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Association of rigid-compulsive behavior with functional constipation in autism spectrum disorder

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AUTHORS' CONTRIBUTIONS

SM and BF contributed to participant recruitment, data collection, data entry, data interpretation and manuscript writing. EL, BP, KW, PL, KM, DB, and JV contributed to study design, data interpretation, and manuscript writing. EM and EM performed the statistical analysis and contributed to manuscript writing. All authors read and approved the final manuscript.

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional review boards and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from parents of all child participants and from all adult participants included in the study. Child participants provided assent, when able. This article does not contain any studies with animals performed by any of the authors.

CONFLICT OF INTEREST

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Abstract

Based upon checklist data from the Autism Speaks Autism Treatment Network, we hypothesized that functional constipation (FC) would be associated with rigid-compulsive behavior in children with autism spectrum disorder (ASD). We used the Questionnaire on Pediatric Gastrointestinal Symptoms - Rome III to assess FC symptoms in 108 children with ASD. As hypothesized, FC was associated with parent ratings on the Repetitive Behavior Scales – Revised (RBS-R) Compulsive, Ritualistic, and Sameness subscales in the overall population. Of note, FC was less common in children who were not taking medications that target behavior or treat FC. In the medication-free children, rigid-compulsive behavior was not significantly associated with FC. More research is needed to understand the mechanisms underlying these associations.

Keywords

Developmental; Gut; Enteric; Medical comorbidity; Obsessive compulsive disorder; Serotonin; Microbiome

INTRODUCTION

Within the diagnostic criteria for autism spectrum disorder, considerable variability can be seen in presentation of core symptoms, particularly in the repetitive behavior domain (American Psychiatric Association, 2013). Those who meet criteria for ASD can also show substantial differences in co-occurring problems, including intellectual disability, language impairment, sleep disorders, and psychiatric diagnoses (American Psychiatric Association, 2013; Esbensen et al., 2009; Georgiades et al., 2007). In addition to variability in behavioral and cognitive symptoms, a number of medical problems are more common in ASD than in the general population and may offer clues to dissect the considerable heterogeneity within this behaviorally defined disorder (Mattila et al., 2010; Munson et al., 2008; Simonoff et al., 2008; Viscidi et al., 2013).

Gastrointestinal (GI) symptoms are four-fold more prevalent in ASD than in the general population, with constipation as the most commonly reported symptom (Aldinger et al., 2015; Doshi-Velez et al., 2014; Greenlee et al., 2016; Kohane et al., 2012; Viscidi et al., 2014). The largest prospective study of GI disorders in ASD found that functional constipation was more common in children who were minimally verbal (Gorrindo et al., 2012). Recent studies have also found GI problems in animal models of autism-associated genes (Bernier et al., 2014; Margolis et al., 2016). If common underlying risk factors can lead to gut and central nervous system pathology, then it is logical to consider relationships between GI symptoms and core or associated behavioral symptoms in ASD.

Based upon clinical experience, we hypothesized that severe constipation would be associated with more prominent rigid-compulsive symptoms in ASD. Our initial evaluation of this hypothesis used data available in the Autism Speaks Autism Treatment Network (AS-ATN) database that includes a large sample of 2–17 year old children and youth with ASD ascertained at medical centers across the U.S. and Canada. In the absence of more detailed data on GI symptoms, we operationalized severe constipation as co-occurring reports of constipation with soiling or diarrhea, suggestive of overflow encopresis, which itself was not directly ascertained within the AS-ATN data set (Peters et al., 2014). In the sub-population with severe constipation, we found significant associations with parent report of compulsive behavior, parent report of repetitive behavior, clinician diagnosis of obsessive-compulsive disorder (OCD), and report of rituals observed on the Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000). Children with constipation alone (without other co-occurring GI symptoms) also showed significant association with clinician diagnosis of OCD. This study had the advantage of substantial breadth of data, including observation from parent report and two different clinicians. On the other hand, the data points were sparse, and the hypothesis was tested retrospectively.

