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Gastrointestinal Tract Symptomatology in Adults with Pica and Autism

Dean D. Alexander
Lanterman Developmental Center, Pomona, California, USA,
ORCID: https://orcid.org/0000-0003-3562-9573,
e-mail: deanalexanderphd@gmail.com

Stanley E. Lunde
Lanterman Developmental Center, Pomona, California, USA,
ORCID: https://orcid.org/0000-0002-5836-4486,
e-mail: stanlunde@gmail.com

Dale E. Berger
Claremont Graduate University, Claremont, California, USA,
ORCID: https://orcid.org/0000-0002-5595-9492,
e-mail: dale.berger@cgu.edu

This study investigated pica behavior in those with and without autism in relation to gastrointestinal (GI) tract symptomatology and disease. A chart review of 64 residential adults with developmental disabilities indicated that individuals with pica had more GI tract diseases, and those with autism and pica had a higher rate of GI diseases compared to those with autism and no pica behavior. These data suggest that individuals with both autism and pica disorders may be a phenotypic subgroup in the autistic spectrum characterized by GI symptomatology, requiring a clinical algorithm for categorization and effective treatment. A behavior-analytic model is presented that conceptualizes pica as part of a chain of events that begins with exploratory behavior and culminates in GI symptomatology and disease. Issues of sensory processing are addressed within this model. Individuals exhibiting pica may benefit from gastrointestinal evaluation, including assessment of the microbiome, and, if indicated, microbiota transfer therapy to normalize gut-brain signaling.

Keywords: pica, autism spectrum disorder, GI diseases, microbiome, microbiota transfer therapy, comorbidity, prevalence, phenotype, sensory processing.

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Желудочно-кишечная симптоматика у взрослых с пикацизмом и аутизмом

Дин Д. Александр
Центр развития Лантерман, Помона, США,
ORCID: https://orcid.org/0000-0003-3562-9573, e-mail: deanalexanderphd@gmail.com

Стэнли Э. Лунде
Центр развития Лантерман, Помона, США,
ORCID: https://orcid.org/0000-0002-5836-4486, e-mail: stanlunde@gmail.com

Дейл Э. Бергер
Университет постдипломного образования Клермонта, Клермонт, США,
ORCID: https://orcid.org/0000-0002-5595-9492, e-mail: dale.berger@cgu.edu

В настоящей работе исследовался феномен пикацизма у людей с аутизмом и без него, а также связь данного феномена с симптоматикой и заболеваниями желудочно-кишечного тракта (ЖКТ). Анализ данных 64 взрослых испытуемых с нарушениями развития, проживающих в интернате, показал, что у людей с пикацизмом чаще встречались заболевания желудочно-кишечного тракта, а у людей с аутизмом и пикацизмом был более высокий уровень заболеваний желудочно-кишечного тракта по сравнению с людьми, имеющими аутизм без пикацизма. На основании полученных данных можно предположить, что люди с аутизмом и пикацизмом могут составить фенотипическую подгруппу в спектре аутизма, характеризующуюся симптоматикой ЖКТ, требующей клинического алгоритма для диагностики и эффективного лечения. Представлена поведенческая аналитическая модель, которая концептуализирует пикацизм как элемент цепи событий, начинающейся с исследовательского поведения и завершающейся симптоматикой и заболеваниями желудочно-кишечного тракта. В рамках данной модели решаются проблемы, связанные с сенсорной обработкой. Лицам, у которых наблюдается пикацизм, может помочь обследование пищеварительной системы, включающее микробиотическую оценку, и, при показаниях, трансплантация микробиоты для нормализации передачи сигналов от кишечника к мозгу.

Ключевые слова: пикацизм, расстройства аутистического спектра, заболевания ЖКТ, микробиота, трансплантация микробиоты, коморбидность, распространенность, фенотип, сенсорная обработка.

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Introduction

Pica behavior refers to the persistent ingestion of non-food items, a behavior that can be life-threatening for many individuals. A recent study supported by the Centers for Disease Control (CDC) reported that 23.2% of those on the autism spectrum exhibit pica behavior. In contrast, pica behavior is seen in 4.5% in children with developmental disabilities other than autism spectrum disorder (ASD) and 3.6% in neurotypical controls [15]. In a study of adults with autism, the percentage identified with a comorbid pattern of pica jumps to 60% [24].

Literatures on pica and autism have focused on GI symptomatology and diseases as sequelae of these disorders. GI problems common in autism include constipation, diarrhea, GERD, bloating, excessive gas, abdominal pain, vomiting, and nausea [13; 18; 43]. In addition, Horvath [19] found approximately 70% of autistic children suffered from esophagitis and duodenitis.

Pica has long been linked to gastritis/helicobacter pylori (H. pylori) [40], colitis [12], and celiac disease [25]. Other researchers have reported pica to result in intestinal perforation and blockage, parasites, surgery to remove objects from the stomach, lead poisoning, and death for individuals who are intellectually challenged as well as neurotypical [1; 10; 16]. With respect to those who are intellectually challenged, Matson [28] described pica as the most dangerous type of self-injurious behavior, as well as the least researched of all types of aberrant behavior.

Studies noted by Xu et al. have shown that "patients with ASD had alterations of the gut microbiota. These alterations were potentially relevant to behavioral and GI symptoms that are correlated with the severity of ASD, suggesting that the gut-brain axis participates in the pathogenesis of ASD" [46, pp. 6, 7]. Krajmalnic-Brown et al. [26] reported a lack of diversity in bacteria strains, while Xu's meta-analysis revealed the percentage and relative abundance of bacterial genera, both harmful and beneficial, in children with ASD and matched controls. Kang and her associates postulated that harmful bacteria can excrete dangerous, disruptive metabolites that can affect the gut, the body, and the brain. Microbiota Transfer Therapy produced significant improvements in GI symptoms, autism-related symptoms, and gut microbiota that persisted for at least two years for children with ASD and GI problems [22]. Pangborn and Baker [35] suggested that maldigestion and malabsorption can foster growth of dysbiotic gut flora, inflammation, and increased gut permeability that can allow entry of toxins and casomorphins. That is, protein, fats, and carbohydrates are not properly broken down so that they can be absorbed across the gut wall. Multiple nutritional deficiencies (e.g., zinc, magnesium, vitamin B6) are common in individuals with autism and may make it difficult for them to metabolize and utilize essential fatty acids [39].

Co-morbidity of autism and pica has been documented in numerous research studies. Kinnell [24] regarded pica to be a *diagnostic* feature of autism based on a study where pica was far more common in individuals with autism (60%) than in people with Down's syndrome (4%)(n = 70 in each group). As noted earlier, Fields et al. [15] found a lower (but still alarming) prevalence rate of pica for ASD children ranging in age from three-to-five years (23.2%).

These findings led us to two unanswered questions:

1. What are the relative prevalence rates of specific GI symptoms and diseases with respect to pica, autism, and autism/pica for adults residing at a developmental center?

2. Do the prevalence rates of GI problems for an adult sample of people with autism approximate the rates reported in the recent literature for children with autism?

Method

Participants

Data were obtained from a Medical Staff Quality Assurance (QA) study conducted at Lanterman Developmental Center to improve services for persons exhibiting pica. The resident population pool of clients included those with diagnoses of autism, autism/pica, and pica. Research groups were matched on gender and age (*see Table 1*) as well as level of cognitive functioning (severe and profound intellectual disabilities). The clients were on similar diets throughout the Center. Names of individuals were not included in the data set.

Table 1

Gender and Age by Diagnostic Group

	Autism	Autism/Pica	Pica	Control
Male	12	12	10	10
Female	3	5	6	6
Age Mean	38.9	42.2	43.7	44.5
Age SD*	9.7	10.8	7.6	7.8
Age Range	24–56	24–58	30–58	31–58

* standard deviation.

Client demographics were available to the authors via the center's computerized client records as well as reports from staff at the residences. Sixteen cases were originally selected in each of four groups. During the course of the study one person in the autism group was discovered to have pica and was subsequently reassigned to the autism/pica group. Group assignment was based upon the following inclusion criteria:

1. Autism: Clients were included if they met the diagnostic criteria of Autistic Disorder [11]. Diagnoses were made prior to the study by both a clinical psychologist and a psychiatrist. Clients with pica were excluded.

