



Possible gastrointestinal symptoms in a subset of children with autism

Amy Brown, Dominic Chow, Satona Murakami, William Goh, Aimee Perreira, Sandi Kwee, Payel Sil & Majdouline LeRoy

To cite this article: Amy Brown, Dominic Chow, Satona Murakami, William Goh, Aimee Perreira, Sandi Kwee, Payel Sil & Majdouline LeRoy (2010) Possible gastrointestinal symptoms in a subset of children with autism, Expert Review of Gastroenterology & Hepatology, 4:2, 125-127, DOI: [10.1586/egh.10.17](https://doi.org/10.1586/egh.10.17)

To link to this article: <https://doi.org/10.1586/egh.10.17>



Published online: 10 Jan 2014.



Submit your article to this journal [↗](#)



Article views: 1655



View related articles [↗](#)



Citing articles: 1 View citing articles [↗](#)

For reprint orders, please contact reprints@expert-reviews.com

Possible gastrointestinal symptoms in a subset of children with autism

Expert Rev. Gastroenterol. Hepatol. 4(2), 125–127 (2010)



Amy Brown, PhD

Author for correspondence
Associate Professor,
Department of
Complementary and
Alternative Medicine,
John A. Burns School of
Medicine, 651 Ilalo Street,
MEB 223, University of
Hawaii, Honolulu,
HI 96813, USA
Tel.: +1 808 692 0907
Fax: +1 808 692 1246
amybrown@hawaii.edu

Dominic Chow, MD

Associate Professor, Departments of Pediatrics
and Medicine, University of Hawaii, Honolulu,
HI 96813, USA

Satona Murakami, MD

Department of Orthopedic Surgery, Graduate
School of Medical Sciences, Nagoya City
University, Nagoya, Japan

William Goh, MD

Fellow, Maternal–Fetal Medicine, Department
of Obstetrics and Gynecology, University of
Hawaii, Honolulu, HI 96813, USA

Aimee Perreira, MD

Research Fellow, Queens Medical Center,
Honolulu, HI 96813, USA

Sandi Kwee, MD

Assistant Professor, Department of Medicine,
University of Hawaii, Honolulu, HI 96813, USA

Payel Sil, MS

Graduate Student, Department of
Complementary and Alternative Medicine,
University of Hawaii, Honolulu, HI 96813, USA

Majdouline LeRoy

Graduate Student, Department of Molecular
Biosciences and Bioengineering, University of
Hawaii, Honolulu, HI 96816, USA

“The fact that certain gastrointestinal problems already exist in some children with developmental delay disorders indicates that children with autism might also be susceptible.”

There is a continuing debate as to whether or not gastrointestinal (GI) problems may exist in a subset of children with autism. If GI disorders are common in some children with developmental disorders, why could they not also exist in children with autism? It is known that constipation and fecal impaction are common in children with mental retardation [1], Rett syndrome [2], Prader–Willi syndrome, Hunter disease and autism [3,4]. It is also an established fact that a certain percentage of children with autism have varying degrees of mental retardation, thus is it not possible that these children may experience the increased risk of GI symptoms associated with mental retardation? A recent review by Buie *et al.* in *Pediatrics* reported that the prevalence of GI symptoms (constipation, diarrhea, bloating, belching, abdominal pain, reflux, vomiting and flatulence) in children with autism spectrum disorders (ASD) range widely from nine to 91% based on 11 studies that average 44% [5]. It is interesting to note that D'Eufemia *et al.* observed that 43% (nine out of 21) of children with ASD had altered intestinal permeability (leaky gut) compared with 0% of controls (zero out of 40) [6].

Other GI problems common in genetically related mental disorders include: possible functional megacolon in Rett syndrome, where 76% of these patients experience GI symptoms [7]; gallbladder dysfunction (gallstones and cholecystectomy) in Rett syndrome [8]; and gastroparesis in Prader–Willi syndrome [9]. Levy even stated that “Down syndrome is recognized as one of the most common predisposing conditions for a group of serious GI anomalies – tracheo–esophageal fistula, duodenal obstruction with or without pyloric stenosis,

annular pancreas, imperforate anus and Hirschsprung's disease” [10]. He added that “intestinal anomalies can be found in many other genetic disorders, with recent evidence suggesting the presence of GI developmental regulatory genes on chromosome 13q.”

In terms of celiac disease, The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition recognizes in their clinical guidelines that at least three developmentally delayed conditions have higher risk rates than the normal population [11]. They reported that strong evidence exists for an association between Down syndrome and celiac disease, with a prevalence rate of 5–12%. Approximately one third of Down syndrome patients with celiac disease exhibit no GI symptoms. Hilhorst *et al.* reported a 43-times higher celiac rate in patients with Down syndrome [12]. According to the 1999 Health Care Guidelines of the Down Syndrome Medical Interest Group, an initial screening for celiac disease is recommended at the age of 2 years [13]. Approximately 4–8% of children with Turner syndrome have celiac disease [14–18], and one study revealed an 8% rate in children with Williams syndrome [19]. The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition also recognized increased rates of celiac disease in children with Type 1 diabetes mellitus. The 2009 American Diabetes Association Standards of Medical Care in Diabetes listed the increased rates of celiac disease to be 1–16% versus 0.3–1% in the general population, and recommended celiac disease screening in these patients [20]. Children with cerebral palsy are also at risk as 43% have high serological celiac markers [21].