In the present study, we used more detailed data, collected prospectively using instruments that have been psychometrically validated, but in a smaller sample of children, to further evaluate the hypothesis that constipation and rigid-compulsive behavior are associated within ASD. Specifically, this study examined the associations between functional constipation and measures of rigid-compulsive behavior, as well as with verbal ability and other measures of symptoms in the repetitive behavior domain, including sensory sensitivity/aversion.

METHODS

Participants

Study procedures were approved by the Institutional Review Boards at XXX and XXX. As previously described, 120 6- to 18-year-olds were recruited through the Autism Speaks Autism Treatment Network and affiliated clinics (Ferguson et al., In Press). Parents of potential participants were screened over the phone using the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III (QPGS-RIII) (Baber et al., 2008), in an attempt to recruit a similar number of participants with and without prominent GI symptoms. In most cases, parents provided consent and children provided assent, when able, with the exception of 18-year-old participants who were competent to provide consent. All participants were

diagnosed with ASD based on clinical interview using DSM-IV-TR criteria (American Psychiatric Association, 2000), with the Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000) used to confirm diagnosis (all previous research-reliable ADOS were accepted and new assessments were conducted in the absence of an existing ADOS). Sixty-eight participants were taking medications that could affect (i.e. increase or decrease) repetitive behavior or gastrointestinal symptoms, including serotonin reuptake inhibitors, atypical antipsychotics, psychostimulants, alpha agonists, and constipation medications.

Assessment of Gastrointestinal Symptoms

GI symptoms were assessed using the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III (QPGS-RIII) (Baber et al., 2008). For most participants, parent-report forms were administered, but four high-functioning participants over the age of 16 years completed the self-report form when the participant and their parent indicated that this would yield the most reliable response. Functional GI diagnoses were derived from standard QPGS-RIII criteria, which utilizes a 5-point scale to measure frequency, severity, and duration of GI symptoms (Baber et al., 2008). QPGS-RIII diagnostic criteria were utilized to identify functional constipation (defined as the presence of two of more of the following symptoms: Two or fewer stools per week, either hard/very hard stools or painful stool, passage of very large stool, stool retention “once a week” or more often, history of large fecal mass in rectum, soiling “once a week” or more often, and does not meet criteria for irritable bowel syndrome) and nonretentive fecal incontinence (defined as a child 4 years of age or older, soiling “once a week” or more often, amount of stool is small or large (not just a stain), soiling for 2 months or longer, and does not meet criteria for functional constipation).

Behavioral and Cognitive Measures

Caregiver report on the Repetitive Behavior Scale-Revised (RBS-R) (Bodfish et al., 2000) was used to assess rigid-compulsive symptoms and other repetitive behavior symptoms. The RBS-R was utilized due to its ability to differentiate subtypes of repetitive behavior in both ASD and intellectual disability. Sensory symptoms were evaluated using caregiver report on the Sensory Over-Responsivity Inventory (SensOR) (Schoen et al., 2008). Interfering behaviors were assessed using caregiver report on the Aberrant Behavior Checklist, Community Version (ABC) (Aman, 1994). If fewer than five words were used during the ADOS (module 1, item A1), participants were defined as minimally verbal (Lord et al., 2000). The full scale intelligence quotient (FSIQ) for each participant from the AS-ATN database (Wechsler Intelligence Scale for Children, Wechsler Abbreviated Scale of Intelligence, or Stanford-Binet, each with a mean of 100 and standard deviation of 15) was used as a measure of general intelligence.

Data Analysis

Initial analyses were conducted with participants with available data on verbal status who were not taking medications that could impact repetitive behavior. Follow-up analyses were conducted including all participants with available data on verbal status. The primary behavioral outcome measure was the Compulsive Behavior Subscale of the RBS-R. Secondary outcome measures included the Ritualistic Behavior and Sameness Behavior

