Reviewer’s report

Title: Of decrements and disorders: assessing impairments in neurodevelopment in prospective studies of environmental toxicant exposures

Version: 1
Date: 8 December 2014

Reviewer: Joseph Braun

Reviewer’s report:

Reviewer Comments
This commentary describes the strengths and limitations of using continuous measures of neurobehavioral traits in studies of environmental toxicant exposures and child neurodevelopment. The authors use the illustrative example of autism spectrum disorders (ASD) to make a compelling argument to study neurodevelopment as a continuum and not simply as a yes vs. no clinical diagnosis. The content of this article is very appropriate for this journal, fills a gap in the current literature when it comes to justifying the use of continuous measurements, and will be of broad interest to the field of children’s environmental health.

Minor Essential Revisions
1. The authors consider clinical diagnosis and continuous traits as the only two measures of neurodevelopment, but there is a large body of literature related to neuroimaging and neurobehavioral traits. In the interest of completeness, I suggest adding discussion of the strengths and limitations of this new and emerging tool that is being used to study environmental toxicants and neurodevelopment (e.g., Rauh, PNAS, 2012 and Cecil, PLoS Med, 2008).

2. I suggest adding some additional discussion of the strengths and limitations of parent-reported measures of neurobehavior. While these are not explicitly mentioned in the text, they are the primary mode of assessing continuous dimensions of social communication and restricted/repetitive patterns of behaviors and interests. This seems important in the context of ASD-related behaviors since the measured value of a trait could be impacted by the content/validity/reliability of the questionnaire or the reporter (teacher vs. parent).

3. Arguably, the nested case-control, case-cohort, or enriched-risk cohort designs are alternative approaches that could be used to study the risk of clinical disorders without the disadvantages of case-control studies that the authors point out. Could the authors please comment on these alternative methods’ strengths and limitations?

Discretionary Revisions
1. Abstract: Specify what standardized psychometric tests are an alternative to.
2. Abstract, last sentence: I suggest changing the phrase “discovery of the role of.” It is clear that some environmental toxicants are risk factors for adverse
neurodevelopment (e.g., lead).

3. Background, 2nd sentence: Is there a citation for the brain being a more sensitive target than other organs?

4. Background, section 1: The amount of measurement error in different measures of exposure is worth mentioning. For instance, some exposures are measured with little error prospectively (e.g., polychlorinated biphenyls), but others likely have substantial error (e.g., bisphenol A). I suggest mentioning that there are not any valid or reliable methods to retrospectively assess exposure to some specific chemicals.

5. Background, section 2, 2nd sentence: I believe the authors are trying to say that the exposure distribution in a case-control study could differ for non-causal reasons related to the sociodemographic or economic factors. I suggest being more explicit if this is what the authors intended to say.


7. Summary, 2nd to last sentence: What is meant by validity standards?

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Declaration of competing interests:**

I declare that I have no competing interests.