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Pica and Autism/Pica in Developmental Disability – Ports of Entry

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ABSTRACT

Introduction: *GI symptoms and disease in neurodivergent individuals who engage in pica are consistently higher than in comparable groups who do not ingest non-food substances. Such statistics serve as a red flag, not only for immediate medical consideration, but also as a baseline against which the impact of long-term interventions for pica and correlated GI issues can be measured. Organic treatment approaches offer effective alternatives to common behavior modification approaches.*

Objective: *Literature draws a sensory-based through line from a hypothesized etiology to the motivation and subsequent treatment of this often life-long aberrant behavior. This paper integrates disciplines to identify key components and research directions for pica and autism/pica.*

Method: *Large field studies, parent reports, and a smaller study based on chart review serve to document prevalence of GI symptoms and disease for individuals with autism with and without comorbid pica, and similarly for individuals with developmental disability, but not autism, with and without comorbid pica. Strengths and limitations of environmental (behavioral) and organic (nutritional, homeopathic) approaches to mitigating pica and identifying research are delineated.*

Results: *Two reports, each with more than 2,000 clients with autism and with and without pica, indicate that GI symptoms are between one and three times higher in those with comorbid pica. In a chart review study of 64 adults ages 24-58 at a developmental center, the disparity between autism groups with and without pica was even greater for a range of gastrointestinal (GI) symptoms, and alarmingly so, for all ten of the most frequently occurring GI diseases.*

Conclusion: *While behavior intervention based on reinforcement principles has been touted as first line treatment, it has significant limitations. Functional analysis of behavior most often points to sensory variables maintaining pica, a finding compatible with organic explanations. A sensory hypothesis is supported by medication efficacy consistent with an addiction model. Thus, an internal (organic) rather than an external (behavior modification) approach is more likely to be successful (durable across settings) in long-term treatment. That said, there is also opportunity for tiered or combined approaches to protect and ensure both the immediate and future health of persons with pica disorder.*

Key words: autism, dopamine; microbiome; neurodivergent; pica.

Introduction

Pica, the ingestion of non-food substances, can have health implications that range from benign (eating blue crayons) to fatal (choking to death on clothing tags from T-shirts). Other items ingested by clients from the first and third authors' state developmental center (now closed) included beads, buttons, rubber gloves, socks, strings, cigarette butts, paper, plastic items, pop tops, trash, small rocks, bark, dirt/soil, feces, plants and grass, leaves, mushrooms, twigs, and indiscriminate small items (Alexander et al., 2020). Still other reports include sharp objects such as nails, pins, and broken glass as well as poisonous substances such as paint chips and swimming pool chlorine tablets (Trajkovski, 2018), clay, ice, sand, hair, chalk, rubber bands, wool, talcum powder, gum (Christiansen, 2022), and starch/cornstarch (Schnitzler, 2022).

Risks and Benefits

Pica has long been linked to gastritis/helicobacter pylori (H pylori) (Sayar et al., 1975), colitis (DiCagno et al., 1974), and celiac disease (Korman, 1990). 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 (Ausman et al., 1974; Danford & Huber, 1982; Greenberg et al., 1958). With respect to those who are intellectually challenged, Matson et al. (2011) described pica as the most dangerous type of self-injurious behavior, as well as the least researched of all types of aberrant behavior.

Autism and Pica Comorbidity

Pica is often comorbid with autism and autistic spectrum disorders (ASD) – a group of complex and heterogeneous developmental conditions. The Centers for Disease Control and Prevention (CDC) estimates that 1 in 44 children are affected with autism; and 23.2% - almost a quarter – of these children exhibit pica behavior (Fields et al., 2019). These percentages stand in contrast to 4.5% prevalence of pica in children with developmental disabilities other than ASD (DD), and 3.6% for neurotypical development (ND) control subjects.

Fields' Data Sets

A CDC follow-up study (Fields et al., 2020) provides comparison data on GI symptomatology for affected populations aged 2 to 5 years. (See Table 1, condensed from Fields et al., 2020.) In both neurodivergent groups (ASD and DD) the prevalence of all five GI symptoms patterns was higher for the children with pica, while not so for children in the ND control group.

Table 1

Symptoms	Autistic Spectrum Disorders (ASD)		Developmental Disability (DD)		Neurotypical Development (ND)	
	Pica	No Pica	Pica	No Pica	Pica	No Pica
	N = 282	N = 962	N = 132	N = 1461	N = 50	N = 1437
Vomiting	7.8%	3.8%	11.4%	2.9%	8.0%	1.6%
Diarrhea	17.4%	11.9%	15.2%	5.5%	12.0%	3.3%
Loose stools	22.0%	16.2%	22.7%	7.7%	10.0%	5.1%
Constipation	30.1%	28.5%	27.3%	18.8%	10.0%	11.8%
Pain on stooling	18.8%	16.2%	19.7%	11.1%	6.0%	6.5%

Note: Data condensed from Fields et al. (2020)

Figure 1 provides information on pica prevalence for subgroups of persons with and without autism (ASD), intellectual disability (ID), developmental disability (DD), and a general population control group (POP). Some key subgroup comparisons follow.