2. Pica: These clients were identified to the first author through a survey and a report as having ongoing problems of pica. Items ingested included beads, buttons, clothing tags, rubber gloves, socks, strings, cigarette butts, crayons, paper, plastic items, pop tops, trash, small rocks, bark, dirt, feces, grass, leaves, mushrooms, twigs, and indiscriminate small items. Clients with autism were excluded.

3. Autism and Pica: Fourteen of the 16 clients received a diagnosis of autism by both a clinical psychologist and a psychiatrist. In two cases, there was one diagnosis of autism and a second of PDD. All 16 clients met criteria for Pica (see above).

4. Control Group: These clients were matched on gender, age, and level of cognitive functioning to the Pica Group.

Measurement

The dependent variables for this study included GI-related symptoms and diseases. A list of GI symptoms/diseases was assembled from medical textbooks, conference proceedings, and intake histories from private practitioners (see Appendix A). This checklist was reviewed for validity by the Quality Assessment and Improvement Committee of the Center's Medical Staff.

Data collection was accomplished by two UCLA pre-doctoral psychology interns at the Center who were trained to search through a 10-year period of clients' medical records. They were blind to the purpose of the study.

Inter-rater reliabilities were calculated by dividing the number of agreements between raters by the number of agreements plus disagreements for four randomly selected charts. The mean ratio for the GI checklist (signs/symptoms/diseases) was 94% which indicated strong agreement between the raters.

The QA study was approved by the Quality Assessment and Improvement Committee of the Center's Medical Staff and by the Lanterman Quality Management Council.

Results

An analysis of the distributions of each of the variables revealed an outlier and positive skew for the number of GI signs/symptoms. A log (base e) transformation was performed, which normalized that variable for use in subsequent analyses. However, the results were substantively the same if the data were left untransformed, or if an outlier in the autism/pica group was dropped or Winsorized.

The mean frequencies for GI diseases and GI signs/symptoms, with respect to the autism/pica, pica, autism, and control groups are shown in *Table 2*.

A multivariate analysis was utilized to examine the two outcome variables with regard to Pica, Autism, and their interaction in a two-by-two factorial design. The Pica condition included both Pica and Autism/Pica groups whereas the No Pica condition included both Autism and Control groups. The Autism condition included both Autism and Autism/Pica groups whereas the No Autism condition included both Pica and Control groups.

The multivariate analysis indicated that Pica was the only significant factor, Wilks' Lambda = .816, $F(2, 59) = 6.65$, $p = .002$. Univariate analyses indicate that both dependent variables significantly differentiated between Pica and No Pica conditions. GI diseases were greater for the Pica condition, $F(1, 60) = 13.34$, $p = .001$, as were GI signs/symptoms, $F(1, 60) = 4.18$, $p = .045$. There were no significant effects for the Autism condition or for the interactions between Pica and Autism with the multivariate analysis. However, the univariate analyses of the interactions indicated that the interaction for GI symptoms was significant, $F(1, 60) = 4.96$, $p = .030$.

Figures 1 and 2 display the means for the four groups for GI diseases and GI signs/symptoms respectively. Both Figures 1 and 2 reflect the high incidence of GI problems for the Autism/Pica group but not for the Autism group.

An analysis of all GI diseases for adults in the Pica vs. No Pica conditions shows much greater co-morbidity of diseases in the Pica condition (*see Figure 3*).

Table 2

Mean and Standard Deviation (SD) for Diseases/Symptomatology by Diagnostic Group

	Autism (n = 15)		Autism/Pica (n = 17)		Pica (n = 16)		Control (n = 16)	
	Mean	***SD***	**Mean**	***SD***	**Mean**	***SD***	**Mean**	***SD***
GI Diseases	0.53	.92	2.88	2.37	2.25	2.02	1.31	1.45
GI Signs/Symptoms *	0.93	0.45	1.41	0.53	1.14	0.34	1.16	0.46

* log transformation (base e)

