

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 29868

Title: "Can gut microbial modification benefit children with autism spectrum disorders?"

Reviewer's code: 02579092

Reviewer's country: Netherlands

Science editor: Ze-Mao Gong

Date sent for review: 2016-09-01 18:34

Date reviewed: 2016-09-06 16:19

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This manuscript gives an overview of the possible role of gut microbiota in children with ASD, but it lacks some depth in different parts. My main concern is table 1. Although I like the idea of a table, I argue that all statements are solid and well explained in the text. The statement that: oral probiotics change fecal microbiota is in mine opinion not true. The authors give some examples were this is shown, but I can give more examples were it was not shown. See Kristensen et al. Genome Med, 8, 52, 2016. The statement IBS also is associated with an abnormal fecal microbiota is no evidence that probiotics might play a role in the treatment of GI symptoms in ASD> page 10, no reference to the study of Parracho is given, but I guess it is the study published in 2010 in the international journal of probiotics and prebiotics. The study has severe drawbacks, and concluding that they found improvements without discussing the limitations of the study is not correct. In the abstract I miss a result/conclusion. page 5, what did Kushak et al. observe exactly. What can be a reason for the contradictory results? minor comments: - et al needs to be italic and with a . - page 4 laboratory measure of intestinal health? - page 5 ..bolster their conclusion that ASD ?..by assessing -page 7 16S DNA - page 9 anxiety and stress stress - table GI tract -references:some names are incorrect, e.g. ref 30



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

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Title: "Can gut microbial modification benefit children with autism spectrum disorders?"

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Reviewer's country: United States

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Overall, this is a reasonable attempt to review a very complex field. It is generally well-written and well-organized. However, many references are missing, and references sometimes seem to be incorrect, so a careful proof of every reference, and a search for other relevant references, is needed. So, at present, it is a good but not great review, but with work it could become a great review. Page 3, top – state approximately how many total patients came to your clinic, and what type of clinic it is (pediatric GI?) P 5, top – 3 other studies did find abnormal digestive enzymes in ASD vs. controls: Kushak RI et al., Intestinal disaccharidase activity in patients with autism: effect of age, gender, and intestinal inflammation. Autism. 2011 May;15(3):285-94. Epub 2011 Mar 17. Horvath K et al, Gastrointestinal abnormalities in children with autistic disorder," J. Pediatrics 135 no. 5 (1999) 559-563. Horvath K and Perman JA "Autistic disorder and gastrointestinal disease," Curr. Opinion in Pediatrics, 14 (2002) 583. P 5, bottom – the following sentence is unclear: "However, the authors did not bolster their conclusion that ASD by assessing serum or fecal inflammatory markers." P 6 top – GIS in ASD also includes alternating constipation/diarrhea P 6, middle – add ref 26 to list of studies showing correlation of ASD severity with GI symptoms P 7 – top – add reference to 2nd

sentence (re. less diverse microbial community) P 7 middle, - need reference for Kang et al P 7, middle - the following sentence seems to have the wrong references: Gondalia et al did not find differences in the gut microbiome between children with autism and their siblings [46,48,49,50]. P 7, bottom - SCFA's have been measured in ASD - for example, see ref 26 and search for other references P 8, middle - define prebiotics; summarize the findings of the RCT's on probiotics for IBS. Mention that current probiotics are aerobic, derived from milk cultures, not normally a significant part of the human gut microbiome which are primarily anaerobic, and short-lived in the human gut P 10, top - discuss results of UK probiotic trial. Also mention several other probiotic trials: West et al 2013; Ka1uzna-Czaplinska et al 2012; Tomova et al 2015: Also mention study by Sandler et al on 8 weeks of vanco, followed (in some cases) by probiotics Several studies have reported increased use of antibiotics in children with ASD (primarily for ear infections) Konstantareas MM, Homatidis S: Ear infections in autistic and normal children. Journal of Autism and Developmental Disorders 1987, 17(4):585-594. Niehus R, Lord C: Early medical history of children with autism spectrum disorders. Journal of Developmental and Behavioral Pediatrics 2006, 27(2):S120-S127. Adams JB et al., Analyses of Toxic Metals and Essential Minerals in the Hair of Arizona Children with Autism and their mothers, Biol Tr El Res 2006, 110:193-209. Adams JB et al., Mercury, Lead, and Zinc in Baby Teeth of Children with Autism vs. Controls J Toxicol Environ Health 2007, 70(12):1046-51. Adams JB et al., Mercury in First-Cut Baby Hair of Children with Autism vs. Typically-Developing Children. 2008, 90(4):739-753. FMT is mentioned in the abstract but not in the paper; it should be discussed Table 1 is a good summary, but also include data that is negative, such as no difference in calprotectin, mixed data on digestive enzymes, etc.