Author’s response to reviews

Title: An in vivo animal study assessing long-term changes in hypothalamic cytokines following perinatal exposure to a chemical mixture based on Arctic maternal body burden.

Authors:

Shawn Hayley Dr (shayley@ccs.carleton.ca)
Emily Mangano Ms (emangano@connect.carleton.ca)
Geoff Crowe Mr (gcrowe@connect.carleton.ca)
Nanqin Li Dr (NLi@hc-sc.gc.ca)
Wayne Bowers Dr (Wayne.J.Bowers@hc-sc.gc.ca)

Version: 3 Date: 24 June 2011

Author’s response to reviews:

We thank the editor and reviewers for their careful attention and useful comments to our manuscript. Please find below our response to the last round of reviewer comments. We have underlined the two sections (one in the results and one in the discussion sections) where we have made final changes in response to the reviewer comments. We have also tried to be especially careful in observing and correcting all formatting as pertains to the journal as highlighted in an email from the editor.

best

Shawn Hayley

Response to reviewer comments (Version 2)

Reviewer 1 has no further comments and finds the paper acceptable.

The second reviewer finds that the manuscript was “...carefully revised...” and has only two additional points.

1. Specifically, the reviewer suggests that there was a misinterpretation of the new LPS data presented for IL-1β in Figure 1. Specifically, the PCB + LPS and full Mix + LPS treatment groups were 2 fold higher than the LPS + vehicle group, but we report no significant difference between the groups.

Our comment in the manuscript stems from the fact that there were actually no significant differences between the groups (as assessed using ANOVA), nor
were any of the follow up comparisons significant. This finding is largely owing to
the variability evident within a number of the groups (likely suggesting that some
animals were responders and some not). Hence, the data are somewhat
inconclusive and it would be scientifically incorrect to state significant differences
between the LPS treated groups.

That said, we do agree with the reviewer in that there was a definite trend
towards increased levels in the LPS + PCB and LPS + full Mix groups and and
this should be acknowledged. To this end, we now include the following sentence
in the results section :” Although variability within the treatment groups prevented
finding statistical significance, it is important to underscore that the IL-1b levels in
the PCB + LPS and full mixture + LPS treatment conditions were elevated by
~2.5 times that of the vehicle + LPS group.”

As well, we have added the following additional sentences towards the end of the
discussion: “...Along these lines, there was a definite trend of increased
hypothalamic IL-1b levels in the PCB and full Arctic mixture perinatally treated
mice that received LPS in adulthood. The variability in the response to LPS
apparent in these mice suggests that some animals were “responders” and some
“non-responders” to the early life chemical priming. Future studies aimed at
better characterizing this effect would benefit from assessing the impact of a
variety of LPS doses. “

2. The second point brought up by the reviewer was that there were marks “-” in
the figures that were not clear. We apologize for this, as these marks were a
result of a problem with the software used to make the figures. We have now
removed these erroneous marks for the figures.