Reviewer’s report

Title: Prenatal and postnatal bisphenol A exposure and social impairment in 4-year-old children

Version: 0 Date: 01 Feb 2017

Reviewer: Joseph Braun

Reviewer's report:

Reviewer Comments

This well-written manuscript examines the association of prenatal and concurrent urinary BPA concentrations with 4-year old children's social behaviors in 304 mother-child pairs from Korea. The authors report null findings when examining linear associations between prenatal or concurrent BPA concentrations among all children, but report that: 1) concurrent BPA is associated with poorer social behaviors in girls, but not boys, 2) prenatal BPA is associated with poorer social behaviors at concentrations >3.0 ug/g, and 3) associations between BPA > 3 ug/g and social behaviors appear to be stronger in girls than boys. The strengths of this study include the prospective design, pre- and postnatal BPA measurements, and reasonable sample size. The major limitations include examination of individual-item level data from the K-SCQ, over-interpretation of the non-linear associations, no formal testing of whether these non-linear effects are significant, and absence of specific methodological details.

Major Comments

1. It is not typical to examine individual level data from psychometric tests like the K-SCQ (Table 2). Conceptually, these individual items were chosen for the K-SCQ because as a whole they represent the construct of social behaviors; however, when examined by themselves they do not. Pragmatically, I believe that their inclusion detracts from what could be a succinct manuscript. I strongly recommend dropping these individual items and focusing on the three summary scales.

2. Did the authors formally test the non-linear association between prenatal BPA and social behaviors? Based on the presented results, I do not believe that there is sufficient evidence to declare a non-linear association. It appears that I could fit a straight line within the 95% CI of the smoothed regression line (Figure 1a) with a great deal of imprecision at the lowest and highest concentrations relative to the median BPA concentration. In addition, there appears to be a positive association between prenatal BPA and SCQ scores at the lowest levels of BPA. What do the authors make of this?
If the authors can verify that the association is truly non-linear, then some caveats around the interpretation on pages 12 and 13 is necessary. The authors should discuss that the range of BPA exposures in this study was quite narrow and this makes it surprising that there is a non-linear association given the narrow range of exposure. If anything, Moreover, the exposures experienced by these mothers and children was not likely to overlap with the doses typically employed in animal neurotoxicity studies. Specifically, low-level human exposure is estimated to be on the range of <1 ug/kg/d (see work by LaKind, Stacy, and others). Animal studies typically employ doses of 5 to 50 ug/kg/d.

3. If the authors do indeed verify a non-linear association, I request that they formally test the difference in association between boys and girls.

4. The authors need to acknowledge that there is the potential for reverse causality of the postnatal BPA-SCQ association. For instance, children with more behavior problems may have different dietary or mouthing behaviors that increase their BPA exposure.

Minor Comments

1. Introduction, line 24: The work of Braun et al, EHP, 2014 also examined social behaviors in children.

2. Introduction, line 9: The detection of BPA in serum does not necessarily indicate exposure and could be indicative of contamination (see the work of Calafat).

3. Introduction, Line 34: Please refer to the official diagnosis of this disorder: autism spectrum disorders.

4. Introduction: Line 36: The European Union did not conduct this study, but it was an extrapolation of the effect and cost of EDCs on neurodevelopmental disorders in the European Union.

5. Methods, page 6: Please clarify why only 2,085 children were selected for follow. Moreover, the high rate of loss to follow-up is troubling (~70%) and should be formally evaluated and discussed. Specifically, could you please compare the baseline characteristics of those not followed-up with those who were?

6. Methods, page 7: Was free and conjugated BPA measured? If so, how was the deconjugation done?
7. Methods, page 8: What log base was used? Was the creatinine-standardized BPA concentration log-transformed?

8. Methods, covariates: How were these covariates selected? Did the authors have data on maternal smoking during pregnancy? If so, I suggest adjusting for it.

9. Conclusion: I think the policy level statement should be dropped and a summary of the strengths and limitations should be provided.

Level of interest
Please indicate how interesting you found the manuscript:

An article of importance in its field

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interest.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report
including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal