Reviewer's report

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

Version: 5 Date: 18 December 2004

Reviewer: Lonnie Zwaigenbaum

Reviewer's report:

General

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

Second review (with reference to recommendations for major revisions from the first review)
1. The authors' hypothesis is that "altered activity of proteolytic enzymes, such as PEP, in children with ASD (children <12 years) might lead to the degradation of some specific neuropeptide hormones and these affect social behaviour and communication". This hypothesis is not tested directly in the paper, but I accept that the authors' initial hypothesis was that there is altered PEP activity in children with ASD.

2. The authors still do not state how they selected the 18 children with autism, and in particular, what medical treatments they were receiving that required anaesthesia – I don't mean to harp on this, but was this a treatment related to ASD, or was this simply a convenience sample of children with ASD undergoing unrelated medical procedures? Also, was there any independent review of diagnosis (or requirement that the diagnosis was by a clinician who specialized in the area etc.)?

3. The authors have noted no gender differences and the possibility that GA may affect measurement. There is some description of the Scand J Clin Lab Invest reference, but there is still no information about the reliability/precision of measurement – which important to report given that the primary finding is increased variability in the autism group.

4. The authors note that both increased and decreased PEP activity has been associated with neuropsychiatric disorder, so it is plausible that increased variability in PEP could increase risk of ASD - that's fine.

Note that only points 2 and 3 require further revisions.

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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)

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Discretionary Revisions (which the author can choose to ignore)

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What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Acceptable
Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests