Reviewer’s report

Title: Occipital event-related potentials to addiction-related stimuli in detoxified patients with alcohol dependence, and their association with three-month relapse

Version: 0 Date: 09 Nov 2015

Reviewer: Geraldine Petit

Reviewer's report:

This study focused on early occipital components of event-related potentials (ERPs) as potential electrophysiological indices to identify the vulnerability for alcohol relapsing after detoxification (3-months). For this purpose, P100 and N170 amplitude and latency in response to alcohol and non-alcohol related cues were compared between alcoholics (relapsers or abstainers for up to three months after detoxification) and non-alcoholics in two conditions: one in which the target was a non-alcoholic drink (NOGO) and the other in which the targets were an alcohol and a non-alcohol related drink (GO). It was found that when compared to abstainers, relapsing alcoholics presented an increased N170 amplitude for the alcohol related cue (beer), this especially in the NOGO condition of the task, which may indicate a vulnerability in relapsing patients to alcohol related indices occurring outside the focus of their directed attention.

This is a very interesting study, well conducted, but the introduction and the description of the data could be much improved and additional statistical analyses would add more weight to the results.

Title:
The "relapse" aspect should appear in the title.

Abstract:

Background and Methods:

Add the fact that the analyses were also made considering the factor relapse/no relapse.

Keywords:
relapse should also appear.
Background

I don't think the problematic is very well introduced in its structure and some elements are missing. (Second paragraph, from line 65).

I would rather follow this plan:

1. Briefly introduce the cue reactivity phenomenon (drugs-of-abuse increasing the salience of drug cues by sensitizing the dopaminergic (DA) system (Robinson & Berridge, 1993), leading to differential attention to drug related cues) + ERPs studies conducted so far.

2. Address the role of cue reactivity in relapse + ERPs studies.

3. Emphasize the fact that the focus has been made so far on late ERPs components (cite studies) and the idea to also look at earlier ones (which would introduce the third paragraph).

Some references are missing their number (Carter and Tiffany, 1999 line 67, Little et al., 2012, line 70, Mundle et al., line 128).

Add references after "Patients with substance use disorder show heightened P300 and slow wave amplitudes in reaction to drug related stimuli" (line 72).

Line 81: add an "s" to disorder.

Line 82: add an "s" to allow.

"In line with this research focus" (line 93): this transition is unclear. The previous idea is that N170 is not only linked to faces. Isn't it thus rather in reference to the idea that N170 is linked to face processing? (earlier idea, line 86).

Line 105 and also further, line 115: value and not valence?

It is unclear why the works of Hinojosa and Hietanen suggest that the effects could be present also for non-target stimuli. (lines 105 and 106).

"and maybe even when attention is focused on non drug stimuli." (line 118). This rationale behind hypothesis is unclear.

A hypothesis on how the electrophysiological parameters could predict relapse is missing.

Methods

Clinical assessments

Did the authors made any assessment of anxiety symptoms?
Line 155: replace "affect" by "have affected".

It is unclear what criteria were used to conclude that a relapse had occurred within the three months following detoxification.

"Eleven patients remained abstinent from alcohol and 12 patients relapsed within the three months evaluation time." (line 161 162). This sentence should appear in the results section instead.

EEG and Task

While the reader very much understand that the focus has been made on early occipital components, did the authors take any look at the NoGo N2 and the NoGo P3 components given that the main differences were observed in the NoGo version of the task which actually constitutes a classical Go/NoGo inhibition Task.

Data analysis

Line 217: Add "and latencies" after amplitudes.

Why was the midline Oz electrode not analysed?

The authors here declare that they will use ANOVAs whereas MANOVAs were actually used.

Results

The results section generally suffers from lack of clarity.

Separate sections with titles for the different results (P100, N170, latencies, amplitudes) would bring more clarity.

It is often unclear why each analyse was conducted (e.g., why an additional analysis only for beer and juice and only for N170? , why separate analysis for Go and NoGo conditions only for amplitudes and not for latencies in relapse assessment?).

Mean values and SD are missing for significant results.

Line 285: heightened N170? amplitudes

Instead of correlations, the authors should run MANCOVAs in order to test for depression as a confounding variable.

Relapse assessment

Did patients with and without relapse differ for mean years of alcohol dependence, mean number of previous inpatient detoxification treatment?
It would be appreciable to have a table showing descriptive and clinical values for both relapsers and non relapsers.

What are the statistics for the difference in depression between both groups?

When describing factors in MANOVAs, please stay consistent by using "task", "condition" or "condition task" throughout the whole results section.

Line 306: isn't the factor "stimuli" missing in the description of the MANOVA?

Line 308: "Within these three months, 11 patients remained abstinent and 12 patients relapsed."

This sentence placed here looks odd. It should appear earlier, in the beginning of the relapse assessment section.

Line 310 "Amplitudes and latencies for patient with and without three months relapse are given in supplementary table 3." This sentence should appear at the end of the relapse assessment paragraph.

Line 314: remove the "s" on both "effects" words in this sentence and add a "a" before "main".

"Due to higher amplitudes to beer stimuli" (line 316). Is it unclear to what it is refered to. Also, begin with the description of the analysed used. Line 317: a main effect of stimuli: add that it is for beer. Line 318: heightened N170? amplitude

Finally, did the authors try to run regression analysis in order to see whether the ERPs parameters could effectively predict relapse (as it is planned in the objectives). And also above and beyond other variables as depression symptoms? This would add more weight to the results.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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