Subscales of the RBS-R (Bonferroni corrected significance threshold $p < 0.017$). Tertiary outcome measures included the other three subscales of the RBS-R, tactile sensitivity/aversion symptoms as assessed by the SenSOR, and the five subscales of the ABC (Bonferroni corrected significance threshold $p < 0.004$). Fisher's exact test and one-way analysis of variance were used to compare categorical and continuous characteristics by QPGS-RIII diagnosis group, respectively. In analyses of behavior, we corrected for verbal status and any demographic characteristics found to significantly differ across GI diagnosis groups. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Among the 120 study participants, 108 had available ADOS verbal status data. Functional constipation (FC) was the most common QPGS-RIII finding in the overall sample, occurring in 43/108 of these patients (40%). As shown in Table 1, participants with GI symptoms (including functional constipation and non-retentive fecal incontinence) did not differ significantly on demographic characteristics, ADOS scores, or FSIQ. RBS-R Compulsive Behavior subscale scores were significantly higher in the FC group compared to those with no QPGS-RIII diagnosis (Table 2, p=0.046, adjusting for age and verbal status). Differences in both the RBS-R Ritualistic Behavior ($p = 0.006$) and Sameness ($p = 0.008$) subscales were also statistically significant. Of the tertiary measures, Self-Injurious Behavior ($p = 0.002$) was significantly higher; ABC Irritability ($p = 0.044$) and SenSOR tactile sensitivity/aversion ($p = 0.006$) were nominally significant; and RBS-R Stereotyped Behavior ($p = 0.078$) and ABC Hyperactivity ($p = 0.066$) were at a trend level of elevation in the functional constipation group before correction for multiple comparisons.

Within the 108 total participants, 62 were taking medications that could affect repetitive behavior or GI symptoms, including serotonin reuptake inhibitors, stimulants, atypical antipsychotics, alpha agonists, and laxatives. Secondary analyses examined the 46 participants who were not taking medications that could impact repetitive behavior or FC. Functional constipation (FC) was the most common QPGS-RIII finding, occurring in 11/46 of these patients (24%), and was significantly less common than in the 62 participants taking medications (51%, Fisher's exact $p = 0.01$). As shown in Table 3, participants with GI symptoms (including functional constipation and non-retentive fecal incontinence) did not differ significantly on demographic characteristics, ADOS scores, or FSIQ.

Within the medication-free subgroup, scores on our primary outcome measure, the RBS-R Compulsive Behavior subscale, were higher for participants with functional constipation compared to those with no QPGS-R III diagnosis after adjusting for both verbal status and age; although this difference was not statistically significant ($p = 0.093$). Neither secondary nor tertiary repetitive behavior measures differed significantly between groups (Table 4).

To examine associations within the participants taking medications, we analyzed the subgroup of children taking behavioral medications (but free of medications targeting FC). No individual medication was used in enough participants to allow separate statistical analysis. Further, the subgroup of children taking medications for FC was also too small to sustain statistical analysis (n = 9). Within the behavioral medication subgroup (n = 46),

functional constipation (FC) was the most common QPGS-RIII finding, occurring in 21/46 participants (46%) (Table 5). Within the behavioral medication subgroup, our primary outcome measure, the RBS-R Compulsive Behavior subscale, was not statistically significant (p=0.99 after adjusting for age and verbal status) (Table 6). Of the two secondary outcome measures, the Ritualistic subscale was significant (p = 0.018) but not the Sameness subscale (p = 0.124). Among the tertiary analyses, the Self-Injurious (p = 0.030) and SenSOR (p = 0.007) variables were nominally significant.

DISCUSSION

As hypothesized, measures of rigid and compulsive behavior showed association with functional constipation, but these associations were consistently observed only in the overall group of participants. The observed association extended beyond the Compulsive Behavior subscale to include ratings of ritualistic and sameness behaviors when including all participants. Significant or suggestive association findings among our tertiary analyses in the full sample extended to measures of self-injurious and stereotyped behaviors, as well as tactile hypersensitivity/aversion, capturing nearly the entire repetitive behavior domain of the DSM-5 criteria, with the exception of restricted interests. In contrast to earlier findings (Gorrindo et al., 2012; Peters et al., 2014), we did not observe a significant association between functional constipation and verbal status, possibly because our population only included ten participants who were minimally verbal.

