



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 42534

**Title:** Increased expression of brain derived neurotrophic factor is correlated with visceral hypersensitivity in patients with diarrhea-predominant irritable bowel syndrome

**Reviewer’s code:** 02155135

**Reviewer’s country:** Italy

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-11-08

**Date reviewed:** 2018-11-13

**Review time:** 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The article is interesting. Moreover I suggest to investigate also another factor implicated in the IBS-D to better understand the effects of BDNF. I suggest making



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the different parts in the abstract more similar by length The discussion is very long and it is difficult to read. It is important a revision of grammatical errors in the document.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- The same title
- Duplicate publication
- Plagiarism
- No

##### ***BPG Search:***

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- No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 42534

**Title:** Increased expression of brain derived neurotrophic factor is correlated with visceral hypersensitivity in patients with diarrhea-predominant irritable bowel syndrome

**Reviewer's code:** 02531171

**Reviewer's country:** Ireland

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-11-08

**Date reviewed:** 2018-11-16

**Review time:** 8 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The manuscript entitled 'Increased expression of BDNF is correlated with visceral hypersensitivity in IBS-D patients' by Zhang and colleagues describes increased BDNF



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in mucosal biopsies from diarrhoea-predominant IBS patients. This is an interesting finding but some issues need to be addressed before this manuscript is ready for publication. General comments: carefully check the entire manuscript for consistent formatting, typos, inappropriate use of capitalisation, use of brackets and grammatical errors. Specific comments: Abstract: This needs to be re-written. Provide context to justify the investigation. Less focus on the IBS symptoms in the results section – focus on the novel findings. Reporting all of the results makes the abstract difficult to read and the conclusions difficult to interpret. Methodology: spell out acronyms on first mention (e.g. H&E). Provide additional details on the biopsies – mucosal pinch biopsies or full thickness samples? Provide details on the power calculations used to select group sizes. Results: This group is unusual with a male prevalence (22 vs 9). This should be commented upon. Age is trending towards being different between patients and controls (similar p value to that of depression, which was commented upon). Should ‘media’ pain be ‘median’? IBD-D should be IBS-D – check carefully throughout. Include p values, or symbol of significance on the histogram in figures 2 & 3. Discussion: The discussion needs significant additional work – some specific comments below. Given that afferents innervating the gut terminate below the mucosa, why did the authors choose to examine neural levels from mucosal biopsies? That authors state that ‘BDNF may have an effect on the intestinal neuronal plasticity in IBS-D patients’, what neurons are you referring to? What is the likely source of mucosal BDNF? The authors should comment on whether there is validity in the findings given that the cohort is not representative in terms of gender. Please provide further explanation/context for the phrase ‘Furthermore, males often had more trust in this study than did females.’ The authors comment that ‘was not statistically significant, possibly due to the relatively small sample size’; was the study under-powered? The authors state ‘Furthermore, we also noticed that IBS-D patients usually complained more about abdominal pain when they were taking



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colonoscopy tests, consistent with visceral hypersensitivity.’ This is not an objective measurement. Please provide data or remove this sentence. Please relate the statement ‘Besides, neuromediators (such as substance P, calcitonin gene-related peptide (CGRP) and serotonin), mucosal inflammation and the intestinal microbiota also have effects on visceral hypersensitivity [36, 38].’ to the study findings. Rather than simply summarising the methods and findings relating to the BDNF experiments, discuss them in the context of the literature. In agreement with the comments of the authors on the limitations of the study, I think and PI-IBS patients should be identified, and potentially excluded from this study.

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- No