

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 9688

Title: New insight in expression, transport, and secretion of BDNF: Implications in brain-related

Reviewer code: 02445242

Science editor: Xiu-Xia Song

Date sent for review: 2014-02-24 20:55

Date reviewed: 2014-03-03 01:18

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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 type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

ESPS Manuscript NO: 9688 Entitled - New insight in expression, transport, and secretion of BDNF: Implications in brain-related diseases

COMMENTS FOR AUTHORS The authors have reviewed both converting (from gene to mature protein) and spatial regulation (transport and secretion) processes of BDNF. They have highlighted recent findings suggesting implications of BDNF in the pathophysiology of the brain-related diseases.

GENERAL COMMENTS (1) The importance of the research and the significance of the research contents This is an area, which has generated considerable amount of research attention. Hence, a review on this subject is timely. (2) The novelty and innovation of the research There are other recent reviews on the subject. To add to them, the authors need to enlarge the sections related to BDNF alterations in individual disorders.

(3) Presentation and readability of the manuscript Currently, this is adequate, but can be improved. (4) Ethics of the research No particular ethical issues involved.

SPECIFIC COMMENTS Title and abstract Adequate Review The initial sections on BDNF gene structure, transcriptional regulation in BDNF gene, and BDNF transport and secretion are well addressed. However, to link this basic physiology of BDNF with alterations in disease states, it would be helpful if the authors could add: 1. A section on neuronal functions of the BDNF in the developing and mature brain. This could include how BDNF acts as a signal for proper axonal growth during development, and how BDNF also serves essential functions in regulating synaptic plasticity in the mature brain,

including its role in learning and memory processes. 2. A section on BDNF polymorphisms, including the most common BDNF single nucleotide polymorphisms (SNPs) resulting in the Val to Met (V66M) protein variant, which is associated with a decrease in the activity-dependent secretion of BDNF, and processing of pro-BDNF to mature BDNF. 3. Actions of the pro-BDNF The sections on implication of BDNF alterations in brain diseases could also be enlarged. Firstly, the influence of BDNF on basic processes such as cognition and memory and stress regulation needs to be mentioned. The link with early trauma and altered HPA axis reactivity would also be helpful in understanding the role of BDNF in various psychiatric disorders. Secondly, the list of neuropsychiatric conditions potentially associated with alterations in BDNF needs to be enlarged. At the very least, its role in Parkinson's disease, stroke, epilepsy, bipolar disorders, substance use, neurodevelopmental disorders, eating disorders and anxiety disorders, and the effects of lithium and electroconvulsive therapy on BDNF need some mention. Thirdly, for each of the disorders covered, e.g. schizophrenia, major depression, or Alzheimer's disease, the findings with regard to the complex and often contradictory BDNF alterations need to be elucidated. - For example, in Alzheimer's disease, although reductions in BDNF or TrkB expression have been found in neurons of the hippocampus and the frontal and temporal cortices, reports have been variable due to brain cohort differences and the variable techniques used to measure their expression in Alzheimer's disease. - In major depression variable expression of BDNF/TrkB has been reported in different brain regions. Animal models have suggested a role of altered stress regulation, as well as effects of antidepressants on BDNF. The contribution of the Val to Met (V66M) polymorphism to the pathological features of major depression, or to suicidality remains unclear. - Similarly, in schizophrenia, most of the studies measuring serum BDNF have documented lower concentrations in patients, but increased or unchanged levels have also been reported. The association between the Val to Met (V66M) polymorphism and schizophrenia is not a consistent finding either. There is s

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Title: New insight in expression, transport, and secretion of BDNF: Implications in brain-related

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

COMMENTS TO AUTHORS

This is a very good manuscript, reviewing the biological role of BDNF in health and disease. Some minor points will help to improve the manuscript: -A figure describing graphically signaling pathways modulating the regulation of BDNF transcription and secretion. -A table describing main evidence for involvement of BDNF and brain diseases in humans. -A table describing main evidence for involvement of BDNF in cell and animal models for brain diseases in humans. -A global description of existing genetic variants in human BDNF gene will be helpful.