Review

Eating and feeding problems and gastrointestinal dysfunction in Autism Spectrum Disorders

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ABSTRACT

Eating and feeding problems, most commonly food selectivity or picky eating, are common among children with ASD. While these behaviors are typically addressed through occupational or behavior-based therapeutic approaches, increasing evidence shows than in many cases, such eating and feeding problems may be organic and stem from some form of underlying gastrointestinal dysfunction. This review highlights the literature on eating/feeding problems in children with ASD, as well as the contributing factors to eating problems and their nutritional implications in this population. In addition, the various manifestations and origins of gastrointestinal dysfunction in ASD are included. Ten relevant studies that address eating and feeding problems and gastrointestinal (GI) symptoms and dysfunction in children with ASD and the possible mechanisms underlying the eating/feeding problems in children with ASD are discussed. This review suggests a strong relationship and significant correlations between eating problems and gastrointestinal dysfunction. Further exploration of their relationship and etiology for the development of interventions are recommended.

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1. Introduction

The recent report by the Centers for Disease Control and Prevention on the increasing prevalence of Autism Spectrum Disorders (ASD) in the United States highlights the need for a deeper understanding of the etiology of this pervasive condition. ASD is a clinically heterogeneous, multi-system disorder with a variety of comorbidities. Once considered a genetically predisposed, hardwired brain disorder, studies are beginning to show that ASD, characterized by social, communication, and behavioral impairments, is not only a whole-body, biological condition, but is affected by both genetic predisposition and environmental factors (Herbert & Arrangab, 2006; Rossignol & Frye, 2012).

One of the common symptoms of children with ASD is eating and feeding problems. A majority of children on the autistic spectrum suffer from some manifestation of food selectivity or picky eating. These behaviors are multi-factorial in origin, stemming from sensory, behavioral and social impairments, and are typically addressed through occupational or behavior-based therapeutic approaches. However, there is increasing evidence that for many children with ASD, such eating and feeding problems may be organic, stemming from underlying gastrointestinal dysfunction (GID). The increased incidence of various types of GID among this population has begun to receive wider acceptance, though previous findings on the subject were mixed. However, despite the evidence that symptoms, such as chronic diarrhea, constipation, gastro-esophageal reflux and abdominal pain, have clear relationships with eating and feeding behaviors in pediatric populations not diagnosed with ASD, the relationship between these two areas among children with ASD, to our knowledge, has yet to be synthesized. This review examines the literature on eating and feeding problems and GID among children with ASD, in an attempt to learn more about the relationships between these two conditions among this population.

We reviewed the available literature on eating and feeding problems and gastrointestinal (GI) symptoms and dysfunction in children with ASD using the following search engines: PsycNET, Pubmed and Google Scholar. Various combinations of the following search terms were used: ASD, autism, PDD-NOS, Asperger, gastrointestinal problems, constipation, diarrhea, gastrointestinal dysfunction, gastro-esophageal reflux, esophagitis, eating and feeding problems, feeding patterns, eating patterns, and food selectivity. English language studies that examined both eating/feeding problems and GID in children with ASD or a related disorder were included and the last search was performed on August 11, 2014. Ten relevant studies addressing the relationship between eating problems and GI symptoms in children with ASD were identified. A narrative review format was chosen due to the understudied nature of this subject area and the wide array of study design, which impeded the conduct of a systematic review. A discussion of the eating problems in ASD and an examination of the possible mechanisms underlying the eating/feeding problems in children with ASD is included.

2. Background

ASD is a neurodevelopmental disorder that includes a wide range of complex developmental disabilities, which, according to the DSM5, includes impaired social interaction and communication, deficits in developing and maintaining relationships, repetitive behaviors, restricted interests, ritualized behaviors, behavioral inflexibility and impaired sensory processing (American Psychiatric Association, 2013). While symptoms of ASD may appear as early as 18 months, diagnosis by age two is considered reliable and standard. In the United States today, the overall prevalence of ASD is 1 in 68 children (Centers for Disease Control and Prevention, 2014).

The etiology of ASD is yet unknown. While certain genetic syndromes, including Rett's and Fragile X, are associated with ASD, only in 6–15% of ASD cases have their genetic origins been identified (Schaefer, 2008). The cognitive and behavioral features of ASD are often thought to arise from dysfunction of the central nervous system (CNS); however many non-CNS, physiological abnormalities have been documented among this population (James et al., 2004; Lombard, 1998; Ming, Brimacombe, Chaaban, Zimmerman-Bier, & Wagner, 2008). Recent research and clinical studies have begun to identify mechanisms such as immune system dysregulation, inflammation, impaired detoxification, environmental toxicant exposures, redox regulation/oxidative stress and energy generation/mitochondrial systems, as well as nutritional disorders as influential in the development of ASD (Ming et al., 2008; Theoharides, Asadi, & Patel, 2013). Common ASD comorbidities include eating/feeding problems, sleep problems (Leyfer et al., 2006), GID (Buie, Campbell, et al., 2010), seizures and epilepsy (Gabis, Pomeroy, & Andriola, 2005), ADHD (Gargaro, Rinehart, Bradshaw, Tonge, & Sheppard, 2011), obsessive-compulsive disorder (Leyfer et al., 2006), and anxiety disorders (Leyfer et al., 2006). Two of the most common co-morbidities are eating/feeding problems and GID.

2.1. Eating/feeding problems

Eating is a natural and essential human activity necessary to support growth and sustain life, which also brings joy and pleasure (Satter, 2007). For infants, feeding is a highly complex developmental skill that matures over the first two years of life (Delaney & Arvedson, 2008). The healthy feeding relationship between a parent and child encompasses both the physiological need of the child as well as an emotional aspect of the feeding responsibility of the parent (Satter, 2005). While mealtimes can be a source of great satisfaction for both infant and parent when feeding skills are intact, problems with eating/feeding can be a potential source of significant stress for both children and parents. Furthermore, as children grow older, preoccupations with food may become compounded by psychological factors such as poor emotional development, low self-esteem and social pressures, increasing the risk of disordered eating.

