



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Psychiatry

**Manuscript NO:** 38857

**Title:** Glutamate transporters, EAAT1 and EAAT2, are potentially important in the pathophysiology and treatment of schizophrenia and affective disorders

**Reviewer's code:** 02465274

**Reviewer's country:** United States

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-03-19

**Date reviewed:** 2018-03-23

**Review time:** 4 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 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 Grade E: Do not publish	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 type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Interesting work addressing a very important topic in the intersection of basic sciences and clinical research.



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- [Y] No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Psychiatry

**Manuscript NO:** 38857

**Title:** Glutamate transporters, EAAT1 and EAAT2, are potentially important in the pathophysiology and treatment of schizophrenia and affective disorders

**Reviewer's code:** 02445267

**Reviewer's country:** Italy

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-04-21

**Date reviewed:** 2018-04-23

**Review time:** 2 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 checked="" 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 main feature and merit of this well done and well written review is that of considering the solely on the Na<sup>+</sup>- dependent EAAT family. Literature search was complete and appropriate. The introduction section should be shortened and focused



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mainly on psychiatric disorders. In the section "EAATs in psychiatric illness" I would suggest authors to add data regarding OCD, for this disorder papers regarding the consequence of excessive release of glutamate into the synapse and glutamate-mediated neuronal degeneration are available.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Psychiatry

**Manuscript NO:** 38857

**Title:** Glutamate transporters, EAAT1 and EAAT2, are potentially important in the pathophysiology and treatment of schizophrenia and affective disorders

**Reviewer’s code:** 02445242

**Reviewer’s country:** India

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-04-21

**Date reviewed:** 2018-05-03

**Review time:** 12 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 checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" 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 checked="" 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**

This was on the whole a well written review, but I had some concerns about its content and organization. • Firstly, there have been several recent reviews on the subject e.g. - Takahashi et al. Glutamate transporter EAAT2: regulation, function, and potential as



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a therapeutic target for neurological and psychiatric disease. Cell. Mol. Life Sci. (2015) 72: 3489. <https://doi.org/10.1007/s00018-015-1937-8> - O'Donovan et al. The role of glutamate transporters in the pathophysiology of neuropsychiatric disorders. npj Schizophrenia (2017) 3:32 ; doi:10.1038/s41537-017-0037-1 The authors of the current review need to ensure that their review has something new to add. • Secondly, I found that a relatively greater proportion of the review was devoted to basic sciences aspects of the topic and comparatively less devoted to the clinical implications among psychiatric disorders. Some of the molecular and genetic aspects appeared too complicated to me. I wonder whether a review on glutamate transporters in the pathophysiology and treatment of psychiatric illnesses requires to go to this depth to discuss neurobiological aspects, or whether this part can be shortened and simplified. • Finally, the authors have covered the role of glutamate transporters in schizophrenia and mood disorders, but (somewhat inexplicably) left out a host of other psychiatric disorders where abnormalities of glutamate transporters may be involved, such as anxiety disorders including OCD and PTSD, neurodevelopmental disorders such as autism and ADHD, neurodegenerative disorders such as dementia, substance use and chronic pain disorders. The authors may want to cover these, at least briefly.

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**Name of journal:** World Journal of Psychiatry

**Manuscript NO:** 38857

**Title:** Glutamate transporters, EAAT1 and EAAT2, are potentially important in the pathophysiology and treatment of schizophrenia and affective disorders

**Reviewer's code:** 02445209

**Reviewer's country:** Czech Republic

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-04-21

**Date reviewed:** 2018-05-07

**Review time:** 16 Days

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 type="checkbox"/> Accept	<input type="checkbox"/> Onymous
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		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
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			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

Dear authors, I only have a few comments on your manuscript: In the part EAAT1, you write about the EAAT1 gene. Is there any epigenetic knowledge related to this gene? The same question related to the part EAAT2 gene. Best regards The reviewer



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