The broad pattern of behavioral association with functional constipation is somewhat consistent with factor analytic and principal components analyses of repetitive behavior in ASD, which report between one and five symptom domains, with the most consistency around a cluster of symptoms variously termed “higher-order,” “complex,” “rigid-compulsive,” or “resistance to change” (Anagnostou et al., 2011; Esbensen et al., 2009; Frazier et al., 2014; Georgiades et al., 2007; Richler et al., 2007; Richler et al., 2010; Scahill et al., 2014; Shuster et al., 2014; Szatmari et al., 2006; Tadevosyan-Leyfer et al., 2003). Further, restricted interests, which were not associated with functional constipation in our population, often separate from other symptoms when more than two symptom clusters are identified within the repetitive behavior domain (Scahill et al., 2014; Smith et al., 2009).

The primary outcome measure, a parent-report subscale specifically focused on compulsive behavior, was associated with functional constipation in the full group of participants but not in either subgroup analysis. This could simply reflect the increase in statistical power yielded by a doubling of the sample size. It could also reflect the higher rate of functional constipation in the subgroup taking medications (p = 0.01). Children with greater functional constipation symptoms at baseline may be more likely to be prescribed medication for behavior (or to relieve constipation), but we do not have longitudinal data to assess whether this is the case. It is also possible that medications prescribed for rigid-compulsive symptoms lead to side effects including functional constipation. Some psychopharmacological medications are well known to impact GI symptoms, such as serotonin reuptake inhibitors, which can cause diarrhea in the first few weeks of dosing, after which the gut serotonin receptors are thought to desensitize, leading to a fairly rapid progression to constipation (Cipriani et al., 2010), and atypical antipsychotics, which can

cause constipation (De Hert et al., 2011). Unfortunately, while we were able to examine a subgroup of children on behavioral medications without GI medications, our sample size does not allow for an analysis of subsets of children on individual medications, or even single classes of medications, in part because children were often taking more than one medication. We also do not have data on the target symptoms for which these medications were prescribed, which could include rigid-compulsive behavior as a logical treatment target based upon randomized controlled trials in both ASD and OCD (Dold et al., 2013; Hollander et al., 2012; McDougle et al., 2005; Soomro et al., 2008) but may also include hyperactivity, anxiety, irritability, or aggression.

These results align closely with our previous retrospective analysis in the AS-ATN data set, despite using very different approaches to assess the hypothesis (Peters et al., 2014). The previous analysis had the advantage of the very large AS-ATN sample, allowing a narrow analysis designed to assess surrogate measures of the most severely affected set of participants with constipation and likely encopresis, but it was limited to individual questions or diagnoses reported by parents or clinicians. Here, dense, psychometrically valid reports of GI and behavioral symptoms were used in a prospectively collected but much smaller sample.

Importantly, this study has a number of limitations. First, data were only available from a single point in time, preventing us from understanding whether changes in functional constipation symptoms predict changes in rigid-compulsive symptoms or vice versa. Second, GI diagnoses were made based on parent/self report using the QPGS-RIII, which a previous study showed is predictive of gastrointestinal diagnoses in ASD but underestimates functional constipation as diagnosed by a gastroenterologist (Gorrindo et al., 2012). Third, behavioral symptoms were measured using well-validated parent report measures that still fall short of the reliability of direct observation. Finally, while we anticipate that common neurodevelopmental mechanisms occurring in the gut and in the brain are the most likely explanation for the observed association, a randomized, controlled treatment study would be necessary to test whether there are causal connections between behavioral and GI symptoms (Margolis et al., 2016).

