Reviewer's report

Title: No interaction between Serotonin Transporter Gene (5-HTTLPR) Polymorphism and Adversity on depression among Japanese Children and Adolescents

Version: 1 Date: 26 March 2013

Reviewer: Brett M McDermott

Reviewer's report:

This is an important area of research and the question is well defined. The methods are appropriate but to account for clinicians being able to generalise these findings some changes are suggested that will clarify issues especially around selection bias. The data is very sound, however, there are some minor errors in describing the data such as the odds ratios. The discussion and conclusion is well balanced. I would have preferred some more comments about allele frequencies by culture given that this was a somewhat unusually low number of LL’s (I know this is mentioned to some extent). The limitation is the homogenous nature of the group. I think the writing is very acceptable.

Major compulsory
1. Page 9, first line of subjects I note that the patients were referred to a (one assumes) research orientated laboratory and some comments probably should be made about potential referral bias around severity, treatment resistance, possible higher SES etc.

2. Page 17 results section, second paragraph There was a odds ratio quoted that was in the millions - clearly there is a missing decimal point, similarly further down the paragraph these is another odds ratio of about 1 billion which I suspect is not correct

3. Page 9, bottom paragraph I note that the control group gender split is very different to the study group (study group approximately 2 boys to 3 girls whilst control group is 2 boys to 1 girls). This may influence the findings.

Minor essential
1. Page 8, last line of first paragraph Hypotheses are often unidirectional whereas this hypothesis is more bidirectional.

2. Page 10, middle paragraph I note that severe psychopathology was measured by a proxy measure of a paediatric psychiatrist referral. It would be worthwhile to note if the group had high levels of suicidality and/or comorbidity which would make them more like a typical clinic population.

3. Page 11 It would be useful to know for measures like the WISC-III whether the clinicians administrating this was blinded to active or control groups. I note some
empirical data is introduced under the heading child behaviour checklist on page 11 and wondered if that should be in the results section.

4. Page 12, the section ‘early adversity’ I note that no control subjects mother had high early adversity - I thought this environmental descriptor could have been more clearly defined.

5. Page 13, second sentence. I note that the group was ethnically homogenous - this is an important consideration for generalising the findings and could probably be more emphasised in the discussion.

6. Page 14 first paragraph I was surprised the observed genotype was similar to the expected Hardy Weinberg equilibrium given that there was only 3% (n=7) LL cases).

**Level of interest:** An article of importance in its field

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare I have no competing interests.