Distinct from eating disorders, in the literature, eating/feeding problems typically refer to some pattern of oral or enteral consumption of nutrients that deviates from the norm enough to lead to negative social and/or health consequences. Eating/feeding problems vary in terms of etiology, behavior and severity (Gal, Hardal-Nasser, & Engel-Yeger, 2011; Laud, Girolami, Boscoe, & Gulotta, 2009; Matson & Fodstad, 2009). They are common in early childhood, occurring among 25–35% of typically developing children, and in up to 80–90% of children with developmental delays (Kodak & Piazza, 2008). Though these are often prominent problems of children with developmental delays, the lack of universally accepted definitions or current classification system for eating/feeding problems presents a challenge in the identification of such problems in infancy and early childhood (Arts-Rodas & Benoit, 1998). Common eating/feeding problems include:

(1) Food refusal – the inability or refusal to eat certain foods. This is defined as a child's refusal to eat all or most foods presented, resulting in the failure to meet caloric needs or dependency on a supplemental formula (Williams, Field, & Seiverling, 2010). This eating/feeding problem is considered to be one of the more severe. It may also manifest as decreased appetite, turning of the head, mouth closure upon presentation of foods, spitting out, gagging, and vomiting of food (Williams et al., 2010).
(2) Food selectivity/restricted food intake – defined as eating only a narrow variety of foods, and is often used to refer to a range of different eating problems, such as selectivity by texture and type, eating a limited repertoire of accepted foods, and high-frequency single food intake (Mari-Bauset, Zazpe, Mari-Sanchis, Llopis-Gonzalez, & Morales-Suarez-Varela, 2013; Matson & Fodstad, 2009).
(3) Aggression and tantrums in the eating/feeding setting – defined as exhibiting aggressive behavior towards self or others during meals such that the mealtime is disturbed, often stemming from sensory or physiological discomfort or behavioral origins (Provost, Crowe, Osbourn, McClain, & Skipper, 2010).
(4) Rumination and pocketing – this is defined as the non-purposeful regurgitation of recently ingested food from the stomach to the mouth following consumption, where it is either expelled or re-swallowed and the pocketing of food in the cheeks for extended periods (Nicholls & Bryant-Waugh, 2009; Seiverling, Williams, & Sturmey, 2010).
(5) Chewing and swallowing problems – many children with ASD have difficulty chewing, or swallowing food; this may lead to food aspiration, choking, or life-threatening respiratory infections (Field, Garland, & Williams, 2003; Nicholls & Bryant-Waugh, 2009).
(6) Poor appetite – poor appetite or a lack of desire to take in adequate amounts of food can result from sensory or physiological origins, such as certain nutritional deficiencies (Beighley, Matson, Rieske, & Adams, 2013).
(7) Vomiting and gastro-esophageal reflux.
(8) Pica – defined as the repetitive ingestion of items without nutritional value, such as paint, hair and dirt, a behavior that results in serious effects and high mortality rate (Matson, Hattier, Belva, & Matson, 2013).
(9) Over-or under-eating – defined as eating too much or too little food as related to physiological needs/requirements (Broder-Fingert, Brazauskas, Lindgren, Iannuzzi, & Van Cleave, 2014; Williams et al., 2010).
(10) Eating rituals – ritualistic or repetitive patterns of behavior are commonly believed to contribute to food selectivity (Matson & Fodstad, 2009; Zandt, Prior, & Kyrios, 2007).
(11) Eating too quickly (Beighley et al., 2013).
(12) Spitting/eating – defined as chewing food and spitting it out without swallowing any of it.

The new DSM5 diagnostic criteria for Avoidant/Restrictive Food Intake Disorder or ARFID, a childhood feeding disorder, encompass some of the problems seen among children with developmental delays. The etiology of eating/feeding problems in these children is complex and research has only begun to explore the variables. These criteria enable researchers to advance the research in eating/feeding disorders because there is one standard definition. However, eating and feeding problems in children with developmental delays and disabilities are caused by a combination of pathology, biological variables and environmental factors (Matson & Fodstad, 2009). The underlying mechanisms of eating/feeding disorders in this population differ from typical disordered eating. Therefore, in light of the lack of previous precision in terminology, for the purposes of this paper, the term eating/feeding disorders will be used to refer to the range of eating/feeding problems described in the literature among children with developmental delays, specifically ASD.

3. Eating/feeding problems in ASD

Many children with developmental delays exhibit a variety of eating/feeding problems, making eating a recurrent challenge and a stressor for many parents. Eating/feeding problems occur more frequently among children with ASD than children with other disabilities (Dominick, Davis, Lainhart, Tager-Flusberg, & Folstein, 2007) and typically developing children (Schreck, Williams, & Smith, 2004). Though few population studies have been conducted, close to 70% of children with ASD are reported to be selective eaters (Twachtman-Reilly, Amaral, & Zebrowski, 2008). They have been repeatedly found to display more of other eating/feeding problems, including food refusal, idiosyncratic mealtime behavior, and acceptance of a limited variety and texture of food items, than typically developing children (Schreck et al., 2004). In one of the first literature reviews on the subject, out of 7 studies performed between 1994 and 2004, it was estimated that 46–89% of children with ASD have atypical feeding habits (Ledford & Gast, 2006) which has since been confirmed by other research

(Provost et al., 2010). Consequently, it comes as no surprise that eating/feeding problems are one of the most pressing concerns and reported by parents to be one of the most frustrating aspects of ASD.

