Nov 15, 2014

Prof. Fang-Fang Ji, Science Editor, Editorial Office

Baishideng Publishing Group Inc

Dear Professor,

Please find enclosed edited and revised manuscript in Word format (file name: ESPS Manuscript NO 14252-revised edited).

Title: Peptides from adipose tissue in mental disorders.

Authors: Andrzej Wędrychowicz, Andrzej Zając, Maciej Pilecki, Barbara Kościelniak, Przemysław Tomasik

Name of Journal: *World Journal of Psychiatry*

ESPS Manuscript NO: 14252

The manuscript has been improved according to the suggestions of reviewers:

The comments of both reviewers were similar, therefore some of them were grouped:
(1A) Please describe mental disorders in detailed.
(1B) what kind of mental disorder in detail are association with adipokines ?
AND
(2A) Please supply pathogenesis between adipokines and mental disorders (from animal and human studies).
(2B)what kind of pathogenesis of adipokines are strong association between animal study and human study in mental disorders ?

Thank you for this comments. We have developed and fully reconstructed introduction according to suggestions

(3B) "*This research still encounter a number of methodological problems often translate into contradictory results of various studies" Please supply proofs of these contradictory results of various studies (add references).*
The references were added in the mention place.
This info is developed in the subsequent paragraphs, – i.e.
a. Conflicting results regarding total adiponectin levels were found in anorexia nervosa (AN) patients. These data have reported that levels in adults with AN were decreased, increased or unchanged.
b. Assessing the adiponectin level in patients with schizophrenia, different results were obtained, regarding the state of nutrition of the patients.
c. However, there are still controversial data whether adiponectin crosses the blood-brain-barrier.

(4B) "*Recently, only one clinical study demonstrated that some AD patients have elevated levels of adiponectin in both plasma and cerebrospinal fluid [37]" Why the levels of adiponectin elevated in AD?*
Yes, this is very important question, however authors (Une et al.) of the mention paper left this question open, and several others as well,
as is listed below:

"Because of the limited data, it is hard to lead to a conclusion whether adiponectin is synthesized intrathecally or whether it flows into the intrathecal space from plasma passing through BBB. It is definite, however, that adiponectin exists in CSF, and further investigations will be needed to clarify where adiponectin is produced, and how it circulates. We have not completely elucidated the pathomechanism of the high adiponectin levels in MCI and AD."

The final suggestion presented by authors (Une et al.) of this paper that *the levels of adiponectin, higher in plasma in MCI and AD ... could be related to the ... weight loss, decrease in fat tissue, and appetite change, observed in the early stage of AD* are very difficult to defense in the light of the same BMI in control and AD group. <u>Therefore we suggest to present this interesting observations without any summary/comment.</u>

(3A) *There are many kinds of adipokines, why you choose these six adipokines such as adiponectin, leptin... ? Are any other adipokines associated with mental disorders not included in this review article ? Why authors chose visfatin, adipsin, FABP-4 (not other adipokies) are not associated with mental disorders ?*
(5B) *"No significant association was found between the concentration of circulating visfatin and eating disorders ..." Now that you did not find any association between visfatin, adipsin, FABP-4 and mental disorders, why you choose these adipokines?*

I am very grateful for these comments. And I feel some kind of shame. These peptides were chosen arbitrarily, due to our scientific interest as a potential direction for OUR future study. Yes, reviewers are completely right that was not fair, and it had need corrections. The paragraph about others adipokines was added, and paras about adipsin as well FABP-4 were diminished and incorporated to this above.

(4A) *Please quote the references in the latest five years as possible as you can.*

A dozen and a half of older references were discarded and over two dozens from last 3 years were added

Some improvements according to editorial policy were done.

The language of manuscript was revised by the Proof Reading Service (UK), certificate is attached as a separate file.

Text was checked with PlagScan without any significant indications. Some small similarities (block of few word only) are normal in reviews.

Thank you again for the possibility of publishing our manuscript in the *World Journal of Psychiatry*

Sincerely yours,

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