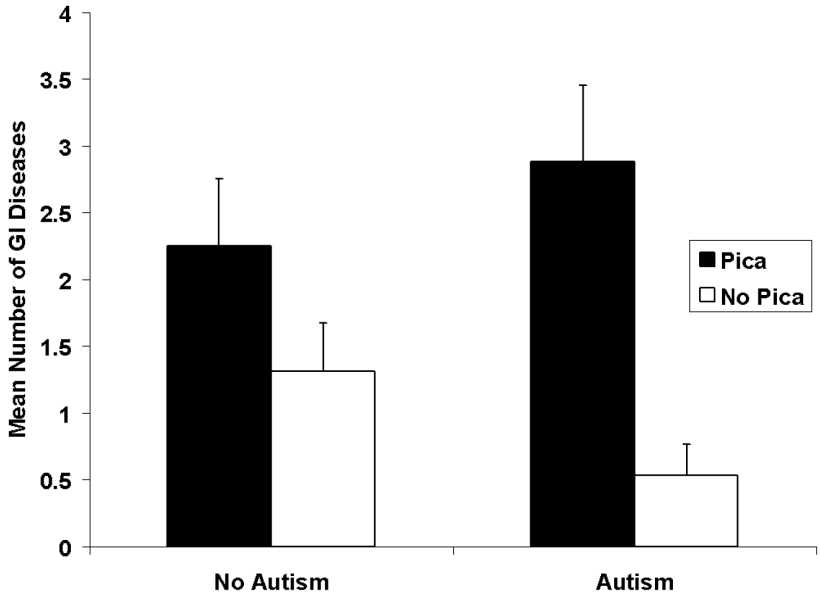

Fig. 1. Mean number of gastrointestinal (GI) diseases by pica and autism conditions with standard error

Those individuals with three or more diseases were identified as severely affected. Almost half of those in the Pica condition can be so identified.

An analysis of the specific types of diseases reveals a predominance of chronic inflammatory diseases: gastritis, esophagitis, GERD, duodenitis, and colitis (*see Table 3*).

In the Pica condition (n = 33), 64% of the persons had at least one of these chronic inflammatory diseases, and 58% had at least two. A comparison of Pica and No Pica conditions reflects higher incidence in the Pica condition across all of these diseases: gastritis, esophagitis, GERD, duodenitis, colitis, hiatal hernia, ulcer, H. pylori, intestinal blockage, and aerophagia.

No significant difference between Pica and No Pica conditions were seen for most frequently occurring GI signs/symptoms. Table 4 shows that vomiting, history of weight loss/difficulty gaining weight, and GI bleeding occurred with about equal frequency in the two conditions.

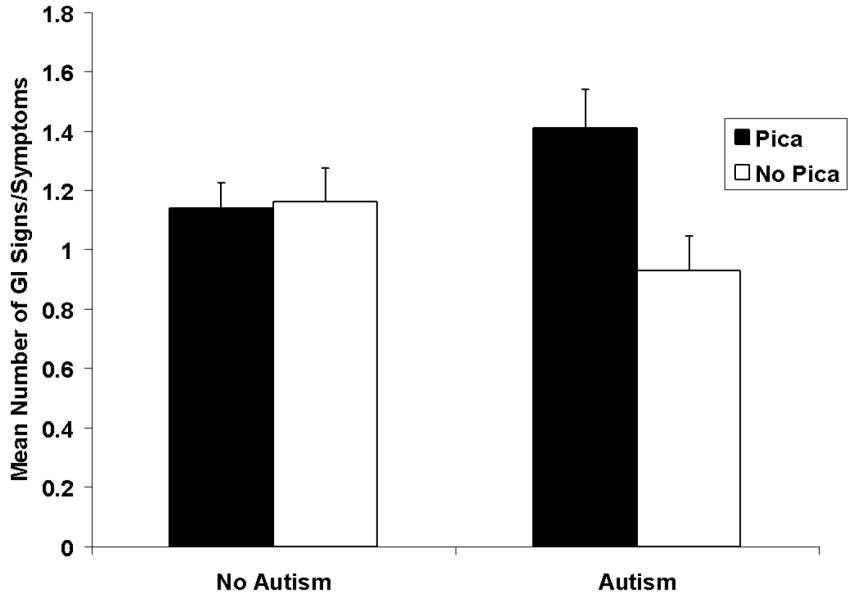

Fig. 2. Mean log (base e) transformed number of gastrointestinal (GI) signs/symptoms by pica and autism conditions with standard error