As previously mentioned, food selectivity is the most common feeding concern documented among children with ASD. In a 2006 review by Ledford and Gast, all studies on children with ASD reported significant feeding difficulties, primarily in the form of food selectivity by type and/or texture (Ledford & Gast, 2006). Many children with ASD who are food selective exhibit a preference for starches, snack foods, and processed foods and display a lack of willingness to eat fruits, vegetables, and proteins. In addition, a multitude of research has associated food refusal with the presence of GER among infants and children with medical problems and developmental delays. A review by Williams et al. (2010) suggests that the most common medical diagnosis found among children with food refusal was GER (69%), followed by other diagnoses including cardiopulmonary conditions (33%), neurological conditions (25%), food allergies (15%), anatomical anomalies (14%), and delayed gastric emptying (6%) (Williams et al., 2010).

3.1. Nutritional implications of eating/feeding problems in ASD

Chronic eating/feeding problems can put children at risk for medical and developmental problems, including under-nutrition, suboptimal growth, social deficits and poor academic progress, as well as risk of nutrient deficiencies, such as vitamins, minerals and amino acids (Sharp et al., 2013). Studies have highlighted the intake of fewer servings of vegetables among children with ASD and lower intake of dairy has been noted as well (Graf-Myles et al., 2013; Johnson, 2008). However, data on the nutritional status of children with ASD is inconsistent; a recent meta-analysis of 17 studies found that children with ASD are subject to lower intake of calcium and protein. Other commonly reported nutrients to be consumed in insufficient amounts include calcium, iron, vitamins A, C, D, B6, B12, E, and K, as well as fiber, folic acid, and zinc (Hyman et al., 2012; Sharp et al., 2013). In a 2000 report on the nutrient status of children with ASD, more than half were abnormally low in vitamins A, B1, B3, and B5 as well as biotin, zinc, magnesium, essential amino acids and EFAs (Kidd, 2003).

Other research has highlighted more mealtime behavioral differences that did not translate to differences in nutritional status (Johnson, 2008). In a study of 164 Turkish children from four autism rehabilitation centers, aged 4–18, the mean intake of 115 children using 3-day food records was assessed. They found that the major feeding problem among this population was food selectivity, though the majority of the children found to be overweight or obese (58.5%) and 11% found to be severely thin. In addition, the calcium, zinc, vitamin B6 and folate intake of the majority of the children was found to be inadequate (Bicer & Alsaffar, 2013).

Indeed, children with eating/feeding problems may also be at higher risk of overweight and obesity. According to the 2003–2004 National Survey of Children's Health, children with ASD are 40% more likely to be obese as compared to typically developing children (Curtin, Anderson, Must, & Bandini, 2010). Despite the array of risks, feeding concerns in ASD are often overlooked in the clinical setting, possibly because findings on the nutritional impact of eating/feeding problems are still not conclusive and such eating patterns do not necessarily associate with compromised growth.

3.2. Factors affecting eating/feeding problems in ASD

The eating and feeding problems seen in ASD are perceived as multi-factorial and include behavioral, physiological, emotional, cognitive, and medical origins. One of the key areas in which the influence of behavior can be seen is one of the defining diagnostic features of ASD: repetitiveness and rituals. According to the DSM5 (APA, 2013), these symptoms include excessive adherence to routines and rituals, excessive resistance to change, restricted or fixated interests with abnormal intensity, stereotyped and repetitive speech, and hypo or hyper-reactivity to sensory input, or unusual interest in sensory aspects in the environment. Restricted interests and repetitive patterns of behavior are commonly believed to contribute to food selectivity (Matson & Fodstad, 2009). Children with ASD often display insistence on specific methods of preparation, food types, and mealtime rules (Raiten, 1986; Williams, Dalrymple, & Neal, 2000), characteristic of higher order repetitive behaviors (Ahearn, Castine, Nault, & Green, 2001; Schreck et al., 2004; Williams, Gibbons, & Schreck, 2005). Anecdotal reports have also documented specific feeding rules, including insistence that all foods on a plate be the same color, eating the same food at each meal, requiring that foods be presented in a particular order, or requiring that foods not touch each other on a plate (Twachtman-Reilly et al., 2008).

Restricted and repetitive behaviors also include hypo or hyper-reactivity to sensory input or unusual interest in sensory aspects in the environment (APA, 2013), also known as sensory processing disorders. Sensory processing refers to the ability to receive, organize and interpret stimuli, including oral, visual, tactile, vestibular, and auditory experiences (Germani et al., 2014). Difficulties with sensory processing have been identified among children with ASD, with differences found between individuals with ASD and controls (Klintwall et al., 2010). Ben-Sasson et al. (2007), found toddlers with ASD are more likely to be under-responsive, display avoidance, and exhibit a low frequency of sensory-seeking behaviors (Ben-Sasson et al., 2007). Hypo or hyper sensory input as a symptom of ASD may also manifest as food selectivity. As a result, it is challenging to separate physiological aspects of feeding difficulty from behavioral aspects. Physiologically based difficulties are often subtle and hard to identify, and "behavioral" difficulties may actually reflect physiological characteristics of this complex disorder (Twachtman-Reilly et al., 2008). It is possible, for example, that early tactile sensitivity may contribute to some of the eating/feeding behaviors, such as avoiding certain foods, textures, tastes, smells and temperatures seen in children with ASD. Indeed, these children are often more likely to accept only low-texture foods, such as those that have been puréed. In

addition, tactile defensiveness and oral defensiveness may be part of a larger problem in modulating sensory input, which can take different forms, and affect various activities of daily living including eating/feeding (Cermak, Curtin, & Bandini, 2010).

Other evidence has pointed to cognitive function as a factor in eating behaviors in children with ASD. In early childhood, executive cognitive functioning can predict a range of life outcomes including health behaviors and academic performance (Allom & Mullan, 2014). The term encompasses interrelated skills required to carry out goal-directed activity, and is comprised of higher order processes related to self-regulation. The executive function hypothesis suggests that since those with ASD are often unable to plan and control behavior, they often 'get locked' into a certain type of food or brand and become easily distraught at changes in eating patterns (Turner, 1999).

Challenges in shifting tasks have been linked with eating behaviors seen in both neuro-typical underweight and obese individuals (Allan, Johnston, & Campbell, 2011). Deficits in inhibitory control are also associated with poorer eating behavior, and consumption of unhealthy foods (Allan et al., 2011). It has also been suggested that snack foods, commonly consumed by children with ASD, may be extremely rewarding for children and impress high emotional and motivational drive upon immature executive cognitive systems, making it difficult to inhibit highly palatable snack foods (Riggs, Spruijt-Metz, Sakuma, Chou, & Pentz, 2010). Conversely, the low motivation associated with less palatable vegetables may result in a decreased emotional motivation to eat them.

The eating and feeding relationship between children and parents is also an important factor in the development of eating/feeding problems. Children's eating is modified by exposure and accessibility to foods, modeling of siblings and parents, the physiological consequences of ingestion, and by liking for and consumption of foods high in calories, sugar, and fat. Parents also shape their children's eating environments through parenting style, choice of feeding methods, the foods made available and accessible, direct modeling influences, and through interaction with children in the eating context (Birch & Fisher, 1998; Ventura & Birch, 2008). In addition, the stress levels of parents of developmentally delayed children may also play a key role in the dynamics and outcomes of the eating/feeding relationship. Another highly influential factor in the eating and feeding behaviors of infants and children and possibly a key way to understand their etiology in ASD is the health and state of their GI tract.

4. Gastrointestinal dysfunction in ASD

The most recent literature confirms that children with ASD have higher rates of GID than typically developing children (McElhanon, McCracken, Karpen, & Sharp, 2014). The prevalence of GI symptoms in children with ASD have been reported to range from 9 to 70% and higher (Buie, Campbell, et al., 2010). A recent meta-analysis of 15 studies found that children with ASD have higher rates of diarrhea, constipation, and abdominal pain than comparison groups. Other forms of GID, such as abdominal pain and GER, which often manifests as vomiting, are harder to identify and may be expressed as problem behaviors, posturing, rejecting certain foods or pointing to the chest (Buie, Fuchs, et al., 2010). Greater incidence of megarectum, an enlarged rectum resulting from muscle dysfunction or fecal impaction, has also been found among children with ASD as compared to controls (Afzal et al., 2003).

Common forms of abdominal distress seen in children with ASD include the following:

1. Chronic abdominal pain – intermittent or constant abdominal pain that exceeds 1–2 months in duration, a challenging assessment in ASDs.
2. Constipation – the occurrence for 2 weeks or so of a delay or difficulty in defecation (note – even children with daily bowel movements may have retention of stool).
3. Chronic diarrhea – when loose stools persist for 2 weeks or longer, with or without an increase in stool frequency.
4. Gastro-esophageal reflux disease – the passage of gastric contents into the esophagus, producing diverse symptoms and complications. Manifests as vomiting, chest pain, heartburn, esophagitis, and/or food refusal (Buie, Fuchs, et al., 2010).

Abnormalities of the GI tissue of children with ASD have been reported in multiple studies. Increased intestinal permeability has been noted (de Magistris et al., 2010; Horvath, Papadimitriou, Rabsztyn, Drachenberg, & Tildon, 1999) with damage to the tight intercellular junctions of gut mucosa noted among children with ASD in several studies (Heberling, Dhurjati, & Sasser, 2013). In addition, elevated levels of fecal ammonia and short chain fatty acids have been identified among the stool samples of children with ASD (Wang et al., 2012).

Other studies have highlighted the role that functional alterations in gut flora may play in ASD (Bolte, 1998; Finegold, Downes, & Summanen, 2012; Midtvedt, 2012). Pathogenic bacterial strains such as clostridia and some strains of candida have been identified in greater numbers among ASD children (Adams, Johansen, Powell, Quig, & Rubin, 2011). Lower levels of beneficial bacterial strains such as bifidobacterium have also been reported (Adams et al., 2011). Pathogens such as clostridia are known to cause illness and produce neurotoxins that may be absorbed from the GI tract. Changes in bacterial flora have been linked with behavioral changes such as hostility, slurred speech, altered mental status, and ataxia. In addition, marked decreases in symptoms of ASD have been identified in children treated with antibiotics specific to clostridia (Bolte, 1998). The use of anti-fungals such as nystatin, have also been shown to lead to an improvement in ASD symptoms (Shaw, 2010). In a trial which gave 10 children with ASD oral vancomycin, followed by a high potency probiotic, communication and behavior gains were seen in 8 of the 10 children while the medication protocol was maintained (Sandler et al., 2000). Indeed, it has

been suggested that certain behavioral problems observed in children with ASD may be indicative of a child's response to, or their attempt to communicate the discomfort of, an underlying GI problem (Bauman, 2010; Horvath et al., 1999). Expressions of GI distress may include sleep disturbances, repetitive behaviors, self-injurious behaviors, aggression, irritability or mood disturbances, and tantrums. Unusual sleep, oppositional behavior, and rigid-compulsive behaviors have all been found to be significantly associated with GI problems among children with ASD (Maenner et al., 2012; Peters et al., 2014). It is important to note that while GI symptoms such as diarrhea and constipation are overtly visible to parents, symptoms such as abdominal pain and GER prove to be a greater challenge to identify in a population with communication challenges. They are often misinterpreted as other comorbid symptoms such as the insomnia or irritability exhibited by children with ASD (Kang, Wagner, & Ming, 2014), therefore, the incidence of GID among this population may be underestimated due to the challenge of accurate identification and diagnosis.

A number of causal and therapeutic hypotheses of ASD involve the GI tract (McElhanon et al., 2014). The leaky gut hypothesis states that large peptides such as the opiate-like peptides gluten and casein are indigestible to many children. They leak through gap junctions in the intestinal tract, into the bloodstream, where they can cause a variety of neuropsychiatric symptoms, as well as gluten and casein sensitivity (Whiteley et al., 2013). Others have focused on the role of functional alterations in gut flora in GID in ASD. In the absence of normal gut bacteria, alterations that may result from the overuse of antibiotics can result in the overgrowth of pathogenic microbes, leading to a number of GI problems (Adams et al., 2011). Normal gut flora are responsible for the breakdown of plant polysaccharides, promoting GI motility and maintaining water balance, production of certain vitamins, and competition against pathogenic bacteria. In addition, gut micro biota have been shown to modulate various neurotrophins and proteins involved in plasticity and brain development (Douglas-Escobar, Elliott, & Neu, 2013). Although the presence of a clear GI pathophysiology specific to ASDs has yet to be identified, elevated risk for GI symptoms in this population remains a critical issue (McElhanon et al., 2014).

The concept of a gut-brain connection in ASD is also supported in the literature. Several different mechanisms involving the peripheral and central nervous systems may mediate the impact that changes in the GI tract may have on ASD symptoms and behavior. Immunological abnormalities in the GI tract have also been proposed to affect the brain, though whether GI abnormalities in autistic individuals contribute to the development, persistence, or intensity of core symptoms is unknown (Hsiao, 2014).

4.1. Gastrointestinal dysfunction and eating/feeding problems in non-ASD pediatric populations

There is clear evidence that GID plays a role in the development of chronic feeding problems in various pediatric populations. In a study of feeding dysfunction in 200 typically developing children with eosinophilic GI disease, Mukkada et al. (2010) found that 84.8% had frequent gagging and vomiting. 88% of the children had food sensitivities and 93.9% displayed a variety of maladaptive feeding behaviors, which persisted even after treatment of the disease (Mukkada et al., 2010). Among 120 children with cerebral palsy, feeding dysfunction was significantly correlated with constipation, as well as lack of functional communication, insufficient chewing, and gagging reflex (Erkin, Culha, Ozel, & Kirbiyik, 2010). In addition, chronically ill toddlers who had shown food refusal have also been found to experience improved eating patterns and emotional health when upper GI problems were treated completely (Zangen et al., 2003).

While the data on non-ASD populations highlights such a connection, a clear relationship between eating problems and GID among ASD populations has yet to be investigated. Furthermore, though a 2008 multidisciplinary panel recommended that for "individuals with ASDs…GI symptoms warrant a thorough evaluation, as would be undertaken for individuals without ASDs" (Buie, Campbell, et al., 2010), evaluation for GI disorders in children with ASD is still not routine in clinical practice. Therefore, the study of symptoms of GI distress and eating problems in these children is of the utmost importance (Kerwin, 2005; McElhanon et al., 2014).

5. The relationship between eating/feeding problems and GI dysfunction in ASD

While an increasing volume of literature highlights the connections between eating/feeding problems and GID in children with ASD, a limited body of research has explored the relationship between the two. The following section reviews studies that explored connections between eating/feeding problems and GID in children with ASD. All studies were descriptive/correlational studies, and five included comparison groups.

Williams et al. (2000) surveyed 100 families of children diagnosed with ASD, Pervasive Developmental Delay, Not Otherwise Specified (PDD-NOS) or related diagnoses, aged 22 months to 10 years of age, regarding their eating habits. The survey questions were grouped by the following eating-related topics: temperament, early eating patterns, and health concerns and nutritional adequacy. While 67% of respondents described their child as a picky eater, 62% reported they felt their child received adequate nutritional intake. Children who were not labeled as picky eaters were perceived to have adequate nutrition (97%), while those described as picky eaters were equally divided between being perceived to have adequate and identified to have inadequate nutrition.

The top health problems identified among the group after ear infections (59%), were GER (28%), current GI problems (17%), previous unspecified GI problems (21%), and food allergies (10%). 23% of the children with GI problems had poor appetite as compared to 2% of their counterparts who did not have GI problems. Furthermore, 6% of those with GI problems were described as having a good appetite for food, versus 23% without GI problems who had good appetite. In addition, a

statistical association was identified between the presence of GI problems and low appetite among the case children. Despite a lack of control data, this study provides valuable preliminary data about multiple eating problems and highlights a possible association between GI problems including gastro-esophageal reflux and decreased appetite.

Field et al. (2003) explored childhood eating/feeding problems and potential pre-disposing factors in a review of medical records of 349 children. The children ranged in age from 1 month to 12 years, 26 of which were diagnosed with ASD. The group provided clear definitions for functional feeding problems, including food refusal, selectivity by texture, selectivity by type, oral motor delays, and dysphagia. Among the subjects with ASD, three were found to have food refusal, 16 had food selectivity by type, eight had food selectivity by texture, four had oral motor delay and three had dysphagia. Food selectivity by type and texture were the most common eating/feeding problems found among children with ASDs.

In this study, GER was the most prevalent form of GID among all children, including those with ASD, and was the factor most associated with food refusal. Each of the three children with ASD who had food refusal also had GER. Children with ASD who were food selective had a significantly lower prevalence of food refusal ($p = 0.01$) and of oral motor problems ($p = 0.002$). Frequencies of every feeding problem were higher among children with GER than other types of GI problems, though frequency of food refusal was significantly higher for children with GER than children without it. Among all three subgroups, GER was associated with more severe eating/feeding problems. Constipation was also found to be very common in children with ASD, which the authors speculated may have been the result of poor diet, and likely reinforced problems by further decreasing appetite and openness to trying new foods. While no causal relations were determined in this study, the findings regarding GER and food refusal are of significance and warrant further study, since early identification of GER, constipation, and their treatment could potentially prevent feeding complications over time.

Kerwin (2005) assessed 89 children between 2 1/2 and 18 years, who were diagnosed for at least 6 months with ASD, Asperger's, or PDD-NOS. 89 participants remained after exclusion criteria were applied and were given a 47-item survey to capture aspects of the child's eating behavior, GI symptoms, and behaviors related to eating and digestion. The mean age of the children was 8.71 years (SD = 3.45) with age range of 3–17 years; 51.7% had PDD-NOS, 39.3% were autistic and 9% had a diagnosis or Asperger's. Like Field et al. (2003) and other reports, this group found the most frequently reported unusual eating pattern was food selectivity. 10% of children surveyed were reported to currently vomit and 6.7% did so in the past. 25–33% of children with PDD in this sample experienced constipation, while 25% experienced loose stools.