Hans Asperger himself suggested a possible link between celiac disease and autism more than half a century ago [22]. Why would the very real possibility of GI problems, including gluten problems, existing in a subset of children with autism even be debated by some researchers? The fact that certain GI problems already exist in some children with developmental delay disorders indicates that children with autism might also be susceptible. This is particularly true since approximately 30% of children with autism exhibit some degree of mental retardation, and that celiac disease is observed in approximately 10% of children with Down syndrome, Turner syndrome and Williams syndrome. Finally, GI symptoms in children with ASD range from 9 to 91%, averaging 44% [5]. In light of these findings, does it make logical sense to eliminate the possibility of GI problems and/or celiac disease existing in a subset of children with autism without thorough scientific investigation? Where is the scientific objectivity when weak research results [4] are nationally promoted as “putting to rest the nagging suggestion that there exists a link between autism and gastrointestinal disease” [23]. This comment in *Pediatrics* was based on a study by Ibrahim *et al.* who reported no significant differences in prevalence of GI symptoms in children with autism (77.2%) compared with controls (72.2%) [4]. Their retrospective study of Mayo Clinic medical records (121 children with autism between 1976 and 1997) attempted to determine whether autistic children had more visits to the hospital for GI symptoms than nonautistic children. The conclusion that there is no link between GI symptoms and autism was used to suggest that parents do not need to place their children on restrictive diets.

Serious limitations of Ibrahim's study include, but are not limited to:

- It was a retrospective study relying entirely upon medical records that tend to be incomplete;
- This was not a clinical study testing the efficacy of diet in autistic children;
- It is not clear whether these were children under the broader ASD or the more specific autistic disorder. Specifically, it was not clear if Asperger syndrome and pervasive developmental disorder, not otherwise classified, were included in the autism diagnosis;
- Subjects were not all formally diagnosed with autism by clinicians, but most frequently as developmental delay (33%), delayed speech and language (42%), attention-deficit/hyperactivity disorder (18%) and mental retardation (16%) [24];
- Categorization of GI problems ranged from very mild to severe, but were grouped together anyway. For instance, gastroesophageal reflux disease is known to be higher in autistic children, but in

this study gastroesophageal reflux disease and vomiting were grouped together, possibly diluting any significant difference;

- Much variability exists among physicians regarding inquiries of GI symptoms in children with or without autism;
- It was not possible to include time-to-event data that are important for dietary reactions;
- They failed to assess or compare the duration, severity and recurrence of the GI symptoms between the autistic subjects and the normal controls;
- Researchers did not document diets (especially gluten-/casein-free diets), dietary supplement use or medications with possible GI side effects;
- The misclassification of symptoms and clinical diagnoses may have reduced the overall power of the study;
- They concluded that the significantly greater prevalence of constipation and food intolerance among children with autism could be behaviorally induced.

“...43% (nine out of 21) of children with autism spectrum disorders had altered intestinal permeability (leaky gut) compared with 0% of controls (zero out of 40).”

Propagating medical conclusions based on a single, retrospective study with the above limitations, in light of the fact that GI problems do exist in subsets of children with developmental delayed disorders (including autism), is not only curious, but may jeopardize the health of a subset of children with autism who may have GI symptoms that need to be treated. Recent recommendations for the evaluation and treatment of common GI problems in children with ASD have been published in *Pediatrics* [25]. The researchers state that children with ASD can benefit from the evaluation of abdominal pain, chronic constipation and other GI symptoms.

Financial & competing interests disclosure

Amy C Brown is CEO of Natural Remedy Labs, LLC, a Cengage textbook author and current grant recipient of the Broad Medical Research Program of the Broad Foundation. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

References

Papers of special note have been highlighted as:

• of interest

•• of considerable interest

- 1 Bohmer CJ, Taminiau JA, Klinkenberg-Knol EC, Meuwissen SG. The prevalence of constipation in institutionalized people with intellectual disability. *J. Intellect. Disabil. Res.* 45(Pt 3), 212–218 (2001).
- 2 Schwartzman F, Vitolo MR, Schwartzman JS, Morais MB. Eating practices, nutritional status and constipation in patients with Rett syndrome. *Arq. Gastroenterol.* 45(4), 284–289 (2008).
- 3 Afzal N, Murch S, Thirrupathy K, Berger L, Fagbemi A, Heuschkel R. Constipation with acquired megarectum in children with autism. *Pediatrics* 112(4), 939–942 (2003).
- 4 Ibrahim SH, Voigt RG, Katusic SK, Weaver AL, Barbaresi WJ. Incidence of gastrointestinal symptoms in children with

