Associations between dietary composition and gastrointestinal symptoms in autism spectrum disorder

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Introduction

- Many children and adolescents with autism spectrum disorder (ASD) have significant gastrointestinal (GI) symptoms, but the etiology is not well understood.
- Studies have shown conflicting evidence on whether there are nutritional deficiencies in the various diets of individuals with ASD. However, little is known about the relationship between dietary intake and GI symptomatology in ASD.
- Many patients with ASD try gluten-free and/or casein-free diets, and this may also impact GI symptomatology or nutritional status.
- A previous study conducted by this team found an association between autonomic functioning, cortisol stress response, and lower GI tract symptomatology. (Ferguson et al., 2016)
- **The present study assessed relationships between GI symptoms and dietary composition in the same sample of individuals that participated in the aforementioned study conducted by our team. We wished to determine if dietary consumption potentially contributed to our finding of a relationship between the response to stress and GI functioning in ASD.**

Methods

Participants

- 75 individuals with ASD were recruited from the Autism Speaks – Autism Treatment Network (ATN) at the University of Missouri Thompson Center for Autism & Neurodevelopmental Disorders. See Table 1 for descriptive statistics.

Assessment of Gastrointestinal Symptoms

- GI symptoms were assessed using the Questionnaire on Pediatric Gastrointestinal Symptomatology-Rome III (QPGS-RIII). A scoring rubric previously created and published by the team was used to create continuous variables for upper and lower GI tract symptoms. See Table 1 for descriptive statistics.

Assessment of Stress Response

- Cortisol response and heart rate variability (pNN50 – marker of parasympathetic tone) in response to vibrotactile and cold-pressor stimulation were utilized as measures of the response to stress. See Table 2.

Assessment of Dietary Composition

- Dietary composition for each participant was assessed using a Food Frequency Questionnaire (FFQ) (Ritter-Gooder et al., 2006) in which the participant's caregiver estimated the participant's food intake over the past month.
- Nutritional information for each food item endorsed on a participant's FFQ was obtained from the on-line, publicly-available USDA Food Composition Database, which provides nutrient information for a given serving size of a food item.
- The micro and macro nutrients contained in each food serving consumed over the past month were summed for each nutritional item (e.g., vitamins, minerals). See Table 3.

Results

	% (n) Mean (SD)	Range	N
Males	89.3% (67)		75
Age at Consent (Years)	12.56 (3.7)	5-18	75
QPGS Rome-III Upper GI Tract Score	4.64 (5.51)	0-24	75
QPGS Rome-III Lower GI Tract Score	20.28 (13.48)	1-63	75

Table 1. Descriptive statistics for sex, age, and QPGS Rome-III upper and lower GI tract scores (higher scores = greater frequency, duration, & severity of GI symptoms).

Biomarker	Covariate	Correlation (95% CI)	p-value	n
Cortisol Response (ln [post stress – pre stress])	Upper GI Score	-0.00 (-0.24, 0.23)	0.9755	75
	Lower GI Score	0.27 (0.04, 0.47)	***0.0207**	75

Table 2. Partial Pearson correlations between Cortisol response and QPGS Rome-III GI scores, controlling for age, gender, and cortisol pre-stress values (cortisol response only). $*p < 0.05$.

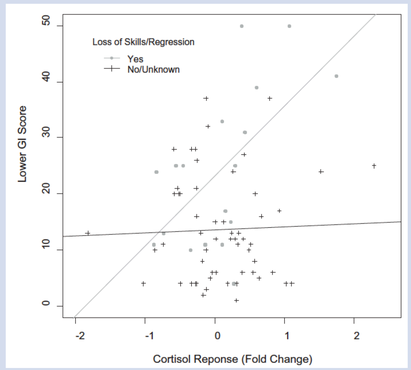

Figure 1. Illustration of the effect modification of history of regressive autism on the relationship between cortisol stress response and lower gastrointestinal tract scores. $p = 0.007$.

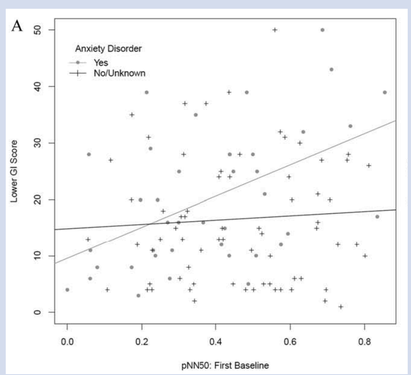

Figure 2. Impact of effect modifiers on the ANS-GI symptomatology relationships. (A) effect of presence or absence of anxiety on relationship between lower GI tract scores and pNN50 baseline. $p < 0.001$.

