Associations between nutrient intake and gastrointestinal symptoms in autism spectrum disorder

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Working collaboratively across North America, to address the physical health of children and adolescents with autism.

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 there is anecdotal evidence of improvement in ASD symptoms with dietary those dietary regimens.
- A previous study conducted by this group has suggested an association between autonomic function and stress response with lower GI symptomatology.
- **The goal of the present study was to assess for potential relationships between GI symptoms and nutrient intake from diet in the same sample of individuals from the previous study, and to determine whether dietary differences might have contributed to our previously observed findings of a relationship between stress responses and GI functioning in ASD.**

Methods

Participants

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

Assessment of Gastrointestinal Symptoms

- Gastrointestinal symptoms were assessed using the Questionnaire on Pediatric Gastrointestinal Symptomatology-Rome III (QPGS-RIII). A scoring rubric was used to create continuous variables for upper and lower GI tract symptoms.

Assessment of stress response

- Cortisol response to tactile stimulation was utilized as a measure of stress response in these individuals. See Table 2.

Assessment of Dietary intake

- Dietary intake of each individual was assessed using a Food Frequency Questionnaire, adopted from a study on Omega-3 intake in cardiac patients by Ritter-Gooder PK et al., in which respondents estimate his/her food intake over the past month.
- Responses were analyzed for nutritional intake using the online, publicly available USDA Food Composition Database that provides nutrient information for a given food.
- Nutrient information for each food marked on a subject's Food Frequency Questionnaire was obtained, and total nutrient intake for each subject was summed to give monthly nutrient intake. 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

Table 1. Demographics for sex and age.

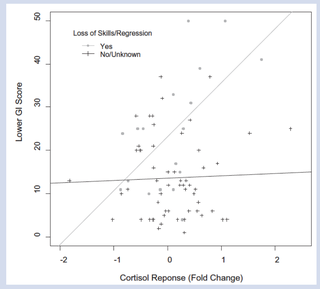

Figure 1. Illustration of the effect modification of history of regressive autism on the relationship between cortisol stress response and lower gastrointestinal tract scores

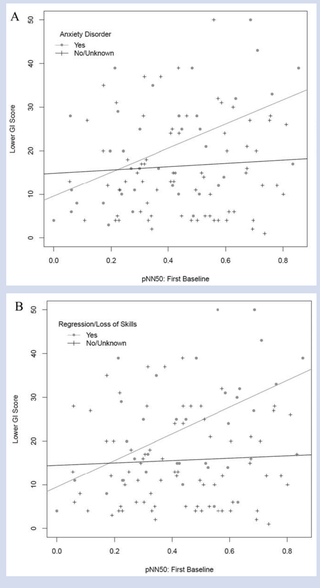

Figure 2. Impact of effect modifiers on the ANS-gastrointestinal symptomatology relationships. (A) effect of presence or absence of anxiety on relationship between lower GI tract scores and pNN50 baseline. (B) Effect of presence or absence of history of regression/loss of skills on the relationship between lower GI tract scores and pNN50 baseline

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
	FSIQ	0.27 (0.02, 0.49)	**0.0365**	64
	ABC Inappropriate Speech	-0.27 (-0.47, -0.04)	**0.0231**	74
	ABC Hyperactivity	-0.28 (-0.48, -0.05)	**0.0186**	74

Table 2. Partial Pearson correlations between Cortisol response and QPGS Rome III GI scores, FSIQ, and selected ABC and Vineland variables, controlling for age, gender, and cortisol pre-stress values (cortisol response only). Significant correlations are in bold ($p<0.05$).