In summary, this study confirms an association between functional constipation symptoms and rigid–compulsive behaviors in children and adolescents with ASD. This suggests that GI symptoms could help to identify a subgroup of children who may share a common pattern of ASD symptoms. Furthermore, investigation of gut function or enteric neurodevelopment in children or in animal models of ASD could prove fruitful to dissect common mechanisms that may also occur in the brain, a much more complex and less accessible organ (Bernier et al., 2014; Margolis et al., 2016). While a connection with the serotonin system is possible (and is long implicated in ASD) (Muller et al., 2015), our assessment of whole blood serotonin levels in this same population did not identify a significant association with rigid-compulsive behavior (Marler et al., In Press). Similarly, associations between GI symptoms and measures of autonomic function were much more modest than the behavioral symptoms observed here (Ferguson et al., In Press). A larger, longitudinal follow-up study, including careful monitoring of any treatment, as well as a control group of participants without ASD, would be necessary to better understand the specificity and directionality of the relationship

between GI and behavioral symptoms. The collection of dietary habits could also prove helpful, as nutritional and feeding habits could affect both GI and behavioral symptoms (Johnson et al., 2014; Kerwin et al., 2005). Direct measures, such as collection of stool or intestinal biopsy samples for microbiome analysis (Li & Zhou, 2016; Mayer et al., 2015), would be particularly helpful in understanding the potential mechanisms that may connect functional constipation with rigid-compulsive behavior.

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Table 1

Total sample characteristics and relationship with GI symptoms

	Total *N*	No QPGS GI diagnosis (*n* = 54)	Functional Constipation (*n* = 43)	Non-Retentive Fecal Incontinence (*n* = 4)	Other Rome-III diagnoses (*n* = 7)	*P* value
Sex	108					0.064
Male (%)		92.6% (50)	88.4% (38)	100.0% (4)	57.1% (4)	
Female (%)		7.4% (4)	11.6% (5)	0.0% (0)	42.9% (3)	
Age: Mean (SD)	108	12.6(4.0)	11.6(3.4)	9.0(2.8)	9.4(3.8)	0.053
Race	108					1.000
Caucasian (%)		88.9% (48)	90.7% (39)	100.0% (4)	100.0% (7)	
Other race (%)		11.1% (6)	9.3% (4)	0.0% (0)	0.0% (0)	
Ethnicity	108					1.000
Non-Hispanic/Latino (%)		94.4% (51)	95.3% (41)	100.0% (4)	100.0% (7)	
Hispanic/Latino (%)		5.6% (3)	4.7% (2)	0.0% (0)	0.0% (0)	
Household income	92					0.455
Less than 50k (%)		37.8% (17)	51.3% (20)	33.3% (1)	20.0% (1)	
50k or greater (%)		62.2% (28)	48.7% (19)	66.7% (2)	80.0% (4)	
ADOS severity score: Mean (SD)	95	7.4(2.4)	7.2(2.1)	7.5(1.7)	7.7(1.7)	0.930
Verbal Status	108					0.153
Verbal		92.6% (50)	93.0% (40)	75.0% (3)	71.4% (5)	
Nonverbal		7.4% (4)	7.0% (3)	25.0% (1)	28.6% (2)	
FSIQ: Mean (SD)	96	87.7(22.6)	80.7(22.4)	64.3(13.9)	91.3(25.2)	0.164

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Table 2

Behavioral relationships with functional constipation in total group of participants with verbal status available.

	Summary Statistics			Adjusting for Age and Verbal Status	
Variable	**Total N**	**0. No Rome III Diagnoses N=54**	**1. Functional Constipation (± Others) N=43**	**Difference (95% CI)**	**P-Value**
RBS-R Compulsive	94	3.9(4.0)	5.6(5.6)	1.94 [0.06,3.83]	0.046*
RBS-R Ritualistic	94	4.8(4.0)	7.2(4.5)	2.45 [0.73,4.18]	0.006*
RBS-R Sameness	94	6.9(6.0)	10.5(7.0)	3.63 [0.99,6.27]	0.008*
RBS-R Self-Injurious	94	2.2(3.2)	4.0(3.1)	2.01 [0.75,3.27]	0.002*
RBS-R Stereotyped	94	4.2(3.9)	5.4(3.5)	1.34 [−0.14,2.82]	0.078
RBS-R Restricted	92	3.6(2.7)	4.1(2.8)	0.52 [−0.61,1.65]	0.369
ABC Stereotypy	94	4.7(4.8)	5.9(5.2)	1.30 [−0.72,3.31]	0.208
ABC Inappropriate Speech	94	3.4(3.0)	4.0(2.9)	0.60 [−0.61,1.81]	0.330
ABC Irritability	94	10.1(10.0)	14.4(9.4)	4.01 [0.15,7.88]	0.044
ABC Hyperactivity	94	13.7(11.2)	17.9(10.4)	4.05 [−0.23,8.34]	0.066
ABC Lethargy/Social Withdrawal	94	10.5(9.3)	9.5(8.3)	−0.65 [−4.23,2.93]	0.721
SensOR Tactile Sensitivity	96	0.2(0.2)	0.4(0.2)	0.12 [0.04,0.20]	0.006

