Author’s response to reviews

Title: Low-Level Environmental Lead Exposure in Childhood and Adult Intellectual Function: A Follow-up Study

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Author’s response to reviews: see over
Drs. Grandjean and Ozonoff,

Please find enclosed a revision to manuscript entitled “Low-Level Environmental Lead Exposure in Childhood and Adult Intellectual Function: A Follow-up Study.” We very much appreciate the comments and suggestions from the two reviewers. Below are point-by-point responses to their comments and concerns.

**Editorial Team comments:**

1. Please consider including results and comments on the association of lead exposure with IQ subtest scores.

We have included results and comments on the association of lead exposure with IQ subtest scores (page 8, paragraph 3).

2. The title page, subheadings and authors’ contribution sections are not in accordance with instructions.

We have reformatted the title page, subheadings and authors’ contribution section in accordance with a recently accepted article.

**Reviewer 1:**

1. The authors should consider describing how this study was instrumental in experts concluding that the 2-year blood lead concentration was the key blood lead variable for predicting subsequent intellectual abilities.

We have added a paragraph to the background that we hope will place the Boston cohort in historical perspective (page 3, paragraph 2).

2. It would be helpful if the authors provided the confidence limits, the p value or both in the text when describing how inclusion of maternal IQ affected the relationship between Full-Scale IQ and average childhood blood levels.

We have included the confidence limits in the text. (page number, para, line).

Suggested additional analyses:

3. The first analysis would test whether the pattern of exposure is an important modifier of lead exposure (see: Hornung, EHP 2009). This could be done by simply adding the ratio of the 10-year or 4-year blood lead concentration over the 2-year blood lead concentration to the model with average childhood blood lead concentration.
We performed the analysis suggested by the reviewer. The ratio of 10 year :2 year lead (and separately, 4 year:2 year lead) to the model with average late childhood level did not show a significant relationship between the ratio and IQ. This is described on page 6, paragraph 2 (methods) and page 9, paragraph 2 (results).

4. The second analysis would be to explore the relationship between Full-Scale IQ and average childhood blood lead levels for the subjects who had a blood lead concentration of <10 micrograms per deciliter.

We attempted to explore the relationship between IQ and lead levels for subjects who had blood lead concentrations of <10 micrograms per deciliter only. There were only 5 subjects who had lead levels of <10 micrograms per deciliter at each measuring point, and so we were not able to perform this analysis. We made a note of this in the text (page 7, paragraph 2).

Reviewer 2:

1. It is unclear what to this reviewer what the authors mean when they refer to lead as a “versatile neurotoxicant.”
We have removed the word “versatile” (page 3, paragraph 1) and refer to lead as a potent neurotoxicant.

2. To avoid confusion, please consider labeling the mean of 4 and 10 year blood lead concentration as Average Late (or later) Childhood Blood Lead.
We have labeled the mean of 4 and 10 year blood lead concentration as average late childhood blood lead throughout the manuscript and tables.

3. Given the small sample size, would it not be more appropriate to use percent change (e.g. 10%) in the lead regression coefficient(s) rather than p-values.
We appreciate the concerns of the reviewer on this point. We decided to keep p-values in our paper. As much as they are overused, they do tell us the difference we observe is (or is not) a result of ordinary sample variation.

4. Again, given the small sample size I think providing parameter estimates and standard errors rather than p-values would be more appropriate.
Please see the above answer

5. Table 1. Blood lead concentrations are arithmetic means -- if so, please indicate.
We reformatted our table to better describe the measures.

6. Table 2 and in general: Do the authors think it is interesting that Performance IQ seems to be more consistently and strongly associated with childhood blood lead concentrations?
We have presented and commented on the relationship between blood lead levels and IQ subtest scores (page 8, paragraph 3).

7. Figure 1: Are these data restricted only to those in your current analyses (n=43)? Some of the outlying blood lead concentrations are quite high (more than 60 micrograms/deciliter) and there is no mention how this was handled in the analyses.
We thank the reviewer for his close attention to the figures. We have updated Figure 1, which now is correctly restricted to only the subjects in our current analysis.

8. Pages 7-9 – grammar errors.
We have corrected the errors found by the reviewer.

Thank you very much for your continued consideration of this manuscript. We look forward to your reply.

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