



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 50316

Title: Nucleus tractus solitarius mediates hyperalgesia induced by chronic pancreatitis in rats

Reviewer's code: 02650654

Reviewer's country: Italy

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-07-31 11:14

Reviewer performed review: 2019-07-31 11:42

Review time: 1 Hour

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 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

Please specify the current meaning of "sensitization" and of "hypersensitivity", as used in clinics.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 50316

Title: Nucleus tractus solitarius mediates hyperalgesia induced by chronic pancreatitis in rats

Reviewer's code: 03026651

Reviewer's country: Lebanon

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-08-01 04:22

Reviewer performed review: 2019-08-04 08:51

Review time: 3 Days and 4 Hours

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 Grade E: Do not publish	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

SPECIFIC COMMENTS TO AUTHORS

Thank you for this interesting basic science paper, study and review

INITIAL REVIEW OF THE MANUSCRIPT



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 50316

Title: Nucleus tractus solitarius mediates hyperalgesia induced by chronic pancreatitis in rats

Reviewer's code: 02734287

Reviewer's country: Croatia

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-08-03 19:36

Reviewer performed review: 2019-08-04 10:00

Review time: 14 Hours

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 checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" 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 checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Valuable insight into mechanisms of processing of pancreatic pain in chronic pancreatitis in rats. Potential use of results includes targeting caudal nucleus of solitary tract for the treatment of pain in chronic pancreatitis.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 50316

Title: Nucleus tractus solitarius mediates hyperalgesia induced by chronic pancreatitis in rats

Reviewer's code: 03257825

Reviewer's country: United States

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-08-02 14:18

Reviewer performed review: 2019-08-05 19:50

Review time: 3 Days and 5 Hours

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

SPECIFIC COMMENTS TO AUTHORS

In this manuscript entitled "The caudal nucleus of the solitary tract mediates visceral hypersensitivity induced by chronic pancreatitis in rats", the authors showed that some neuroplastic changes in the caudal nucleus of the solitary tract contributed to chronic



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pancreatitis-induced pain syndrome. The finding is interesting and the paper is well written. However, some issues need to be addressed. (1) In chronic pancreatitis, the progressive impairment of pancreatic tissues lead to the development of a chronic pain syndrome. However, the longest time point of studying NR2B and GluR1 expressions in Fig 4 is 4 weeks, which already have a trend of down-regulation. What are the expression levels of NR2B and GluR1 at a later time point? If their expressions are further decreased at a later time point, how can we explain the role of NR2B and GluR1 in the chronic pain syndrome? (2) The authors showed that deactivating excitatory neurons within NTS alleviated the pain in chronic pancreatitis. This approach, however, could block the pain caused by peripheral sensitization and pancreatic neuropathy. This should be discussed. (3) It has been shown that 80% of TNBS-treated rats exhibit morphological changes mimicking features of chronic pancreatitis in humans. The percentage of TNBS-treated rats that have had the pathological changes mimicking chronic pancreatitis in this study should be shown.

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[Y] No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 50316

Title: Nucleus tractus solitarius mediates hyperalgesia induced by chronic pancreatitis in rats

Reviewer's code: 00182054

Reviewer's country: Germany

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-07-31 13:47

Reviewer performed review: 2019-08-06 19:01

Review time: 6 Days and 5 Hours

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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input 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 checked="" 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 checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The following points should be corrected: 1) The article is written well but it is too long to read; therefore the text should be summarized, especially in the methods part. 2) Small typing mistakes should be corrected like on page 6 (celiac lexis not plexus) and



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(An increasing not A increasing). 3) A list of Abbreviations is missing. 4) Graphic 1 shows multiple Brain slices with immunochemical staining, but the small pictures are not as informative as the bar graph, this needs modification.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 50316

Title: Nucleus tractus solitarius mediates hyperalgesia induced by chronic pancreatitis in rats

Reviewer's code: 00070583

Reviewer's country: Romania

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-08-03 21:14

Reviewer performed review: 2019-08-07 08:40

Review time: 3 Days and 11 Hours

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

SPECIFIC COMMENTS TO AUTHORS

The study by Yang Bai et al provides evidence of the role of the nucleus of the solitary tract in the visceral hypersensitivity induced by chronic pancreatitis. It is a well-conceived study that respects all major regulatory and scientific rigors. The



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methodology is sound and statistics are appropriate. The number of study animals is sufficient. Experiments were done properly and results are satisfactory. The manuscript is well written, grammar and style are sufficient. Minor corrections can be made (for instance, one word in the core tip has an extra "s"). Minor points: Was chronic pancreatitis achieved in all treated rats (i.e. histologically-proven pancreatic lesions)? Regarding the time-frame of the experiments, in particular experiment 3: Have the authors considered following the values after these 28 days? The manuscript can be published with minor future corrections, being of interest for a certain part of the scientific community.

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