*Statistically significant after correction for multiple testing

Table 3

Medication-free sample characteristics and relationship with GI symptoms

	Total *N*	No QPGS GI diagnosis (*n* = 32)	Functional Constipation (*n* = 12)	Non-Retentive Fecal Incontinence (*n* = 1)	Other Rome-III diagnoses (*n* = 2)	*P* value
Sex	46					0.641
Male (%)		90.6% (29)	100.0% (11)	100.0% (1)	100.0% (2)	
Female (%)		9.4% (3)	0.0% (0)	0.0% (0)	0.0% (0)	
Age: Mean (SD)	46	12.2(4.6)	9.2(2.5)	7.0	7.0(1.4)	0.052
Race	46					0.641
Caucasian (%)		90.6% (29)	100.0% (11)	100.0% (1)	100.0% (2)	
Other race (%)		9.4% (3)	0.0% (0)	0.0% (0)	0.0% (0)	
Ethnicity	46					0.521
Non-Hispanic/Latino (%)		96.9% (31)	90.9% (10)	100.0% (1)	100.0% (2)	
Hispanic/Latino (%)		3.1% (1)	9.1% (1)	0.0% (0)	0.0% (0)	
Household income	39					1.000
Less than 50k (%)		50.0% (14)	44.4% (4)	100.0% (1)	100.0% (1)	
50k or greater (%)		50.0% (14)	55.6% (5)	0.0% (0)	0.0% (0)	
ADOS severity score: Mean (SD)	40	6.8(2.6)	6.5(0.8)	6.0	7.0(1.4)	0.972
Verbal Status	46					0.666
Verbal		87.5% (28)	100.0% (11)	100.0% (1)	100.0% (2)	
Nonverbal		12.5% (4)	0.0% (0)	0.0% (0)	0.0% (0)	
FSIQ: Mean (SD)	42	88.1(24.7)	88.8(24.9)	76.0	88.5(20.5)	0.967

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Table 4

Behavioral relationships with functional constipation in participants who were not taking medications likely to affect repetitive behavior or FC

	Summary Statistics			Adjusting for Age and Verbal Status	
Variable	**Total N**	**0. No Rome III Diagnoses N=32**	**1. Functional Constipation (± Others) N=11**	**Difference (95% CI)**	**P-Value**
RBS-R Compulsive	42	3.6(3.5)	5.5(6.0)	2.74 [−0.41,5.89]	0.093
RBS-R Ritualistic	42	5.0(3.6)	6.6(4.4)	1.08 [−1.74,3.90]	0.454
RBS-R Sameness	42	6.8(5.5)	9.9(6.9)	3.34 [−1.08,7.76]	0.144
RBS-R Self-Injurious	42	2.1(3.5)	3.0(2.7)	1.82 [−0.52,4.16]	0.133
RBS-R Stereotyped	42	4.0(4.2)	4.7(2.8)	0.91 [−1.89,3.71]	0.523
RBS-R Restricted	41	3.7(2.6)	4.5(2.8)	0.87 [−1.18,2.91]	0.408
ABC Stereotypy	42	4.2(4.9)	5.8(5.7)	2.26 [−1.46,5.98]	0.238
ABC Inappropriate Speech	42	3.2(2.9)	3.5(2.4)	−0.33 [−2.39,1.73]	0.754
ABC Irritability	42	8.4(9.5)	13.1(9.6)	3.94 [−2.54,10.41]	0.237
ABC Hyperactivity	42	10.7(8.7)	14.5(9.6)	2.32 [−3.59,8.22]	0.443
ABC Lethargy/Social Withdrawal	42	10.2(9.2)	8.4(5.2)	−0.97 [−7.20,5.25]	0.759
SensOR Tactile Sensitivity	42	0.3(0.2)	0.4(0.2)	0.13 [−0.03,0.28]	0.115