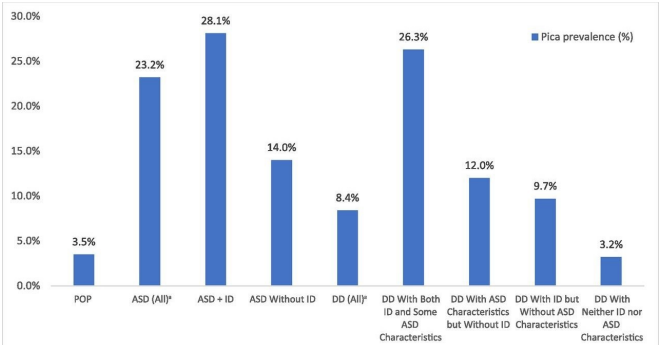
1. Prevalence of pica for those with ASD + ID (28.1%) is twice that for those with ASD without ID (14.0%). The difference in pica prevalence is greater when DD groups with both ID and some ASD characteristics (26.3%) are compared to DD groups with neither ID nor ASD characteristics (3.2%).
2. Clearly persons with ID or ASD have greater pica prevalence, and prevalence is greatest when these characteristics are combined.
3. ASD ALL (23.2%) exceeds DD ALL (8.4%); ASD + ID (28.1%) exceeds DD + ID (9.7%); ASD without ID (14%) exceeds DD without ID (3.2%).

Pica prevalences for ASD groups are consistently higher (nearly three to four times higher) than for corresponding DD groups. These data suggest that *autism per se may perpetuate pica* to a greater extent than developmental disability alone. This also stands in contrast to an earlier hypothesis (Alexander et al., 2022) that *pica potentiates autism, even though the possibility of reciprocal potentiation is subject to further study.*

Fields and her colleagues (2021) pushed the use of subgroups for pica even further than Alexander (2020) and afford increasingly sophisticated comparisons. While each subgroup comparison can be useful in research designs, four key groups emerge: ASD + ID, ASD without ID, DD + ID but without ASD characteristics, and POP. These subgroups heretofore referred to as a "core group," build a foundation for how components can contribute to an understanding of pathophysiology and clinical efficacy.

Figure 1

Pica prevalence in asterisk SEED (Study to Explore Early Development) study groups and subgroups (Fields et al., 2021)



Study to Explore Early Development

The Autism Research Institute Data Set

A large data set (N = 2291) provided by Dr. Stephen M. Edelson (2020) at the Autism Research Institute in San Diego, California included parent surveys (E2) of GI symptoms for ASD clients ages 3 to 62. As shown in Table 2, clients with pica (ASD-P) showed higher incidence of all six GI symptoms than clients without pica (ASD).

Table 2

GI Symptoms for ASD Clients Ages 3-62
With and Without Pica Symptoms

	ASD-P N = 1011	ASD N = 1280
GERD	24%	15%
IBS	12%	7%
Abdominal pain	41%	30%
Diarrhea	39%	27%
Loose stools	37%	25%
Smelly stools	44%	29%

Note: Data from Edelson, Autism Research Institute

Alexander Study: Pica vs. No Pica

A bacterial correlations with three GI symptoms and five diseases occurring AT LEAST three fold more in the pica groups would be invaluable (Alexander et al., 2020) compared four groups of adults with developmental disabilities (total N = 64) ages 24-58 on patterns of GI symptomatology and disease. The groups included clients diagnosed with autism only, pica only, autism and pica, and a control group with developmental disability only (i.e., no comorbidities). Data were based on checklists for 24 GI signs and symptoms and 15 diseases found in medical records over a ten-year period. Chart reviews were compiled by two UCLA predoctoral interns blind to the purpose of the study. Inter-rater reliability was 94%, indicating strong agreement between the raters.

Comparing the autism-pica group to the autism-only group, we found higher symptomatology on measures of GI distress: GERD (35% vs. 7%); abdominal pain (29% vs. 0%); constipation (94% vs. 80%); vomiting (41% vs. 27%); and alternating diarrhea/constipation (29% vs. 7%). The results for number of diseases were especially striking: clients with autism and pica (ASD-P) averaged 2.88 diseases; clients with developmental disability and pica (DD-P) averaged 2.25 diseases; and clients with only autism, 0.53 diseases; and clients with only developmental disability, 1.31 diseases. When data were combined for the two groups with pica disorder (ASD-P and DD-P, N = 33) vs. no pica disorder (autism only and developmental disability only, N=31), the percentages for all ten of the most frequently occurring GI diseases were higher for clients with pica disorder (see Table 3).

Table 3

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
H Pylori	15	0
Aerophagia	12	0
Intestinal Blockage	9	3

GI Diseases for Adults with Intellectual Disabili-

ties, Ages 24-58, With and Without Pica

Note: Data adapted from Alexander et al., 2020.

These data indicate that non-food ingestion takes a heavy toll on health over time and are consistent with reports of higher mortality rates (Bell & Stein, 1992). Pica may largely explain the link between autism and gastrointestinal problems (Alexander, 2019). The substantial disparity here between the two autism groups (with and without pica) suggest that individuals with ASD-P disorder may be a phenotypic subgroup on the autism spectrum characterized by GI disorder, requiring a clinical algorithm for categorization and effective treatment (see Alexander et al., 2020).

