Author’s response to reviews

Title: No Evidence of Association Between Catechol-O-Methyltransferase (COMT) Val158Met Genotype and Performance on Neuropsychological Tasks in Children with ADHD: A case-control study

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PDF covering letter
Dear Dr. Puebla,

Re: MS: 2087104726282591

Following receipt of your email, dated 16/04/04, I am writing to return our revised manuscript taking into consideration and addressing the points made by the two reviewers.

With respects to this, we provide a point-by-point response to the reviewers comments:

**Reviewer 1:**

**Minor Essential revisions:**

1. We acknowledge that working memory was not directly assessed and have noted this (pg 5 & 7).

2. Both the forward and backwards sections of the Digit Span were performed and this information has been added (pg 7).

3. We agree with the reviewer that using the WCST as in the Egan paper would have been preferable. However, this test was not included in the original protocol. Further acknowledgement of this limitation has been included in the discussion section (pg 10).

4. The CPT used in this study was a CPT-Identical pairs with display durations of 1 second and Inter-stimulus delays of 1.5 seconds. These details have been added to the methods section (pg 7).

5. The neuropsychological tests were performed in school (in almost all cases). This information has been reiterated (pg 7).
Discretionary revisions:

1. We note the reviewer’s point that age may be an important factor and have reanalysed the data using age as a covariate. This did not alter the results and this has been noted (pg 8).

2. Psychiatric diagnosis was performed by trained, graduate level, Psychologists. This has been noted (pg 6). Although we acknowledge that the CHATTI may be associated with diagnostic error, this assessment was used to ascertain pervasiveness of symptoms only, for which it has good reliability. This has been noted (pg 6).

3. Demographic data has been summarised in greater detail in our previous papers. In the interests of succinctness, it was not repeated here. Readers have been referred to this previous paper (pg 7). Male patients were analysed separately without alteration to the results. Therefore, we decided to utilise the full sample in this study. References to the male only analysis are on page 8, which indicates that further information can be requested from the authors.

Reviewer 2:

Discretionary Revisions:

1. The reviewer makes a valid point about power. Comments regarding power calculations have been added to the discussion section.

2. Although ethnic stratification may be a problem, our sample was caucasian to the index child’s grandparents and so it is unlikely in this case. This information has been added (pg 6). A comment on the possibility of genotyping parents and performing family-based analyses has been included (pg 10).

We trust that we have satisfactorily addressed all the points made by the reviewers and revised the manuscript accordingly.

If further information or changes are necessary, please do not hesitate to contact us.

Thank you for your interest in our paper,

Kate Langley