Reviewer's report

Title: Structural and cognitive deficits in chronic carbon monoxide intoxication: a voxel-based morphometry study

Version: 2 Date: 25 February 2013

Reviewer: Shawn D Gale

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Major Compulsory Revisions
1. Please be more specific with your ANOVA and ANCOVA findings. For example, in terms of education you report the F and p value for the overall ANOVA that was significant but you do not report the post-hoc analysis to determine which groups are different. By looking at the data in Table 1 it can be seen that the it is likely that the control group mean is much larger than the DNS and non-DNS CO groups yet in the text (p. 15) you indicate that these two groups differed on education level. This procedure is repeated for your interpretation of the differences between DNS and non-DNS groups on cognitive measures and I find it difficult to believe that the difference between these two groups on the percent conceptual level from the WCST is statistically different (49.8% vs. 52.3% while the controls are at 71.9%). The effect size here is only 0.1. I believe you have interpreted your overall F test to indicate differences between all groups when in reality it is the control group that is different from the two CO groups. Please review this and also report the post-hoc analyses.

2. Please be consistent with your use of DNS which you refer to as both “delayed encephalopathy” and also “Delayed Neuropsychiatric syndrome.” I understand there are differences in the literature regarding what the N stands for (neurologic, neuropsychiatric, neuropsychologic), for example see Choi (1983) which used the term Delayed neurologic sequelae, but need to be consistent.

3. Your statement on page 4, “Findings of conventional neuroimaging show no significant difference between patients with or without DNS” isn’t completely accurate. Please see Ku et al. (2010) in Gen Hosp Psychiatry that found those with DNS were more likely to have positive CT findings than those without DNS.

4. Where there any differences in COHb between the DNS and non-DNS groups? Differences in length of exposure? Differences in acute treatments (e.g. hyperbaric vs. normobaric)? Looks like you mention this on page 23 but should be evident elsewhere when the reader is trying to ascertain any group differences. Any differences on initial neuroimaging like demyelination?

5. On page 18 you claim that the DNS group had “relatively decreased pre-frontal executive function…” can you really claim this when the only difference was supposedly in percent conceptual response, which was only different by 3% (see comment #1) and all other measures from the WCST were similar between groups?
Minor essential revisions

1. In the subjects section of methods can you explain what you mean by “chronic” phase after poisoning? Days, weeks, months? Looks like this information is in Table 1 but would be nice to tie those two together. You also have this information on page 7 perhaps moving it up in the subjects section would be helpful.

2. On the bottom of page 7 you mention the word/face recall test. Where are these data? If not going to be used in this paper then no reason to specifically name the other cognitive measures administered. Though of course it would be interesting to know if the groups differed on this measure and if regional GMV correlated with it.

3. Make sure you explain an acronym before you use it. Example you use DARTEL on page 9 but the definition is on page 11.

4. Heading on page 16 says “aberration” do you mean atrophy?

5. The large section at the top of page 21 regarding anterior cingulate should cite supporting references.

Discretionary Revisions

1. Consider discussing issues related to your findings of changes in the hypothalamus since the structure is so small and your scans are at 1.5x1.5x1.5mm.

2. Should reference your comment at the bottom of page 22 regarding 10% of cases.

3. On page 8 you go into detail of what the WCST stimuli consist of. I would suggest you simply refer the reader to an article/book (like Lezak’s) that describes this and instead you report what cognitive abilities this test purportedly measures and which scores you are investigating.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests