but not the ASD only group, differed significantly from the Atypical groups. These results suggest that individuals with comorbid ASD and GI issues have greater deficits in adaptive functioning compared to what could be explained by ASD alone. GI issues may be related to difficulties with feeding and toileting, which may contribute towards greater deficits in the adaptive domain. For the personal-social domain, children with ASD alone had lower functioning than those without ASD (i.e., Atypical group, Atypical + GI group). This is to be expected, as deficits in social skills constitute one of the core characteristics of ASD. Interestingly, children with comorbid ASD and GI issues differed from the Atypical group but not the Atypical + GI group, which suggests that GI issues may also be related to social functioning. Difficulties with feeding and/or toileting may limit a child's participation in social activities. In the communication domain, two group differences were found, children with ASD (i.e., ASD group, ASD + GI group) had significantly lower functioning than those with atypical development without GI issues, suggesting that ASD is the main contributor towards communications difficulties. Similar to social functioning, this is not surprising, as deficits in communication are a core feature of ASD. As for the cognitive domain, discrepancies were found only between the Atypical + GI group and both ASD groups, indicating that the presence of ASD, but not GI issues, is related to impaired cognitive functioning. No significant group differences were found in the motor domain.

The study of GI problems in children with ASD is challenged by difficulties in accurate diagnoses of the presence of GI issues in this population. Due to deficits in communication, children with ASD might experience difficulties communicating pain and discomfort (Buie et al. 2010). Another potential interfering factor is food selectivity, a common problem experienced by individuals with ASD (Mari-Bauset et al. 2014), which often leads to restricted diets and inadequate intake of fiber, fluids, and other food constituents (Kuddo and Nelson 2003). In addition, medications may also complicate the diagnosis of GI problems in ASD as many of them may cause

disruptions to gut functions (e.g., abdominal pain, diarrhea, constipation; Kuddo and Nelson 2003).

The prevalence of GI issues reported here (4.1%) was lower than rates noted previously (9–61%; Black et al. 2002; Ibrahim et al. 2009; Mazefsky et al. 2014; Mazurek et al. 2012; Molloy and Manning-Courtney 2003). The young age of participants in this study might be related to this difference as younger participants are less able communicate their discomfort. Additionally, primary care physicians may be less likely to refer to specialists or treat with medications for younger children, thus GI issues may be undiagnosed in toddlers. It is also possible that the prevalence of GI issues may also increase with age in children with ASD compared with those without (Bresnahan et al. 2015). In this study, current GI problems instead of accumulative history of GI issues were utilized to measure the prevalence of GI issues, which may have also contributed to the low prevalence rate.

The following limitations of the study should also be considered when interpreting the results. Most notably, diagnostic classification of ASD was determined using a diagnostic algorithm designed for research purposes, rather than clinical assessment. Further, information regarding the presence of GI problems was collected through parent report, which may be subject to recall bias. In addition, the current study was not able to document the specific types of GI symptoms. Other studies that were able to examine different categories of GI issues have found differential results regarding the impact of specific GI issues on ASD symptoms (Ibrahim et al. 2009; Postorino et al. 2015). Lastly, no control group of typically developing children was included in this study, limiting its ability to compare the effects of atypical development and ASD. In future studies, researchers may consider using data collecting methods other than parent report (e.g., medical records), and more detailed information on specific GI symptoms should be recorded to better enable researchers to discern the relationship between ASD and GI issues.

If GI issues do not yet manifest themselves as increased severity of ASD symptoms or decreased developmental functioning in young children as suggested in this study, perhaps toddlerhood would be the best time to intervene to help make identification and evaluation of GI issues later on easier. Detection of GI issues could be facilitated by teaching young children with ASD ways to indicate pain and discomfort to caregivers. Consistent with previous research findings, the current study does not support the supposed relationships between GI problems and ASD. When GI symptoms are present, children with ASD should be treated with similar methods used with those without ASD. Dietary treatments should not be used to remediate core symptoms of ASD; instead, they should be only used when there is a diagnosis of intolerance or allergy suggesting a need for limitation or removal of certain allergens (Buie et al. 2010; Mari-Bauset et al. 2014). More studies on young children are needed to further investigate the relationships between ASD and GI problems and subsequently improve quality of life in this population.

Compliance with Ethical Standards

Funding This study did not receive external funding.

Conflict of Interest Deann Matson, Dr. Johnny Matson's wife, is the sole owner of the Baby and Infant Screen for Children with aUtism Traits (BISCUIT) and sells the scale. The authors declare that they have no conflict of interest.

Ethical Approval The university Institutional Review Board and the Louisiana State Department of Health and Hospitals Institutional Review Board have approved the use of data from EarlySteps for research purposes. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent A deidentified database containing select variables was provided by the EarlySteps program for research purposes. All personal identifiers of EarlySteps participants, including name and date of birth, were removed from the database by OCDD before receipt.

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