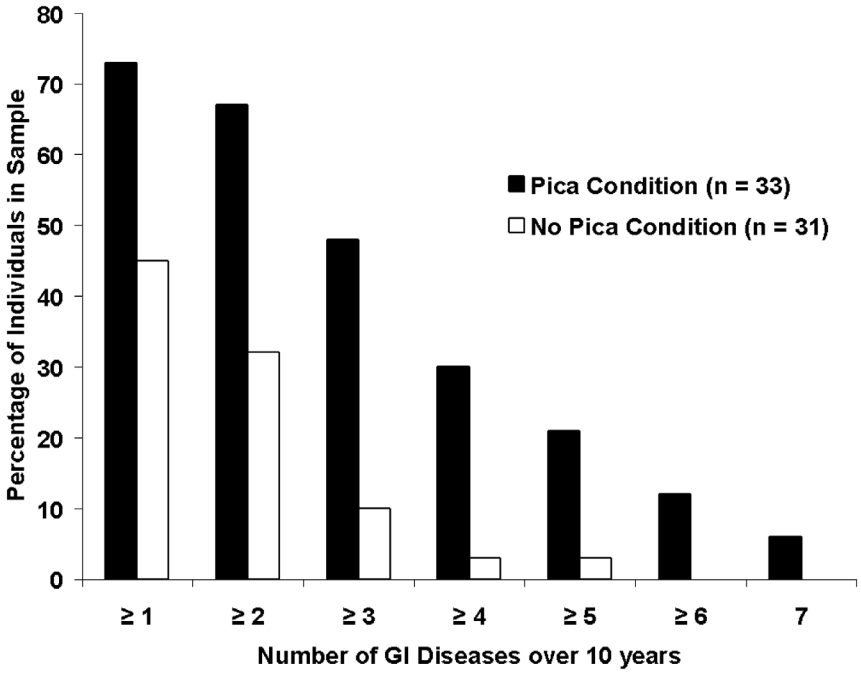

Fig. 3. Prevalence of gastrointestinal (GI) diseases by pica condition

Table 3

Percentage of Most Frequently Occurring Gastrointestinal (GI) Diseases by Pica Condition

Disease	Pica (n = 33) %	No Pica (n = 31) %
Gastritis	58	26
Esophagitis	39	13
GERD*	30	23
Duodenitis	27	13
Colitis	15	6
Hiatal Hernia	15	6
Ulcer	15	3
Helicobacter Pylori	15	0
Aerophagia	12	0
Intestinal Blockage	9	3

* gastroesophagitis reflux disease

Table 4

Percentage of Most Frequently Occurring Gastrointestinal (GI) Signs and Symptoms by Pica Condition

Signs and Symptoms	Pica (n = 33) %	No Pica (n = 31) %
Constipation	97	81
Vomiting	39	35
Weight Loss	21	23
GI Tract Bleeding	21	19

However, the significant interaction between Pica and Autism conditions suggests that adults with both Pica and Autism have an especially high rate of GI symptoms, including signs/symptoms such as alternating diarrhea/constipation, night awakening, abdominal cramps, and chronic/seasonal diarrhea (*see Figure 2*). A post hoc *t*-test (LSD) showed that the average number of symptoms for the Autism/Pica group (1.41) was significantly greater than the average for the Autism only group (0.93), t (30) = 3.02, p = .004.

Discussion

GI disease showed a significant overall effect associated with pica, but not with autism. Those persons diagnosed with pica had 2.8 times as many GI diseases, and 4.8 times as many were severely affected. Persons with pica had 2.6 GI diseases on average compared to 0.9 for those without pica. As shown in *Table 3*, adults with pica showed higher prevalence of each of the 10 most frequently recorded GI diseases.