Longitudinal study can help to determine over time which method or methods can most effectively reduce pica and associated GI symptomatology across affected children and adults. Data on 10,109 caregivers of children with pica were analyzed from the Avon Longitudinal Study of Parents and Children (ALSPAC). Prevalences of pica were obtained across subgroups including the overall group divided between male and female, and the presence or absence of both autism and developmental disability. Pica prevalence was assessed in "waves" designated at 36 months, 54 months, 65 months, 77 months, and 115 months. Prevalence information from Papini et al., 2024 are shown in Table 4 in a condensed format.

Papini et al., 2024

Table 4

	36 months	**54 months**	**65 months**	**77 months**	**115 months**
Overall prevalence	(2.29%)	(0.78%)	(0.62%)	(0.55%)	(0.33%)
Male	(2.33%)	(0.77%)	(0.64%)	(0.58%)	(0.49%)
Female	(2.24%)	(0.81%)	(0.59%)	(0.52%)	(0.16%)
Autism present	(12.5%)	(11.11%)	(10.17%)	(13.6%)	(10.71%)
Autism not present	(2.22%)	(0.70%)	(0.55%)	(0.46%)	(0.25%)
DD present	(3.53%)	(1.81%)	(1.16%)	(1.60%)	(0.98%)
DD not present	(2.08%)	(0.55%)	(0.41%)	(0.38%)	(0.21%)

Pica prevalence across five data collection waves.

Note: Data condensed from Papini et al., 2024.

Compared to other groups, there is proportionately more continuity, i.e. less variability in prevalence changes for the autism group over ages 3 to about 9 ½ (9.58). Prevalence decreases substantially more in the overall group (2.29% to 0.33%) and the DD group (3.53% to 0.98%) than in the autism group (12.5% to 10.71%). In fact, there is a high value of 13.6% for the autism group at 77 months. Why? Furthermore, the marked disparity between these elevated statistics and the even higher (23.2%) prevalence for young autistic children (24-60 months) in Fields et al. 2021 deserves scrutiny beyond the scope of this paper.

At these end points, the overall group ratio decreases 6.9 times, the DD ratio decreases 3.6 times, while the autism ratio decreases only 1.2 times. Even more striking are progressive comparisons of prevalence ratios between groups: autism to overall at 36 months: 5.5 times; autism to overall at 115 months: 32.5 times; autism to DD at 36 months: 3.5 times; and autism to DD at 115 months: 10.9 times. Thus by age 9 ½ the odds of a child with autism demonstrating pica behavior are much greater than for the general population of children or those with developmental disability only. Though pica prevalence is very similar for males (2.33%) and females (2.24%) at 36 months of age, prevalence is greater for males (0.49% vs. 0.16%) at 115 months. This 3:1 ratio somewhat parallels the 4:1 ratio of males to females with ASD.

These data, like Fields et al., 2021, suggest then that autism potentiates pica in some unspecified manner and not the other way around. Moreover, these data also make a strong argument for adding age or age ranges as an additional subgroup to core group considerations. Both the Alexander 2020 study (age range 24-58 years) and the ARI/Edelson 2020 data (3-62 years) might have looked at age or age ranges vis-a-vis pica symptomatology and disease, but neither did. Opportunity lost.

Etiology and Addiction

Consideration of pica as an addiction disorder (Hull, 2020) best starts with speculation on etiology. Sayetta (1986) provides an overview of theories of etiology, including nutritional, sensory and physiologic, and psychosocial. Nutritional theories posit that persons seek out/crave non-food items in an attempt to rectify deficiencies in specific minerals such as iron or zinc. Sensory and physiologic theories suggest that pica is attributed to the taste, texture, or smell of the non-food items. Psychosocial theories link pica to stressors in the family or outside environment and lowered social support (see also Papini et al., 2024). Freud would conceptualize pica as behavior that arises out of the exploratory stage of development observed in all children, but persists beyond toddler age (Schnitzler, 2022).

Alexander et al. (2020) proposed a seven-step model for the etiology of pica based on sensory/physiologic, and nutritional considerations:

1) Persistent exploratory mouthing of environments associated with or governed by sensory reinforcement, sensory sensitivity (Ristori et al., 2019; Spek et al., 2020), sensory hyperresponsivity, sensory craving, and sensory-processing disorder (Edelson, 2019; Edelson & Johnson, 2016).
2) The ingestion of harmful bacteria, the metabolites of which may affect the body and brain (Kang et al., 2019; Kang et al., 2017; Krajmalnik-Brown et al., 2015; Xu et al., 2019).
3) Maldigestion and malabsorption or faulty metabolism (Horvath et al., 1999; Pangborn & Baker, 2005).
4) Nutritional deficiencies (Pangborn & Baker, 2005) and micronutrient deficiencies (Miao et al., 2014).
5) Pica disorder.
6) GI symptomatology and inflammation (worsening over time).
7) GI disease.

Establishing Operations for Pica

This model raises questions around developmental age and stage, sensory craving and processing disorder, and microbiome and dietary interventions.

The American Psychiatric Association (2013) regards pica as the eating of non-nutritive, non-food substances inappropriate to the developmental age of the individual. Mouthing and eating of non-food objects is observed in almost all children up to 4 years of age but is considered "normal" rather than deviant. Of note is that most individuals with developmental disability who demonstrate pica have a developmental age between 1 and 3 years throughout adulthood; hence, these early behaviors may be more likely to be maintained. (This observation may shed light on the stable prevalences across more than six years' duration reported in the Papini et al. 2024 study.)

Parent data from the Autism Research Institute reflect that 57% of the total ASD-P group demonstrated craving for certain foods (Edelson, 2020). If left untreated, children with autism and early pica behavior and food cravings may be more likely to maintain pica throughout life. Ristori et al. (2019) suggested a possible correlation between the specific cravings associated with pica and pronounced sensitivities to the smell, taste, texture, visual appearance of food, and food selectivity. We cannot use preferences or cravings demonstrated by persons developing typically as guidelines. Those who consume raw starch likely find the texture of chunks of laundry starch as appealing as geophagists find clay (Schnitzler, 2022). Question: If texture dimensions are altered per microwave to preserve nutrient content (Sharma & Sharma, 2022), are there changes in client responsivity?

In behavioral terms, these describe possible establishing operations. The physiological description of *addiction* provided by Ratey et al. (2008, 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" (Miller & Misher, 2016, p 143).

Maintenance of Pica

In our 7-step model, sensory reinforcement maintains the persistent mouthing of environments, which leads to an ensuing cascade of events culminating not only in pica, but in symptomatology and inflammation (worsening over time) and GI disease. Maintenance of pica behavior may be tied to the "Dopamine Motive System," which Schnitzler (2022) considers to be the "neurobiological basis of addictive behaviors." Quite possibly the processes called out in Steps 1-4 of our model lead to "aberrations in the system which result in depletion of dopamine." (This in turn) "leads to deregulations that manifest as compulsive, repetitive behaviors such as addictions and possibly the stereotypies typical of ASD. It would seem that the characteristics of pica resemble those of addictions as evidenced by the obligate-driven goal-directed motivation to ingest inedible substances. This suggests that the behavior is rewarding to the individual albeit in an atypical aberrant way" (Schnitzler, 2022, p 535).

Pica, Dopamine and Beyond

There is research to support the hypothesis that pica may increase depleted dopamine levels in a manner consistent with the effects of eating, and even with using drugs of abuse (see Salgado & Kaplitt, 2015). Schnitzler (2022) recommended fMRI studies for individuals with pica with a focus on corticostriatal and limbic connectivity. But look first to the online report of Singh et al. (2009) for

their 1994 article "Does Diminished Dopaminergic Neurotransmission Increase Pica?" Compared to placebo, when subjects were taking Methylphenidate, a dopamine agonist, lowest levels of pica were observed. However, all subjects given Thioridazine, a dopamine antagonist, engaged in higher levels of pica compared to baseline. These findings suggest that some people may use pica to compensate for dopamine depletion. If so, the rewarding role of pica could be decreased by replenishing dopamine in the system through diet and/or supplementation.

Commenting on neurochemical and physiological explanations of pica, Schnitzler (2022) surmised that dopamine transmission may be disrupted in pica disorder: "The association between iron deficiency anemia (IDA) and pica lends further credence to this hypothesis since IDA has been associated with decreases in D2 receptors in the Nucleus Accumbens" (p. 535).

Iron, IDA, and Other Iron Indicators

Iron is an essential element for human life involved in oxygen transport, immunity, cell division and differentiation, and energy metabolism (Piskin, et al., 2022). Studies from the mid-20th century rested upon the nutritional hypothesis that a mineral deficiency – in this case iron – led to craving non-foods to try to correct deficiency not addressed by diet. Plasma iron was significantly low in the Danford and Huber (1982) study of persons with developmental disability. In a comparable population, Swift et al. (1999) reported that adults with low serum iron had 5.43 times the odds of having pica. More recently, Johnson et al. (2010) reported low ferritin in children with ASD and associated pica.

Other reviews focus on the relationship of IDA and pica in non-disabled populations (Miao et al., 2015); or IDA in autism without specific reference to pica (Baj et al., 2021; Herguner et al., 2011). Results from the Miao meta-analysis (N = 43 studies) revealed that for 6,407 participants with pica behaviors and 10,277 controls, pica was associated with 2.4 times greater odds of anemia, lower hemoglobin, and lower hematocrit concentration. Herguner et al. indicated that 24.1% of children with ASD had IDA, and 15.5% had anemia. Baj et al., among others, suggested that the coexistence of ASD and iron deficiency is significantly higher in children with ASD than in children without these disorders. The authors pointed out that observed decreases in iron concentration in the ASD brain may lead to alterations in dopaminergic and serotonergic systems and therefore impaired cognitive development and functionality. Implicated are frequently observed low levels of serum ferratin, a protein associated with iron storage in the liver. De Giacomo et al. (2023) reported significantly lower levels of serum ferratin (but not transferrin, hemoglobin, or hematocrit) for 93 children with ASD compared to 74 typically developing children. Noteworthy at this point is the high prevalence of pica in children with ASD (23% or greater in Fields et al., 2019) in conjunction with the astonishing continuity in prevalence from 3 years of age to almost 10 (Papini, 2023).

Yet iron supplementation to correct deficiency is only a starting point in any consideration of the pathophysiology or treatment of pica, much less autism and pica. Notable change may result from supplementation of a different essential element (Lofts et al., 1993), or from a treatment package of nutrients that does not contain iron (Adams et al., 2018). Baj et al. (2021) reviewed other possible "agents missing in action" – zinc, copper, chromi-

um, magnesium, calcium, manganese, cobalt, selenium – and possible toxic "culprits" – mercury, arsenic, cadmium, aluminum, lead (see also Adams et al., 2018, and Hessabi et al., 2019). The former can be considered for supplementation; the latter controlled by removal from the environment or chelation. In some instances, mineral panels for pica revealed no trace elements outside of normal range, or only slightly (Alexander, 2002, unpublished results) for six adults with longstanding pica behavior at the Lanterman Developmental Center, Pomona, California (results limited by no evaluation of possible toxic burden). In fact, iron-deficient African children receiving iron-fortified wheat flour had unfavorable results reflected in higher ratios of harmful (fecal enterobacteria) to helpful (bifidobacteria and lactobacilli) bacteria at baseline (Zimmerman et al., 2010). In this regard, the focus on iron indicators and IDA here remains somewhat unresolved and is exemplary rather than conclusive.

Our Unique Microbiomes

The unique microbiome of each person undoubtedly enters into any equation of success or failure as well. Why does pica become established for some but not for others? Forty-three percent of the ASD-P children in the ARI data set *did not* crave certain foods (Edelson, 2020). Each individual develops uniquely, living in one's own physical environment, experiencing one's own psychological environment, and eating one's particular diet. Each person creates a unique microbiome, the collection of all microbes such as bacteria, fungi, viruses and their genes, based upon developmental history. "Some microbes alter environmental substances in ways that make them more toxic, while others act as a buffer and make environmental substances less harmful" (National Institute of Environmental Health Sciences, 2024). This may explain the bifurcation between an unhealthy and a benign trajectory for exploratory pica in typical development. The estimated 100 trillion gut microorganisms are far from being well understood (Buford, 2017; Christiansen, 2022; Jeffery et al., 2015; Gill et al., 2006). Yet if success or failure is spread out over so large a range of essential elements, toxins, picas, and unique microbiomes, is there then a core-defining issue underlying pathology and treatment (Al-Beltagi et al., 2023)? That common denominator may be microbiome-mediated gastrointestinal inflammation in dysbiosis (Dorsey & Miller, 2020).

Lighting the Way

Inflammation is pivotal to much theorizing. An evolutionary anthropologic look at geophagia (ingestion of clay and soil) and amylophagia (starch) considers an adaptive role in protecting the body from toxins and pathogens (Dorsey & Miller, 2023). Kaolin or clay can adsorb drugs and toxins from the GI tract, while corn starch has both absorptive and adsorptive properties (Schnitzler, 2022). Almost all picas listed in the introduction clearly do not have such potentially adaptive functions. Paint chips and sharp objects are anything but protective. Yet much of the proposed Dorsey and Miller model is worth consideration:

"We propose… that gastrointestinal inflammation causes both pica and IDA mediated by the microbiome (p. 21) and geophagy and IDA are caused by inflammation, but neither causes the other (p. 23). … In testing our hypothesis that the microbiome is the key to understanding both IDA and geophagy, we would expect to see a reduction in inflammatory markers like circulating hepcidin and fecal calprotectin, improvement of intestinal barrier function, and lower levels of translocation of bacteria

and endotoxins after [pica] cravings and behaviors subside. Similarly, when other antibiotics, probiotics, or other interventions that reduce inflammation in the gut are provided, we expect an association with reduced pica (pp. 23-24)."

Importantly, how do these inflammation markers change for different picas serving (theoretically) adaptive versus maladaptive functions? Should we expect increased inflammation for the latter? Neurochemical assessment – presently lacking (Schnitzler, 2022) – could provide insight here into pathophysiology.

Search and Re-Search into the Gut

Recovery of health may depend in large part upon healing a permeable "leaky gut" – a dysfunctional, dysbiotic, inflamed barrier tasked to produce about 90% of the neurotransmitters that bear directly upon brain function (the gut-brain axis). Fu et al., 2021 concluded that GI disorders can arise from gut dysbiosis, immune dysfunction, food sensitivities, digestive enzyme deficiencies, and sensory processing and integration differences. Yet underlying these various organic states and functions, tied to mineral metabolism, are trillions of gut bacteria, many beneficial, many harmful, all connected through the gut-brain axis. Beneficial bacteria in the gut or microbiome can affect body weight, the body's susceptibility to infection, aid in food digestion, produce vitamins, and protect against harmful bacteria. If left unchecked, harmful bacteria can excrete dangerous metabolites that can affect the gut, the brain, and the rest of the body. Some Clostridia strains, for example, are believed to secrete neurotransmitters/neurotoxins/metabolites which interfere with hosts' central neural pathways (Rosenfeld, 2015) and lead to GI problems and a range of behavioral deficits (Taniya et al., 2022). Examples of beneficial ("healthy") bacteria include Prevotella, Akkermansia, Bacteroides, Bifidobacterium, and Lactobacillus. Examples of harmful bacteria include Faecalibacterium, Escherichia Coli, Ruminococcus, and Clostridium. Fu et al. (2021) noted 18 bacteria significantly correlated with ASD symptoms and 11 bacteria significantly correlated with constipation. Similarly, bacterial correlations with three G.I. symptoms and five diseases occuring AT LEAST three-fold more in the pica groups would be invaluable (see Alexander et al., 2020, page 4.)