Nutrient	N	Mean	SD	QPGS Rome-III Upper GI Tract Score	QPGS Rome-III Lower GI Tract Score
Water (g)	75	16572.97	11460.77	0.013	0.103
Energy (kcal)	75	20488.04	10495.77	-0.004	0.102
Protein (g)	75	1173.56	577.61	-0.081	0.063
Total Lipid Fat (g)	75	839.27	471.00	-0.111	0.011
Carbohydrate (By Difference; g)	75	2155.64	1280.66	0.129	0.178
Dietary Fiber (Total; g)	75	236.28	170.27	**.235***	0.168
Sugars (Total; g)	75	903.46	766.05	0.224	0.132
Calcium (mg)	75	18807.42	16132.60	-0.055	0.085
Iron (mg)	75	124.27	83.14	0.088	0.088
Magnesium (mg)	75	4071.20	2601.42	-0.017	0.085
Phosphorous (mg)	75	21675.08	13352.86	-0.067	0.085
Potassium (mg)	75	43572.57	26575.61	0.01	0.117
Sodium (mg)	75	26558.41	16553.72	-0.028	0.071
Zinc (mg)	75	158.42	86.66	-0.002	0.106
Vitamin C (Total Ascorbic Acid; mg)	75	1460.16	1742.43	0.17	0.098
Thiamin (mg)	75	17.15	9.36	0.016	0.152
Riboflavin (mg)	75	28.66	20.36	-0.083	0.078
Niacin (mg)	75	267.65	135.11	-0.089	0.024
Vitamin B6 (mg)	75	36.26	29.70	**0.338***	0.184
Folate (DFE; µg)	75	4106.64	3945.34	0.033	0.083
Vitamin B12 (µg)	75	79.59	52.50	-0.07	0.034
Vitamin A (RAE; µg)	75	8888.35	7170.05	-0.076	0.05
Vitamin A (IU)	75	69048.11	73514.22	0.001	0.056
Vitamin E (Alpha Tocopherol; mg)	75	110.16	79.69	-0.032	0.005
Vitamin D2 + D3 (µg)	75	84.82	79.37	-0.202	-0.043
Vitamin D (IU)	75	3410.78	3262.99	-0.203	-0.044
Vitamin K (Phylloquinone; µg)	75	1109.33	1096.81	0.107	0.106
Total Saturated Fatty Acids (g)	75	283.16	168.10	-0.073	0.029
Total Monounsaturated Fatty Acids (g)	75	308.11	191.03	-0.119	0.009
Total Polyunsaturated Fatty Acids (g)	75	176.61	106.67	-0.162	-0.031
Total Trans Fatty Acids (g)	75	8.32	11.99	-0.096	0.106
Cholesterol (mg)	75	3314.17	1822.61	-0.061	0.01

Table 3. Monthly nutrient values and Pearson correlation coefficients between nutritional composition values and QPGS-Rome III upper and lower GI tract symptom scores. ***not significant at $p < 0.05$ after correction for multiple comparisons.**

Results

Gastrointestinal Symptoms

- The most frequently occurring GI disorders based on parental report on the QPGS-RIII in the sample were functional constipation (42.5%), irritable bowel syndrome (11.7%), lower abdominal pain associated with bowel symptoms (9.2%), and upper pain associated with bowel symptoms (7.5%).

Stress Response, GI Symptoms, & Effect Modifiers

- A significant positive relationship was found between cortisol response to stress and QPGS-RIII lower GI tract scores. See Table 2.
- Presence of regressive ASD significantly modified the relationship between QPGS-RIII lower GI tract score and cortisol response to stress. See Figure 1.
- Presence of ASD + a co-occurring anxiety disorder significantly modified the relationship between QPGS-RIII lower GI tract score and parasympathetic tone at baseline. See Figure 2.

Dietary Composition + GI Relationships

- Initial analyses found that QPGS-RIII upper GI tract symptoms were positively associated with total dietary fiber (p=0.042), and vitamin B6 intake (p=0.03), but were no longer significant after adjusting for the 32 nutrients examined. See Table 3.
- There were no significant correlations between QPGS-RIII lower GI tract symptoms and any nutrient.

Discussion

Lower GI tract symptoms were positively correlated with cortisol response to stress-inducing stimuli.

- This association was greater for children with a history of regressive ASD.

Nutritional composition was not associated with upper or lower GI tract symptoms in this sample of individuals with ASD.

- This supports the hypothesis that there may be other factors associated with lower GI tract disorders in ASD, such as an increased stress response.
- Diet is not likely a driving factor for the previously observed relationship between stress response and GI functioning in ASD.
- Further studies are needed to explore non-diet associations with GI disorders in ASD.

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