Reviewer’s report

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

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Reviewer: Erin Bigler

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The investigation of the neuropathological effects of carbon monoxide (CO) poisoning continues to be improved based on advances in neuroimaging analysis techniques and it appears that this study adds to the literature, although there are numerous points of clarification needed. One important aspect of this study, unlike many earlier studies is that this investigation examined both those with typical timeframe onset of CO poisoning and those with delayed neuropsychiatric syndrome (DNS). While there are a number of anoxic brain injury VBM studies, the authors are correct in the absence of studies that have focused on gray matter and neuropsychological outcome.

In the introduction the authors state that DNS may occur “... from 3 to 240 days after acute CO exposure...” I would suggest not referencing specific number of days, because I think those are a bit arbitrary and more a reflection of the design of other experiments of CO exposure. For me, the key element is that the CO patient has some degree of “recovery” and is medically deemed to not be under the acute adverse effects of CO intoxication. The typical sequence is that the patient is discharged after being medically cleared but returns later with obvious decline. In the Material and Methods section, criteria for inclusion seems vague and not everyone received COHb determination. More details are needed, especially for those who were only seen at the out-patient clinic.

A variety of neuropsychological measures were administered but no details were given about the standardization of these measures with a non-English speaking cohort. The Wisconsin Card Sorting Test and Wechsler Adult Intelligence Scale were used, but the reader is not informed as to what adaptations were used as both of these methods in terms of instructions and normative standards are based on North American norms, even referenced by the authors. The authors list three different WAIS references, but do not report which one. These kinds of details are essential, because a major part of the current findings relate to the neuropsychological outcome in relation to the neuroimaging findings. These points are major compulsory revisions in my opinion.

Image analysis procedures appear appropriate but it was unclear to me how multiple comparisons were controlled for given the number of neuropsychological variables and neuroimaging methods that were used. Towards the end of the Discussion section there is a fair amount of speculation without much in the way of supporting references.
There are several places where abbreviations are not clearly identified, some noun-verb non-agreement and neuropsychological does not require a hyphen.

**Level of interest:** An article whose findings are important to those with closely related research interests

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

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