A central "port of entry" for pica research could similarly include correlations for healthy and harmful bacteria with different types of pica – ideally across core groups and over time. Olesen and Alm (2016) advocated "the need to show that differences in the microbiota can be used to predict or ameliorate disease (…e.g. pica disorder/GI diseases) and not just show that differences exist" (p. 2). This research could then in turn lay the foundation for testing clinical efficacy of interventions that currently include diet/nutrition, exercise, antibiotics, prebiotics, probiotics, postbiotics, microbial fermentation, and Fecal Transplant Therapies. The goal is to recolonize and rebalance gut microbiota to treat biologically driven patterns of aberrant behavior and associated symptoms and disease, even while issues of cause and effect persist (see Olesen and Alm for similarities and differences in perspective.)

Alexander (2022) reviewed three ASD research methodologies – each with some subgroup comparisons, but which could be reformulated around a unifying hypothesis: we predict greatest disturbance in function, i.e., deviation on biological measures, for clients with pica compared to other

matched subgroups without pica in a core group approach. These three methodologies utilize different sets of dependent measures – salivary (Beversdorf, 2022), metabolic (James et al., 2004), and bacterial (Xu et al., 2019).

Hypothesis 1

Utilizing measures associated with saliva, RNA, transcriptome analyses, adult clients with pica and autism/pica will show a higher percentage of GI symptoms and diseases than pica-free ASD, DD, or TD (typically developing) clients.

Hypothesis 2

Based on plasma concentrations of metabolic biomarkers, adult clients with pica and autism/pica will show greater oxidative stress and impaired methylation capacity than pica-free ASD, DD, or TD clients.

Hypothesis 3

Using measures associated with bacterial taxonomy, percentage, and relative abundance, adult autism/pica clients and clients with only pica will show higher percentages and greater relative abundance of "unhealthy bacteria," and lower percentages and less relative abundance of "healthy bacteria," as well as less diversity in bacteria strains than pica-free ASD, DD, or TD clients.

Additional Compass Directions

Innovative methodologies may follow suit based upon microbiome therapeutics in conjunction with the same type of predictions for the presence of pica. Whereas additive therapy utilizes a cocktail of beneficial microbes (FMT), probiotics to restore the healthy composition of the gut microbiome, subtractive therapy uses bacteriocins and bacteriophages to target pathogens in the gut without causing harm to other microbes in the ecosystem. Modulatory therapy seeks to restore healthy balance in the gut microbiome by changing diet (macro- and micronutrients), exercise, and antibiotics. The goal is the colonization of beneficial microbiota over pathogens (see Yadov and Chauhan, 2021, and Taniya, et al., 2022.) These are all ports of entry for core group research.

Still other intriguing directions for pica research include fMRI and neurochemical studies (Schnitzler, 2022); microbiota transplant therapy "fast-tracked" for autistic children by the FDA in 2019 (Adams et al., 2019); and possibly a series of studies to examine additional prevalence and treatment impact. A 2x2 for constipation/no constipation and pica/no pica could provide data on the role of Turicibacter. Or consider a core group design featuring the impact of FMT or probiotic intervention as measured by change in the relative abundances and percentages of each selected bacterial strain, together with bacterial diversity. Lastly, organic approaches to restore intestinal microecology, notably bacterial diversity, have been effective in treating certain recalcitrant GI diseases. FMT is particularly effective for Clostridium Difficile; while FMT and probiotic VSL #3 have reduced active ulcerative colitis (Dang, et al., 2020). The literature on pica cited in the introduction (e.g., di Cagno et al., 1974 and Sayar et al., 1975) and data in Table 4 (Alexander et al., 2020) reflect an unmistakable linkage between inflammatory ("itis") diseases and prevalence of pica. What impact then could these microbiota -based approaches have on concurrently reducing pica in association with GI diseases leading to dysfunction of gut microbiota, or (sensory-driven) pica in isolation? Such reductions, if observed, would, moreover have bearing upon issues arising from our model for the etiology

of pica, e.g., biotics decreasing "leaky gut" (Fuentes, et al., 2017) and addressing nutritional and micronutrient deficiencies. Pica warrants a place on the growing list of conditions targeted by microbiota applications and precision medicine.

First Efforts: Simplicity First

A rule of thumb familiar to parents and professionals in the helping disciplines is *simplicity first.* Before trying out FMT or additive or subtractive therapies, there are simpler approaches which can be assessed preferably under professional (physician, nutritionist, behavior analyst) supervision. For example, if texture happens to be the most salient dimension for pica, can alternative foods serve as a substitute? Caramels for the ingestion of plastics/rubber? Grape Nuts cereal for sand or certain dirt? Hard candies instead of pebbles/small rocks? Color, contour, taste and smell may require assessment separately or in combination to determine possible treatment benefit beyond any simple trial and error. Two paths back to health will be highlighted: nutrition and behavior.

Bio-nutritional approaches are receiving increasing attention (Adams et al., 2018; Alexander, 2021, 2023; Alexander & Frank, 2023; An et al., 2019; Coman & Vodnar, 2020; Wastyk et al., 2021; Willett, 2023). “What we eat matters, or more accurately, whatever you are eating has eaten, matters” (Wastyk et al., 2021). Intake impacts gut microbiota composition, and our ability to alter it through short-term and long-term dietary changes (Coman & Vodnar, 2020; Wastyk et al., 2021). That is, we can influence our systemic health/brain function by properly or improperly feeding gut microbiota. Assessment for possible nutritional deficiencies, foremost zinc, iron, and other minerals, should be a starting point (Christiansen, 2022). Bio-nutrition would appear to be a straightforward and often effective approach to address sensory-driven – (non-operant) pica.

Coprophagy: Contrasting Two Approaches

Organic Approach

Coprophagy, ingestion of feces, is particularly challenging from health perspectives (diarrhea, intestinal parasites, blood-borne pathogens (Ing et al., 2011), poor oral hygiene along with various oral infections, and from social perspectives (peer rejection). A 1993 study by Bugle and Rubin decreased coprophagy in each of three persons with developmental disability using a Standard Vivonex formulation. Standard Vivonex contains all essential nutrients in a readily absorbable powdered form. This highly successful study employed both multiple baseline and reversal methodologies to demonstrate intervention efficacy.

Behavioral Approach

The first author unsuccessfully employed a discrimination training procedure (unpublished, 1970) to treat long-term coprophagy in a 50-year-old adult male with autism (no expressive speech other than grunting, no social interaction or eye contact; frequent body rocking, profound intellectual disability). Preferred foods including sweets, carbohydrates, and favorite mealtime foods were initially positioned alongside feces. In later trials, the feces sample was also placed at 10-15 feet further away. In every instance, the client sought out the feces obtained that day from other residents. His approach appeared driven or compulsive and was not deterred by prior staff interruption/prevention.

This attempt to mitigate coprophagy was conducted solely as a clinical intervention rather than as a treatment guided by functional analysis (Ing et al.

2011). Both clinical teams suggest automatic (sensory) reinforcement maintaining the aberrant behavior. Both approaches were closely supervised and focused on one individual with autism. Both approaches evaluated NCR (non-contingent reinforcement) procedures based on preferred foods. But here the similarity stops. My intervention was centered around a 50-year-old man with a long history of coprophagy; Ing's subject was a 6-year-old girl, who underwent ten-minute sessions in a non-residential environment. Of greatest contrast, however, is that the Ing staff employed "artificial feces" created to resemble actual feces in color and texture, but *without* the (perhaps critical) olfactory (sensory) component, as the authors appropriately point out. Therefore, the youngster's preference for readily available snack foods (Froot Loops, M&Ms, Mentos, gummy bears) over artificial feces cannot be viewed comparably to a coprophagic penchant for actual feces outlined in the 1970 discrimination procedure. Future trials could be based on response latencies to actual samples before staff intervene protectively.

Dietary Supplements

Other successful treatments of pica have been noted by Pace and Toyer (2000) using a multivitamin (Polyvisol), and by Adams et al. (2018) introducing a gluten-free, casein-free, soy-free diet. In Case "C," Adams et al. postulated that the quick resolution of pica they observed was linked to addressing serious nutritional deficiencies and/or an underlying metabolic problem with Cobalamin. Perhaps resolution may be achieved through the removal of allergens or irritant foods in the usual diet that cause inflammation in the gut lining (Trajkovski, 2018). Alexander and Frank (2023) reported the elimination of pica (bar soap, shampoo) through homeopathic-based remedies for an adolescent male with autism except under high-stress conditions (serious illness and death of a grandparent). A multiple baseline across-subjects design could further test the merit of homeopathy using core subgroups.

Behavior-Based Pica – Etiology and Treatment

Reinforcement/reward *may* play a simple but central role in the etiology and treatment of behavioral pica. A child or adult putting non-foods to or into the mouth draws the immediate attention of caregivers, especially for items that carry risk. The individual may then come to use pica instrumentally as a means of getting attention on demand. Does the behavior occur only when parents or staff are watching, i.e., attention? Or when a client is attempting to escape from or avoid a particular setting? Does the behavior increase when he or she resides in an environment with limited social interaction and alternative activities? Here then is a behavioral path to pica disorder that may follow early development patterns of oral exploration and stimulation, and/or social/sensory deprivation at any age.

Behavior-based Treatments

ABA approaches using primary (food) or secondary reinforcement (social or tangible reward such as toys, money, tokens) may be helpful here. These have been employed in the contexts of non-contingent reinforcement, and several differential reinforcement procedures. Behavioral approaches have included response-effort manipulations, response-blocking/interruption, brief contingent holds, self-protective devices, discrimination training, replacement-behavior training, time-out procedures, overcorrection, water mist and aromatic ammonia, ecological modifications, or some combination of the above procedures (Ausman, et al., 1974;

Bell & Stein, 1992; Call et al., 2015; Hagopian et al., 2011; Matson et al., 2013; McAdam, 2014; Schnitzler, 2022; Williams & McAdam, 2012).

Example of a Simple, Successful Behavior Treatment to Eliminate Cigarette Butt Pica

The first author successfully employed differential reinforcement of incompatible behavior (DRI) to eliminate the health risks associated with cigarette butt pica for a 50-year-old man with ASD-P. Although he was not a smoker, baseline nicotine and cotinine levels obtained through laboratory measurement were consistent with chain smoking. At his residence, the client was observed to carry around a rubber ball continuously, and he also loved soda. Treatment involved cleanup around his dorm; then sending him to his work site one-quarter mile away with his ball in one hand and a can of soda in the other. This walk was a main source of discarded butts. Carrying items in both hands was incompatible with picking up butts. The soda served as a reward both to and from work. Nicotine and cotinine dropped to zero levels over a six-month measurement period (Alexander, 2005).