Table 5

Behavioral-medication only sample characteristics and relationship with GI symptoms

	Total *N*	No QPGS GI diagnosis (*n* = 19)	Functional Constipation (*n* = 21)	Non-Retentive Fecal Incontinence (*n* = 3)	Other Rome-III diagnoses (*n* = 3)	*P* value
Sex	46					0.019
Male (%)		100.0% (19)	90.5% (19)	100.0% (3)	33.3% (1)	
Female (%)		0.0% (0)	9.5% (2)	0.0% (0)	66.7% (2)	
Age: Mean (SD)	46	12.9(3.1)	12.1(3.3)	9.7(3.1)	11.0(4.6)	0.349
Race	46					0.834
Caucasian (%)		84.2% (16)	90.5% (19)	100.0% (3)	100.0% (3)	
Other race (%)		15.8% (3)	9.5% (2)	0.0% (0)	0.0% (0)	
Ethnicity	46					0.737
Non-Hispanic/Latino (%)		89.5% (17)	95.2% (20)	100.0% (3)	100.0% (3)	
Hispanic/Latino (%)		10.5% (2)	4.8% (1)	0.0% (0)	0.0% (0)	
Household income	39					0.190
Less than 50k (%)		20.0% (3)	47.4% (9)	0.0% (0)	0.0% (0)	
50k or greater (%)		80.0% (12)	52.6% (10)	100.0% (2)	100.0% (3)	
ADOS severity score: Mean (SD)	40	8.3(1.8)	7.9(2.1)	8.0(1.7)	9.0(1.7)	0.738
Verbal Status	46					0.055
Verbal		100.0% (19)	90.5% (19)	66.7% (2)	66.7% (2)	
Nonverbal		0.0% (0)	9.5% (2)	33.3% (1)	33.3% (1)	
FSIQ: Mean (SD)	41	88.5(20.3)	78.4(22.0)	58.5(13.4)	91.3(36.7)	0.178

Table 6

Behavioral relationships with functional constipation in participants who were taking behavioral medications and no GI medications

	Summary Statistics			Adjusting for Age and Verbal Status	
Variable	**Total N**	**0. No Rome III Diagnoses N=19**	**1. Functional Constipation (± Others) N=21**	**Difference (95% CI)**	**P-Value**
RBS-R Compulsive	38	4.5(4.7)	5.3(5.1)	−0.02 [−2.51,2.48]	0.990
RBS-R Ritualistic	38	4.4(4.7)	8.1(4.0)	3.36 [0.69,6.04]	0.018
RBS-R Sameness	38	7.5(7.1)	11.3(6.4)	3.26 [−0.83,7.35]	0.124
RBS-R Self-Injurious	38	2.4(2.9)	4.4(2.4)	1.86 [0.23,3.49]	0.030
RBS-R Stereotyped	38	4.4(3.5)	5.3(3.3)	0.33 [−1.52,2.19]	0.727
RBS-R Restricted	37	3.7(2.9)	4.1(2.8)	0.12 [−1.62,1.87]	0.889
ABC Stereotypy	40	5.4(4.8)	5.0(4.0)	−0.46 [−3.16,2.24]	0.739
ABC Inappropriate Speech	40	3.4(3.1)	4.3(3.0)	1.05 [−0.80,2.90]	0.270
ABC Irritability	40	11.6(10.4)	13.8(8.2)	1.82 [−3.72,7.36]	0.520
ABC Hyperactivity	40	17.9(13.6)	19.6(9.8)	0.44 [−6.57,7.45]	0.903
ABC Lethargy/Social Withdrawal	40	11.4(9.8)	8.6(6.9)	−3.18 [−8.29,1.93]	0.227
SensOR Tactile Sensitivity	40	0.2(0.2)	0.4(0.2)	0.18 [0.05,0.30]	0.007