Children who presented with gestures of abdominal pain tended to have bloated stomachs and gagged more frequently during meals. In general, feeding behavior was more highly correlated with report of bowel function than other symptoms of GI distress. Exhibiting cycles of the amount or variety of food consumed was associated with chronic loose stools and working hard to move the bowels. A more frequent passing of gas was associated with less strong dislike of specific foods. Other GI related behaviors were reported in the type of head banging or hitting the head. These were significantly associated with a history of vomiting, burping and belching, chronic, loose and frequent stools, and in cycling variety of foods consumed (defined as periods of good eating followed by periods of poor eating patterns, lasting 1 week to 6 months). Frequent and chronic loose stools, infrequent bowel movement, cycling the amounts of food consumed, food cravings, and pica were also all associated with hitting the ears.

While, again, no causality could be established, this study both echoed previous findings about eating/feeding problems, and shed light on the association between common self-injurious behaviors and their connection with different types of GID. This indicates that it could be a possible sign of pain and distress. In addition, its larger, heterogeneous sample size included a large range of children and eating/feeding problems. In addition, the findings about pica were novel and should be explored further to determine the cause (i.e. sensory or nutrient related), considering the serious health risks known to accompany this disorder.

In a smaller cross-sectional study of GI symptoms in children with ASDs, another group examined 50 children with ASD (Valicenti-McDermott et al., 2006). They included 2 control groups: 50 children with typical development and 50 with other developmental delays, who were matched for age (±6 months), sex, and ethnicity. The age range for study eligibility was 1–18 years, as well as active patient status receiving regular follow up at the pediatric neurology and developmental pediatric programs of the Albert Einstein College of Medicine. Diagnosis of ASD was made by a neurologist or developmental pediatrician and confirmed by record review and interview, as well as a score of 30 or more on the Childhood Autism Rating Scale (CARS). Structured interviews were utilized as well as a revised GI questionnaire, which allowed for the identification of lifetime GI and eating/feeding problems, including special diets, prior diagnosis of food allergy, food and types of selectivity, frequent vomiting, reflux diagnosis and a familial autoimmune questionnaire.

Within the sample, 70% of children with ASD were found to have a history of GI symptoms, including abnormal stool pattern, frequent constipation, frequent vomiting, and frequent abdominal pain (not associated with constipation). This is as compared with 28% of the group with typical development and 42% of the group with developmental delay. The most common GI symptom among case children with ASD was constipation. In addition, 60% of children with ASD were found to have food selectivity, which was far higher than either of the control groups. Multivariate analysis confirmed food selectivity to be associated with GI symptoms among children with ASD. Though once again, no causation could be identified, in this study, an association was found between food selectivity and GI symptoms in this cross-sectional study population. The strengths of this study are in its inclusion of two matched control groups as well as an analysis of lifetime prevalence of GI problems versus the focus on current symptoms seen in other studies.

Later research by Ibrahim, Voigt, Katusic, Weaver, and Barbaresi (2009) drew contrasting conclusions to previous studies. They examined 121 subjects with ASD and matched them with two control subjects for each case subject. GI diagnoses and

symptoms were grouped into five categories based on the literature review: (1) constipation, (2) diarrhea, (3) abdominal bloating, (4) GER and (5) feeding issues or food selectivity. Patients were followed from date of birth to date of last follow up before age 21. Significant differences were found between ASD case and control subjects in the cumulative incidence of constipation by 20 years and in feeding issues and selectivity. However, in contrast to other studies, this group found no significant difference in overall cumulative incidence of GI symptoms between case and control subjects. In addition, no significant association was found between ASD status and overall incidence of GI symptoms, diarrhea, reflux/vomiting, or bloating/discomfort/irritability. However, subjects with ASD were found to have a higher incidence of both constipation and feeding issues/food selectivity. Among the ASD group, 33.9% had constipation, as compared to 17.6% among controls ($p = .003$) and 24.5% of the ASD group had food selectivity, as compared to 16.1% among controls ($p = .009$).

One of the unique features of this study is the long-term population based assessment of the incidence of GI symptoms, compared to the shorter-term survey studies of previously discussed research. No significant difference was found between case and control groups. While these authors postulated that behaviorally related food selectivity (routine, insistence on sameness) may lead to constipation due to limited variety in dietary intake or the taking of stimulant medications, other groups have not confirmed such a causal relationship (Gorrindo et al., 2012).

In their study on GI disturbances in patients with ASD from Poland, Kazek et al. (2010) examined 30 patients with ASD (17 children) or autistic features (13 children) suffering from various GI complaints. The patients were aged 3–13 years, and all had upper GI endoscopies performed. Chronic abdominal pain was observed in 80% of the patients and impairment in peristaltic reflexes was noted in 97% of the autistic children, with 57% of the cases manifesting as diarrhea and 67% as constipation. Vomiting and regurgitation was reported by 33% of the patients, with 63% of the parents reporting eating disorders, and 33.3% reporting a refusal to eat over several days. In addition, 20% of the children were found to have esophagitis and another 20% had macroscopic changes of the gastric mucosa. 70% of patients had chronic inflammation of the duodenal mucosa and 40% were diagnosed with chronic duodenitis. The parents of 18 children (60%) reported symptoms of food allergy.

The high percentage of abnormal endoscopic findings of this population along with the high percentage of food allergies seen are significant. Together with the novel finding about increased numbers of intraepithelial lymphocytes not joined with the immunological indicators of celiac disease, this study, which utilized physical GI examination, sheds further light on the possible etiology of GID in children with ASD and the role of GI inflammation resulting from ingestion of potentially allergenic foods.

Gorrindo et al. (2012) compared parental reports and characterized GID of 121 children who were split into three groups: one with co-occurring GID and ASD; one with ASD and without GID; and one with GID only. Children with GID were evaluated by a pediatric gastroenterologist and all ASD diagnoses were confirmed using the Autism Diagnostic Observation Schedule (ADOS). GI health was evaluated using the questionnaire on pediatric gastro symptoms (Rome III version (QPGS)). Parents were asked to keep a 7-day diet log for the purpose of a dietary analysis. Subjects ranged in age from 5.1 to 17.9 years; no difference was found in ADOS classification among the ASD groups.

As found in previous studies, the most frequent type of GID among children with ASD was functional constipation, which 85% of the ASD group and 44.4% of the GID only group experienced. The next most common GI diagnosis was GER (20%). While elevated BMI has been associated with functional constipation among typically developing children, in this study, BMI was not significantly associated with a diagnosis of constipation in ASD. In contrast to the postulation of Ibrahim et al, no differences in constipation were found among those children with ASD taking potentially constipating medications. Younger, more socially impaired children with ASD had increased odds for functional constipation. While behavioral problems were not assessed, this study did find that children with ASD and co-occurring GID lacked expressive language, and had more social impairment. No differences in dietary habits were found among the three groups, which the authors noted may be attributable to the older age of the children. They suggested it is unlikely that dietary habits play a causal role in GID among this population of children. This study found no evidence of food selectivity beyond what is seen in a non-ASD population. The authors suggest that GID is not a result of dietary or eating habits.

In 2012, Badalyan and Schwartz (Badalyan & Schwartz, 2011a, 2011b) conducted two studies on feeding problems and mealtime feeding behaviors and GID. One study was conducted among children diagnosed with classic autism and the second among children diagnosed with Asperger syndrome (AS) or PDD-NOS, both in comparison to typical siblings. The latter study was a cross-sectional online survey of 64 children with Asperger syndrome and 44 with PDD-NOS (total of 108), between the ages of 3 and 12 years. They conducted an online survey from February 2009 to April 2009 which included 41 questions pertaining to feeding behaviors, unusual mannerisms, food preferences, and GID starting from when the child was between the ages of 3–12; the survey was used both for the child with AS or PDD-NOS and his or her sibling. Frequency of feeding behaviors and GI problems were categorized as follows: never, rarely (less than 10% of the time), sometimes (10–50%) and often (more than 50%). Diarrhea was defined as passing at least three watery, unformed stools in a day and constipation was defined as hard or painful stools passed less than three times per week.

Children with high functioning autism were found to have a greater likelihood of frequent (more than 50% of the time) feeding behavior problems and GID. The eating/feeding problems identified included insistence on unusual presentation, unusual preferences, and poor social behavior at mealtimes. These same children also had higher odds of frequent constipation and fecal incontinence. 57% of AS/PDD-NOS group had frequent unusual preferences as compared to 5% of the controls. 48% had frequent food dislikes compared to 6% controls. Frequent constipation was found 30% of the time among AS/PDD-NOS compared to 4% of the time among controls, and 22% of case children had fecal incontinence compared to 2% of the sibling controls.

The same group conducted a second study of near identical methodology on 79 children with classic autism and their matched sibling controls (Badalyan & Schwartz, 2011b). The two groups differed significantly, with respect to prevalence of frequent problematic feeding behaviors, unusual food preferences, insistence on eating foods with specific utensils/dishes, dislike of new foods, fear of new foods, poor mealtime social behavior, unusual posturing during meals, and oral motor problems. Significant differences in the groups were also found with respect to GID, including constipation, soiling, diarrhea, and failure to thrive but not in rates of vomiting, abdominal pain, reflux, or dysphagia. Dislike of new foods and bizarre mealtime mannerisms were found to be more frequent among those with ASD ($p < 0.01$) and higher odds of constipation and fecal incontinence ($p < 0.01$) were also identified among the case subjects ($p < 0.01$).

These studies are unique in their inclusion of a sibling control group and the separation of the classic autism and PDD-NOS diagnoses. The abnormally high prevalence of unusual mealtime and feeding habits as well as various types of GID among children with ASD is noteworthy. Though verification of diagnosis was not obtained for either study, and no correlation nor causation were determined, these findings warrant further exploration.

Finally, Kang et al. (2014) described the clinical characteristics of GID of 164 children with ASD who were evaluated at a pediatric neurology practice. The study was conducted using a 14-page clinical intake form and a retrospective chart review. Six of 12 children who underwent an endoscopy had inflammation of the gut. Chronic GID was defined as diarrhea or unformed stools, constipation, vomiting/GER, or bloating and gassiness. Food intolerance was defined as chronic GI symptoms or eczema, which dissipated after removal of a specific food group. 49% of the children in the cohort reported one or more GI disorder and 34% had one or more chronic GI complaint. 26% had constipation, 22% of the children had diarrhea, 13% of parents reported bloating or gassiness in their children, and 10% reported vomiting or reflux. They also found that subjects with any of the above GI symptoms had significantly higher rates of food intolerance ($p < 0.001$). The authors postulated that food intolerance could lead to mucosal inflammation and cause symptoms of GID, reflux, gas and bloating, diarrhea, or constipation (Kang et al., 2014).

6. Discussion

A large subset of children with ASD suffer from both eating problems and GID (Buie, Campbell, et al., 2010; Ledford & Gast, 2006; Mannion, 2013). The impact of these problems on the short and long term health of children with ASD is an understudied area of importance (Sharp et al., 2013; McElhanon et al., 2014). Such eating/feeding problems have multi-factorial causes, including behavioral, sensory, social-emotional, and cognitive aspects. A growing body of research indicates that various types of organic GID may also influence eating/feeding problems (Kerwin, 2005; McElhanon et al., 2014; Williams et al., 2010). While the research has shown that GID, such as GER, gastroenteritis, and food allergies, may play a role in the development of chronic feeding concerns, in other pediatric populations, a clear mechanism among populations with ASD has yet to be clearly elucidated (Mukkada et al., 2010; Zangen et al., 2003).

Among the majority of the studies reviewed, eating and feeding problems and GID were both found to be more prevalent among ASD populations than non-ASD groups. Food selectivity was found to be the most common type of eating problem among children with ASD, a confirmation of previous findings (Kerwin, 2005; Valicenti-McDermott et al., 2006). Constipation and GER were the most common types of GID in most studies (Badalyan & Schwartz, 2011a; Field et al., 2003; Gorrindo et al., 2012; Valicenti-McDermott et al., 2006). Both conditions have been shown to be associated with food selectivity and refusal and low appetite both in ASD and non-autistic populations (Field et al., 2003; Williams et al., 2000).

The pain and discomfort caused by GER in which food and stomach acid back up into the esophagus, causing pain which is not easily visible, may lead to food selectivity or refusal and low appetite (Buie, Fuchs, et al., 2010). In addition, GER may also be caused by delayed gastric emptying, resulting from constipation (Buie, Fuchs, et al., 2010). Possible causes of constipation include limited food variety, low fiber and low fluid intake, food allergies or intolerances, including to gluten and casein, control/behavioral issues, functional issues, or fear of pain from defecation. While some have postulated a connection to potentially constipating medications, other studies have found no differences in constipation among those children with ASD taking such medications (Gorrindo et al., 2012; Ibrahim et al., 2009). The self-injurious behaviors found to be associated with infrequent bowels among others may be a sign of pain and distress among some children (Kerwin, 2005). Thus examination on a case-by-case basis is warranted. In addition, one study found pica to be associated with self-infliction of pain; the causes and etiology of this potentially dangerous eating behavior warrants further investigation as well.

Diarrhea was also found to be a common GI symptom among children with ASD. Some have suggested the changes in stool consistency and appearance reported by parents may be related to food allergy (Buie, Fuchs, et al., 2010), the intake and malabsorption of carbohydrates or other macronutrients, although the condition has multiple causes (Buie, Fuchs, et al., 2010). What appears to be diarrhea many times is actually leakage of stool around an impacted stool, resulting from ongoing constipation. Diarrhea may also result from frequent use of antibiotics and result in a known phenomenon known as antibiotic-associated diarrhea; this occurs when antibiotics disturb the natural balance of bacteria in the intestinal tract and cause harmful bacteria to multiply beyond their normal numbers (Johnston, Goldenberg, Vandvik, Sun, & Guyatt, 2011). Others experience diarrhea-like symptoms with the malabsorption of disaccharide carbohydrates in the small intestine. When these carbohydrates are malabsorbed, the osmotic load produced by the high amount of low molecular weight sugars and partially digested starches in the small intestine can cause abdominal distension, rapid peristalsis, and diarrhea, changes in stool pH and consistency (Hammer, Santa Ana, Schiller, & Fordtran, 1989; Robayo-Tores, Quedzada-Calvillo, & Nichols,

2006). Special diets such as the Specific Carbohydrate Diet, which restricts disaccharide intake, have been reported to be beneficial to children and adults suffering with chronic diarrhea (Horvath et al., 1999).

In addition, two studies identified high percentages of food allergy and intolerance among their patients and an association with GID. Food intolerance has been speculated to lead to chronic mucosal inflammation, contributing to many symptoms of GID, GER, gas and bloating, diarrhea or constipation (Guo et al., 2012; Kang et al., 2014). Proper identification and removal of offending foods may play a key role in easing both GI symptoms and related eating problems. In addition, a bloated abdomen, posturing, and infliction of self-pain warrant further exploration to rule out causes (Buie, Fuchs, et al., 2010).

This review has several limitations. To date, there is a limited number of studies published in this subject area and of the few that have been, most include a limited number of subjects and rely on parental report, which is inherently subject to bias. In addition to potential under-reporting of food intake or eating problems, many parents may not be aware of, and therefore may not report, the occurrence of some GI problems. This may include diarrhea, despite the fact that their child experiences chronic loose or soft stool; constipation, which may also be present even when there is a regular, small movement of the bowels, around fecal impaction and posturing, which may indicate GI distress, but may be mistaken as a behavioral issue. Finally, some forms of GID, such as GER are not visible and may go undiagnosed. The perception of symptoms by parents who are subject to the stresses inherent in raising and caring for a child with developmental delay, and their reporting of their child's nutritional intake may also contribute to bias.

A majority of the studies reviewed lack consistency in the definitions used for GI symptoms and dysfunction and eating problems, making it difficult to effectively compare findings. In addition, the use of medical chart review may be compromised if parents did not fully report symptoms to their physicians, or if physicians did not enter complete data into patient records.

Finally, the number of studies on the subject is few and due to their design, causality could not be established in the studies included in this review. Less than half of the studies included a comparison group, and only several studies presented information regarding participants' definitive diagnostic status (i.e. autistic disorder, PDD-NOS, AS), which limits generalizability of findings. While this review suggests a strong relationship and significant correlations between eating problems and GID, the direction and specific mechanisms that link the two are still unclear. It is likely variables may affect one another, with GI problems affecting eating, and vice versa, therefore further studies in this field are required.

7. Conclusion

The high prevalence of both eating problems and GID in children with ASD make it pertinent to further explore their etiology and relationship, and to develop interventions for core and comorbid symptoms. Successful treatment depends upon the proper identification and management of medical problems that may be contributing to the feeding difficulty or vice versa, to prevent worsening of the eating/feeding problem as the child grows older. In addition, eating/feeding problems are complex and multifactorial, yet lack universally accepted definitions and classification systems. Therefore, health professionals are forced to rely on and implement regular clinical assessments to determine the presence of GI problems as well as food allergies and sensitivities, which play a role in feeding and eating problems (Arts-Rodas & Benoit, 1998). A multi-disciplinary approach including physicians, nurses, nutritionists, occupational therapists, and speech-language pathologists, is important for the successful resolution of the multi-factorial roots of these problems. Further studies are recommended to identify the direction of correlations and specific mechanisms.

Acknowledgments

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