Limitations of Behavior Treatments

In the majority of instances, behavioral treatment fails or is discouraged due to staff training costs and availability, considerations of treatment averseness, environmental restrictions, and issues around generalization (effectiveness across settings) and maintenance (effectiveness over time) (Call et al., 2015; Hagopian et al., 2012; Williams & McAdam, 2012). A spectrum of behavioral issues surfaced in a recent article titled "Parent Treatment of Complex Pica in a Teen with Autism" (Thomas et al., 2023). There was need to train parents in multiple procedures (competing stimulus, response interruption, redirection, and finally response cost). A second topography of pica arose when the original object-oriented pica led to increases in untargeted body-oriented pica (e.g., ingestion of skin, hair, and nails). The time-consuming training required very close parental proximity, which in turn necessitated fading. Though eventually deemed successful, the endeavor itself was complex and arduous. Fortunately, none of these limitations were applicable in the cigarette butt case study. But more often, what appears successful (and publishable) under tightly controlled experimental conditions does not hold up under more naturalistic conditions or over time. Where success is observed, it is likely to be only a temporary fix – a Band-Aid on a wound (Alexander, 2021). This may not be surprising when we look at the most frequent results obtained in state-of-the-art functional analysis (Williams et al., 2022). The majority of studies describing functional analysis of pica report the consumption of non-foods to be maintained by non-operant *sensory* or "automatic" reinforcement (Christiansen, 2022; Halgopian et al., 2012; Halgopian et al., 2011) or amelioration of nutritional deficits, variables outside of the therapist's control (Call et al., 2015). The deeper "wound" must await healing at the level of the microbiome, i.e., organic recovery, where trip-wire issues for behavioral intervention such as staff availability, intensive training, and generalization do not apply.

Combining Treatment Methods

A final consideration is the tiered use or combined use of methods to protect and ensure the lasting health of persons with pica disorder. Behavioral approaches to pica prevention may be needed immediately to protect and guarantee safety. This

may involve cleanup of the immediate environment, temporary environmental restrictions, enhanced staff training and team collaboration, functional analysis of the pica behavior by a trained psychologist or behavior analyst, and field testing a proposed intervention. These can be readily implemented prior to a bio-nutritional approach, or concurrently with recommendation of medical staff. Given risk, one pica behavior may be one too many. A bio-nutritional approach more often (but not always – Adams et al., 2018; Wastyk et al., 2021) will require a longer evaluation period. Medical staff may review functional analysis findings to determine if patterns of GI symptoms signaled by maladaptive behaviors may first need medical attention and possibly gastroenterologist consultation (Trajkovski, 2018). The health implications of a non-food diet are apparent in cross-sectional looks at children (Edelson, 2020; Fields et al., 2020) and adults (Alexander et al., 2020; Edelson, 2020) with and without pica. Symptomatology is almost always worse when pica is present and may severely worsen over time (Table 3). Longitudinal study can further verify. Early intervention – possibly behavioral and certainly nutritional – is warranted in response to GI red flags.

Revisiting the 7-Step Model for Etiology of Pica

The order of the seven steps in the Alexander et al., 2020 paper depends on the theorizing of different writers. Dorsey and Miller's (2023) proposal that inflammation leads to geophagy and IDA might add microbial dysbiosis to Step 2. That is, the harmful neurotoxins/metabolites from the ingestion of unhealthy bacteria lead to inflammation and resulting microbial dysbiosis. This leads to a next step of maldigestion, malabsorption, faulty metabolism – including dopamine dysregulation, and nutritional deficiencies, and pica together.

On the other hand, Al-Beltagi et al. (2023) seemed to favor placing pica per se at the forefront of the cascade. Pica increases the risk of developing GI issues that include irritation of the digestive system, blockages in the digestive tract, bacterial or parasitic infections, and nutritional imbalances. Diarrhea, having the highest prevalences for all subgroups with pica in the Fields et al. (2020) study, may predictably result. A third possibility, perhaps the best, considers feedback loops in which pica is both a precipitant and a consequence of GI inflammation and dysregulation. Future research is needed to shed light on these long-debated cause and effect relationships.

Conclusion

Pica produces especially high rates of GI distress for those on the autism spectrum, both among children (Edelson, 2020; Fields et al., 2020) and adults (Alexander et al., 2020; Edelson, 2020). Efficacy of some medical treatments tends to support an addiction model of pica. Internal (organic) treatments show promise as an important supplement or even replacement for external (behavior modification) treatments.

This paper takes a further step toward closing the gap between an aberrant pattern of behavior - sometimes lethal - and a paucity of effective LONG-TERM treatment approaches. Pica research remains "a poor cousin" compared to a wealth of research on autism, even while ingestion of non-foods affects approximately a quarter of the individuals on the ASD spectrum. Research methodologies for persons with autism can and should be extended to include pica as a factor of almost certain clinical significance. The expansion of such investigation would undoubtedly allow a deeper

dive into the pathophysiology of pica (Beversdorf et al., 2022; Dang et al., 2020; James et al., 2004; Krajmalnik-Brown et al., 2015) and the roles of neurology and addiction (Schnitzler, 2022; van Wijngaarden-Cremer & van der Gaag, 2015). Numerous suggestions were made in this paper to stimulate new pica research utilizing a "core group approach." Addressing how microbes alter environmental substances (NIEHS 2024) should help to refine or revise etiology models. These represent new ports of entry for advancing an underserved field.

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