	Mean	SD	N
Rome III GI Upper Score	4.64	5.51323	75
Rome III GI Lower Score	20.28	13.48128	75
Water (g)	16572.9673	11460.771	75
Energy (kcal)	20488.0367	10495.7657	75
Protein (g)	1173.5551	577.60532	75
Total Lipid Fat (g)	839.2664	471.00048	75
Carbohydrate (By Difference; g)	2155.6363	1280.66155	75
Dietary Fiber (Total; g)	236.2797	170.27214	75
Sugars (Total; g)	903.4632	766.04648	75
Calcium (mg)	18807.42	16132.6032	75
Iron (mg)	124.2673	83.14305	75
Magnesium (mg)	4071.2	2601.42227	75
Phosphorous (mg)	21675.0833	13352.8603	75
Potassium (mg)	43572.57	26575.607	75
Sodium (mg)	26558.4067	16553.7216	75
Zinc (mg)	158.421	86.6629	75
Vitamin C (Total Ascorbic Acid; mg)	1460.161	1742.43404	75
Thiamin (mg)	17.1451	9.35754	75
Riboflavin (mg)	28.6636	20.36107	75
Niacin (mg)	267.6509	135.11402	75
Vitamin B6 (mg)	36.2633	29.69813	75
Folate (DFE; µg)	4106.6433	3945.33584	75
Vitamin B12 (µg)	79.5947	52.5026	75
Vitamin A (RAE; µg)	8888.3467	7170.05499	75
Vitamin A (IU)	69048.1067	73514.2181	75
Vitamin E (Alpha Tocopherol; mg)	110.1635	79.68801	75
Vitamin D2 + D3 (µg)	84.8217	79.3749	75
Vitamin D (IU)	3410.783	3262.99249	75
Vitamin K (Phylloquinone; µg)	1109.334	1096.80656	75
Total Saturated Fatty Acids (g)	283.1597	168.1027	75
Total Monounsaturated Fatty Acids (g)	308.1146	191.03401	75
Total Polyunsaturated Fatty Acids (g)	176.6071	106.67456	75
Total Trans Fatty Acids (g)	8.317	11.99395	75
Cholesterol (mg)	3314.1667	1822.61335	75

Table 3. Mean nutrient intake values

	Rome III Upper GI Score	Rome III Lower GI Score
Rome III Upper GI Score	1	**.531****
Rome III Lower GI Score	**.531****	1
Water (g)	0.013	0.103
Energy (kcal)	-0.004	0.102
Protein (g)	-0.081	0.063
Total Lipid Fat (g)	-0.111	0.011
Carbohydrate (By Difference; g)	0.129	0.178
Dietary Fiber (Total; g)	**.235***	0.168
Sugars (Total; g)	0.224	0.132
Calcium (mg)	-0.055	0.085
Iron (mg)	0.088	0.088
Magnesium (mg)	-0.017	0.085
Phosphorous (mg)	-0.067	0.085
Potassium (mg)	0.01	0.117
Sodium (mg)	-0.028	0.071
Zinc (mg)	-0.002	0.106
Vitamin C (Total Ascorbic Acid; mg)	0.17	0.098
Thiamin (mg)	0.016	0.152
Riboflavin (mg)	-0.083	0.078
Niacin (mg)	-0.089	0.024
Vitamin B6 (mg)	**0.338****	0.184
Folate (DFE; µg)	0.033	0.083
Vitamin B12 (µg)	-0.07	0.034
Vitamin A (RAE; µg)	-0.076	0.05
Vitamin A (IU)	0	0.056
Vitamin E (Alpha Tocopherol; mg)	-0.032	0.005
Vitamin D2 + D3 (µg)	-0.202	-0.043
Vitamin D (IU)	-0.203	-0.044
Vitamin K (Phylloquinone; µg)	0.107	0.106
Total Saturated Fatty Acids (g)	-0.073	0.029
Total Monounsaturated Fatty Acids (g)	-0.119	0.009
Total Polyunsaturated Fatty Acids (g)	-0.162	-0.031
Total Trans Fatty Acids (g)	-0.096	0.106
Cholesterol (mg)	-0.061	0.01

Table 4. Correlation matrix between nutrient intake values and QPGS Rome III GI scores

Results

Gastrointestinal Symptoms

- The most frequently occurring GI disorders 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%). See Table 1.

Stress response

- A significant positive relationship was found between cortisol response to stress and a greater lower GI tract score. See Table 2.
- Presence of regressive ASD significantly modified the relationship between lower GI tract score and cortisol response to stress. See figure 1.
- A significant positive correlation was identified between cortisol response to stress and FSIQ. See Figure 2.

Dietary nutrient intake

- Upper GI tract symptoms were significantly correlated with total dietary fiber intake and vitamin B6 intake; however, these relationships did not survive correction for multiple comparisons (Bonferroni Correction). See Table 4.
- There were no significant associations between lower GI tract symptoms and dietary intake.

Discussion

Lower GI tract symptoms were positively associated with post-stress cortisol concentration.

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

Nutritional intake is not associated with GI symptomatology in this sample of individuals with ASD.

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

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