In their conclusions Valicenti-McDermott et al. [44, p. S135] stated: "Gastrointestinal symptoms seem to be a common comorbidity of autism. Specific GI symptoms may help identify a phenotypic subgroup within the heterogeneous group of individuals who meet behaviorally defined criteria for autism". Of note, Valicenti-McDermott et al. found that the settings in which individuals were recruited were not biased toward GI symptoms, thus supporting generalizability of the findings. However, their study did not address pica. The significant interaction observed in the current study between autism and pica on GI signs and symptoms suggests that it is important to distinguish Autism and Autism/Pica diagnostic groups. On the types of indicators used by Valicenti-McDermott et al. the autism/pica group in the current study had higher rates of GI dysfunction than the autism-only group; that is, GERD (35% vs. 7%), vomiting (41% vs. 27%), abdominal pain (29% vs. 0%), constipation (94% vs. 80%), and alternating diarrhea/constipation (29% vs. 7%). The data strongly suggest that the high rate of GI symptoms observed among people with autism can be accounted for by pica.

Ousley and Cermak noted that the "study of gastrointestinal disorders [...] has begun to provide insights into the pathophysiology of well-defined ASD medical/genetic subgroups" [33, p. 23]. Indeed, our study suggests that individuals with both autism and pica may be a phenotypic subgroup. In their comprehensive consensus report, Buie et al. noted "Given the heterogeneity of persons with ASDs and the many inconsistent research findings regarding ASDs, it is imperative that the phenotype (biological, clinical, and behavioral features) of future study subjects be well defined [5, p. s13]. Coury et al. included "behavior phenotypes related to poor nutritional status" [8]. They pointed to the establishment of clinical algorithms for categorization and effective treatment.

From a behavior-analytic viewpoint that tentatively but promisingly reaches across to new research on the autistic gut and microbiome, we suggest conceptualizing pica here primarily as part of a chain of events: (1) persistent exploratory mouthing of environments associated with or governed by sensory reinforcement, sensory sensitivity [38; 41], sensory hyper-responsivity, sensory craving, and sensory processing disorder [13; 14], (2) the ingestion of harmful bacteria, the metabolites of which may affect the body and brain [22; 23; 26; 46], (3) maldigestion and malabsorption or faulty metabolism [19; 35], (4) nutritional deficiencies [38] and micronutrient deficiencies [30], (5) pica disorder, (6) GI symptomatology and inflammation (worsening over time), and (7) GI disease**.** A more comprehensive model would no doubt incorporate feedback loops, e.g., pica behavior impacting digestion and absorption. We suggest that nutritional deficiencies and imbalance be conceptualized as an "establishing operation," *ibid* for pica, and that individuals exhibiting pica may benefit from nutritional and gastrointestinal evaluation.

Pica may be only the "tip of the iceberg" because this behavior may serve as a marker for GI symptomatology and disease. The risks associated with these underlying dysfunctions and dysbiosis may be greater than the risks posed by most physical acts of ingestion. In contrast to earlier research on the prevalence of health conditions

associated with pica [9; 10], the current study specifically calls attention to the occurrence and co-occurrence of diseases of chronic inflammation. In this study, the higher means for both GI diseases and GI signs/symptoms for the Autism/Pica group versus the Pica group as shown in Table 2 may suggest that the pathophysiology of autism, while not wholly understood, further contributes interactively to disease processes. Adults with pica (with and without autism), but not autism-only, compare with the seriously affected children in the recent autism literature. In view of this literature a replication of the current study that focuses on children with pica-only, autism-only, and autism/pica is indicated. Other research designs should consider including these groups for comparison purposes, along with individuals with autism with and without GI disorders.

Both the pica and autism literatures have advanced promising specific and broad spectrum nutritional interventions to modify biochemical imbalances and patterns of aberrant behavior. Investigators were able to reduce pica through supplementation with iron [17], a liquid multivitamin, Polyvisol [34], and also with Standard Vivonex, a product containing all essential nutrients in a readily absorbable form [4]. In the autism literature, clinical improvement is reported using antioxidant therapy (Vitamin C, E, B-6, magnesium, and manganese if warranted) and zinc supplementation (as Zn picolinate] [39], and using folinic acid, betaine, and methyl B-12 to address issues of increased oxidative stress and impaired methylation [21]. These findings are particularly important in view of Coury et al.'s [8] conclusion for 12 studies of nutritional quality for children on the autism spectrum: "Collectively to date, these indicate a trend for clinically significant suboptimal nutrient intake in children with ASDs ..."