- autism: a population-based study. *Pediatrics* 124, 680–686 (2009).
- 5 Buie T, Campbell DB, Fuchs GJ 3rd *et al.* Evaluation, diagnosis, and treatment of gastrointestinal disorders in individuals with ASDs: a consensus report. *Pediatrics* 125 (Suppl. 1), S1–S18 (2010).
 - **First practice-based focus article in *Pediatrics* evaluating gastrointestinal disorders in patients with autism spectrum disorders.**
 - 6 D'Eufemia P, Celli M, Finocchiaro R *et al.* Abnormal intestinal permeability in children with autism. *Acta Paediatr.* 85(9), 1076–1079 (1996).
 - 7 Lotan M, Ben-Zeev B. Rett Syndrome. A review with emphasis on clinical characteristics and intervention. *ScientificWorldJournal* 6(6), 1517–1541 (2006).
 - 8 Percy AK, Lane JB. Rett syndrome: model of neurodevelopmental disorders. *J. Child Neurol.* 20(9), 718–721 (2005).
 - 9 Prater CD, Zylstra RG. Medical care of adults with mental retardation. *Am. Fam. Physician* 75(5), 622, 624 (2007).
 - 10 Levy J. The gastrointestinal tract in Down syndrome. *Prog. Clin. Biol. Res.* 373, 245–256 (1991).
 - 11 Hill ID, Dirks MH, Liptak GS *et al.* Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J. Pediatr. Gastroenterol. Nutr.* 40(1), 1–19 (2005).
 - **Practice guideline recommendations for children with celiac disease.**
 - 12 Hilhorst MI, Brink M, Wauters EA, Houwen RH. Down syndrome and coeliac disease: five new cases with a review of the literature. *Eur. J. Pediatr.* 52(11), 884–887 (1993).
 - 13 Cohen WI. Current dilemmas in Down syndrome clinical care: celiac disease, thyroid disorders, and atlanto–axial instability. *Am. J. Med. Genet. C Semin. Med. Genet.* 142C(3), 141–148 (2006).
 - 14 Gravholt CH. Clinical practice in Turner syndrome. *Nat. Clin. Pract. Endocrinol. Metab.* 1(1), 41–52 (2005).
 - 15 Bonamico M, Pasquino AM, Mariani P *et al.* Prevalence and clinical picture of celiac disease in Turner syndrome. *J. Clin. Endocrinol. Metab.* 87(12), 5495–5498 (2002).
 - 16 Gillett PM, Gillett HR, Israel DM *et al.* Increased prevalence of celiac disease in girls with Turner syndrome detected using antibodies to endomysium and tissue transglutaminase. *Can. J. Gastroenterol.* 14(11), 915–918 (2000).
 - 17 Ivarsson SA, Carlsson A, Bredberg A *et al.* Prevalence of coeliac disease in Turner syndrome. *Acta Paediatr.* 88(9), 933–936 (1999).
 - 18 Rujner J, Wisniewski A, Gregorek H, Wozniwicz B, Młynarski W, Witas HW. Coeliac disease and *HLA-DQ 2 (DQA1* 0501 and DQB1* 0201)* in patients with Turner syndrome. *J. Pediatr. Gastroenterol. Nutr.* 32(1), 114–115 (2001).
 - 19 Giannotti A, Tiberio G, Castro M *et al.* Coeliac disease in Williams syndrome. *J. Med. Genet.* 38(11), 767–768 (2001).
 - 20 American Diabetes Association. Standards of medical care for patients with diabetes mellitus. *Diabetes Care* 32(Suppl. 1), S13–S61 (2009).
 - 21 Stenberg R, Dahle C, Lindberg E, Schollin J. Increased prevalence of anti-gliadin antibodies and anti-tissue transglutaminase antibodies in children with cerebral palsy. *J. Pediatr. Gastroenterol. Nutr.* 49(4), 424–429 (2009).
 - 22 Asperger H. [Psychopathology of children with celiac disease.] *Ann. Paediatr.* 197, 346–351 (1961).
 - 23 Gilger MA, Redel CA. Autism and the gut. *Pediatrics* 124, 796–798 (2009).
 - 24 Barbaresi WJ, Katusic SK, Colligan RC, Weaver AL, Jacobsen SJ. The incidence of autism in Olmsted County, Minnesota, 1976–1997. *Arch. Pediatr. Adolesc. Med.* 159, 37–44 (2005).
 - 25 Buie T, Fuchs GJ III, Furuta GT *et al.* Recommendations for evaluation and treatment of common gastrointestinal problems in children with ASDs. *Pediatrics* 125(Suppl. 1), S19–S29 (2010).
 - **Second article in *Pediatrics* focusing on treating gastrointestinal disorders in children with autism spectrum disorders.**