Reviewer's report

Title: Plasma Prolyl Endopeptide Activity in Children with Autistic Spectrum Disorders

Version: 5 Date: 8 December 2004

Reviewer: Vijendra Singh

Reviewer's report:

General

Authors have attempted to address questions and concerns raised by this reviewer previously but there are still some important problems (see Discretionary Revisions below).

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

The following revisions would improve the quality of the manuscript:

1. To better describe their finding, the title should begin with "Alterations of....." instead of "Altered Levels of......."
2. In the Background, second para, it would be appropriate to say that "They were classified...... in DSM-IV" and cite Ref. #6 only, simply because the DSM-IV is the updated revision.
3. In the Background, second para (last line), the reference #9 cited for "a cascade of complex gene-interactions" is not related to this topic. They should either find a more suitable reference or simply leave the statement without a citation. The reference #9 is appropriate for the topic of "Oxytocin and related peptide hormones in autism".
4. Then, continuing on the next page under Background, authors should delete their unpublished manuscript about the "high levels of arginine-vasopressin (AVP)" even if they have already submitted their manuscript for publication. But if this manuscript has been found to be accepted for publication then they can leave it in and list the reference in the list by saying "Accepted for Publication." If they really feel confident then I suppose they can say within brackets as "(our unpublished observation) and so it would be something like this "high levels of arginine-vasopressin (AVP)(our unpublished observation)".
5. Authors have added a new reference which is Ref. #15. There is no need for that and it should be excluded.
6. Under Discussion, the "Blood Brain Barrier" should be described as "blood-brain barrier (BBB)."
7. The Conclusions should be changed to something like this: "Our preliminary finding suggests a role for PEP enzyme in the pathophysiology of autism but further research should be conducted to establish its role in the aetiology of psychiatric and neurological disorders, including autism and related spectrum disorders."

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Discretionary Revisions (which the author can choose to ignore)

By and large, the authors have responded to previous questions adequately but it would be
important for them to clarify the health and treatment status of "Control Children" in their study. As stated by authors, the control children are children who were attending hospital for other treatments, which means they were "non-ASD children" but not "healthy children". Thus the authors need to comment on the validity of their data resulting from non-ASD children, i.e., could the disease status of non-ASD children and the nature of treatment given to them potentially alter the level of PEP enzyme activity. This is just as important an issue as their observation and if the control value is not appropriate then their finding becomes scientifically unsound.

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.