More recently, Ristori et al. [38] investigated autism, GI symptoms, and modulation of gut microbiota by nutritional interventions. Their emphasis on pronounced sensitivities to the smell, taste, texture, visual appearance of food, and food selectivity *may* correlate with specific *cravings* associated with pica [41; 43]. For example, do pronounced food sensitivities/selectivities such as texture preferences (e.g., hard candies, hard objects; chewy foods, plastics, foam materials, or rubber) predict pica preferences? Earlier literature raises the possibility that pica may represent an early, if not the earliest, pattern of addiction [27]. Recent literature on pica and substance abuse addresses possible linkage [20]. The physiological description of addiction provided by Ratey and Hagerman [37, p. 172], may be explanatory here: "... the basal ganglia goes on autopilot when you see/hear/smell/feel the stimuli, and the prefrontal cortex cannot override your actions even though you may know better...". Stated differently, pica may be a "failure to inhibit 'abnormal' stimulation rather than a choice to obtain particular stimuli" [31, p. 143]. If this is the case, we are clearly pointing to early identification efforts to reduce the effect on developmental trajectory [2].

Finally, a promising new intervention based on microbiota transfer to alter the gut ecosystem may be directed not only to children with ASD, but also to those with pica. "Bacterial and phagedeep sequencing analyses revealed successful partial engraftment of donor microbiota and beneficial changes in the gut environment" [23, p. 1] (see also [22]). In the current study H. Pylori bacterial infection and ulcer each occurred in 15% of the combined Pica group versus 0% and 3% of the combined No Pica group. Gastritis was identified through chart review in 58% of the Pica group versus 26% of the No Pica group, i.e., more than twice as frequent. Microbiota Transfer Therapy may then be an option for dysbiotic gut ecosystems associated with pica.

Conclusions

Although this study was limited to chart reviews, it raises both research and treatment issues regarding pica and autism. The gap in comorbidity prevalence between 23.2% for children and 60% for adults should be addressed by cross-sectional and longitudinal study [15; 24; 32]. Although reported prevalence of GI disorder in children with ASDs ranges from 9% to 70% or higher, potential problems with pica are not routinely considered in ASD evaluations [8]. Adult and child survey analyses are needed to accurately determine the prevalence of autism, pica, and autism/pica within specific populations.

An online toolkit for professionals described a multifaceted approach to diagnosing, treating, and preventing pica [29]. Based on the findings in this study and the current research literature, we suggest including additional neurometabolic measures, such as copper/zinc ratios, trace minerals, essential fatty acids, GABA, dopamine-beta hydroxyylase, serotonin, epinephrine, and norepinephrine. The critical "gut-behavior axis" involves neural, hormonal, immune, and metabolic pathways [3; 42]. A personalized metabolic therapy approach to intestinal microbiota may have import [36]. Also, we suggest a behavior-analytic framework for considering the development of pica within a multidimensional chain of events with feedback loops. Furthermore, the development of any comprehensive treatment strategy should include a review of medical history as one component and behavioral history as another [8].

In consonance with Buie's GI Consensus Statement [5], the present authors recommend gastroenterology referral for new diagnoses of autism, pica, or comorbidity. Diagnostically, pica may alert to undiagnosed GI symptoms or disease, or vice versa, or they may present co-morbidly. Thus, pica can be viewed as a behavioral indicator important in identification of risk factors for GI problems. Trace mineral evaluation can also be included in medical screening. If the results are out of range or out of balance, nutritional intervention is essential as part of a complete treatment strategy. Such intervention may augment, if not replace, more rapidly introduced behav-

ioral intervention, while not subject to some of the same concerns, such as staff training, costs, and availability, treatment averseness, environmental restrictions, and issues related to generalization and maintenance [45]. Carbone [7] and Buie et al. [6] have also stressed the importance of a focus on both medical and behavioral assessment and treatment.

Pica is a critical problem sorely underrepresented in research, especially given the risks it poses, and that biological approaches make up but a very small percentage of all pica studies to date. Important next steps may include a comparison of biomarkers for oxidative stress and methylation capacity [21] across the four groups in this study, and similarly obtaining comparative data on microbiome indices [23]. Future research should also focus on laboratory analysis of trace minerals, EFAs, and metabolic indicators, Cu/Zn ratio, and essential fatty acids. GABA, dopamine-beta hydroxylase, epinephrine, and norepinepherine are also variables of interest. Deficits can then be targeted specifically or globally through supplementation or, if indicated, through Microbiota Transfer Therapy [22] to normalize body chemistries, and behavioral interventions can be used to reduce or eliminate health-threatening behavior.

Appendix A

Clinical Signs and Symptoms of Dysfunction and Diseases of the Gastrointestinal (GI) Tract

Please check those that apply to this client

Signs and Symptoms	Diseases
( ) Abdominal pain or cramps	( ) GERD (gastroesophagitis reflux disease)
( ) Abnormal posturing (that puts pressure on the abdomen)	( ) Gastritis
( ) Night-awakening	( ) Esophagitis
( ) Rumination	( ) Duodenitis
( ) Vomiting	( ) Colitis or Enterocolitis
( ) 3 or more large BMs per day	( ) Visceral hyperplasia or Ileocolonic lymphonodular hyperplasia
( ) Excessive belching	
( ) Excessive gassiness or bloating	( ) Leaky Gut Syndrome / increased intestinal permeability
( ) Abnormal stools (malodorous or poorly formed or shiny or black or containing mucous)	( ) Ulcers
( ) GI Tract bleeding	( ) Crohn's disease
( ) Poor appetite or lack of interest in eating	( ) Kidney infections or kidney stones
( ) Difficulty gaining weight / history of weight loss	( ) Intestinal polyps
( ) Constipation	( ) Irritable Bowel Syndrome
( ) Chronic or seasonal diarrhea	( ) Diverticulitis
( ) Alternating diarrhea and constipation	( ) Gall bladder disease
( ) Malodorous stool	( ) Celiac disease (coeliac)
( ) Impaired digestion/maldigestion	( ) H. Pylori (Helicobacter Pylori)
( ) Inflammation of GI tract	( ) Hiatal Hernia
Altered bowel flora microbial growth	( ) Intestinal blockage
( ) fungal overgrowth / hypersensitivity	( ) Aerophagia
( ) bacteria	
( ) parasites	
( ) viral	
( ) Malabsorption	
( ) Food allergies / sensitivities	

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Information about the authors

Dean D. Alexander, PhD in Psychology, Principal Investigator, Quality Assurance Study, Lanterman Developmental Center, Pomona, California, USA (retired), ORCID: https://orcid.org/0000-0003-3562-9573, e-mail: deanalexanderphd@gmail.com

Stanley E. Lunde, PhD in Psychology, Director of Research, Lanterman Developmental Center, Pomona, California, USA (retired), ORCID: https://orcid.org/0000-0002-5836-4486, e-mail: stanlunde@gmail.com

Dale E. Berger, PhD in Psychology, Professor of Psychology, Claremont Graduate University, Claremont, California, USA (retired), ORCID: https://orcid.org/0000-0002-5595-9492, e-mail: dale.berger@cgu.edu

Информация об авторах

Дин Д. Александр, PhD in Psychology, главный исследователь, отдел по оценке качества исследований, Центр развития Лантерман, Помона, Калифорния, США (на пенсии), ORCID: https://orcid.org/0000-0003-3562-9573, e-mail: deanalexanderphd@gmail.com

Стэнли Э. Лунде, PhD in Psychology, Директор по исследованиям, Центр развития Лантерман, Помона, Калифорния, США (на пенсии), ORCID: https://orcid.org/0000-0002-5836-4486, e-mail: stanlunde@gmail.com

Дейл Э. Бергер, PhD in Psychology, профессор психологии, Университет постдипломного образования Клермонта, Клермонт, Калифорния, США (на пенсии), ORCID: https://orcid.org/0000-0002-5595-9492, e-mail: dale.berger@cgu.edu

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