Reviewer’s report

Title: “Free won’t” after a beer or two: Chronic and acute effects of alcohol on neural and behavioral indices of intentional inhibition

Version: 1 Date: 25 Nov 2019

Reviewer: Ann-Kathrin Stock

Reviewer's report:

Q1: General Background:

Initial Review comment:

In the general background section, as well as in some parts of the following manuscript, the authors state that "In terms of drinking, the priming dose effect of alcohol, i.e., loss of control over further consumption after a priming dosage, reflects the insufficiency of intentional inhibition rather than stimulus-driven inhibition (Field, Wiers, Christiansen, Fillmore, & Verster, 2010)." While this is most certainly a big issue in individuals with AUD, a few alternative explanations could also be conceivable in individuals with non-pathological drinking habits: In the investigated samples, the priming dose could also lead to a shift in plans/motivational values, or simply to changes in delay discounting. So while investigating alcohol effects in healthy samples is of course interesting and valid research question, I am skeptical whether this allows for valid conclusions on AUD mechanisms. -After all, loss of control over drinking is one of the key symptoms in AUD, which likely sets affected individuals apart from the general population.

Author response:

We thank the reviewer for pointing out this important issue. Indeed, three criteria of DSM-5 in diagnosing AUD are relevant to the loss-of-control behavior. However, loss of control is thought to play important roles in different stages of addiction, including initial use of a substance and transition from recreational use to heavier use and abuse, rather than only when one is diagnosed with AUD. For instance, if a binge drink occasion happened on a Friday night in the student bar, this event is unlikely to add to a diagnosis of loss of control related to AUD. However, the same behavior on a Thursday night, before big exams on Friday could add to the diagnosis. Therefore, we would argue that loss of control over drinking among healthy samples can still be relevant, especially when there is no adaptive adjustment to (changing) circumstances (cf., Albertella, Watson, Yücel, & Le, 2019). Second, loss-of-control is the behavioral output, and shifting in plans/motivational values, or changes in delay discounting could all be relevant underlying processes. Such reasons may or may not differ between people with AUD and healthy recreational users. In sum, we admit that it is necessary to clarify that we focused on healthy recreational users and that findings cannot be generalized to people with AUD.
In the Abstract under the Conclusion (p. 2) "These findings suggest that both past-year increases in risky alcohol consumption and moderate acute alcohol use have limited effects on stimulus-driven inhibition and intentional inhibition. These conclusions cannot be generalized to alcohol use disorder and high intoxication levels."

In the general discussion

p. 22 "Accordingly, our conclusions cannot be generalized to the population with AUD."
Also in our reply to Q3.

Reviewer reply:

I would generally agree with your statement that "loss-of-control is the behavioral output, and shifting in plans/motivational values, or changes in delay discounting could all be relevant underlying processes." However, I would like to remark that loss of control is often critically defined by whether or not there has been a change in plans or motivational values. The way I would define it, loss of control can only be declared in situations where there has been no shift of goals so that these match current behavior.

I would suggest to use a slightly different wording: p. 22 "conclusions cannot be readily generalized".

Q2: Experiment 1:

Initial Review comment:
The authors stated that they wanted to investigate the effects of "long-term" or "lifetime" alcohol use on inhibition. These should not be used as interchangeable terms as lifetime use usually refers to lifetime prevalence, while long-term use is more commonly defined as prolonged and continuous consumption. Unfortunately, the assessed measures of alcohol consumption do not allow to answer this particular research question. More specifically, neither the AUDIT, nor the CORE provide proper measures of long-term alcohol use (supposing that all participants reported lifetime use, I assumed that the authors most likely wanted to focus on longterm use): The AUDIT was initially developed to distinguish heavy drinkers with AUD from rather strictly abstinent controls. Nowadays, this fact is mostly disregarded and it has become a widely tool which provides increasing scores with increasingly risky drinking behavior. While this application of the test seems warranted, I doubt that this score provides an accurate measure of long-term alcohol, especially as the AUDIT neither assesses the time of first consumption, nor any changes in consumption frequency and patterns over time. Compared to this, the long version of the CORE assesses age of first consumption, binge drinking within the past two weeks, and recent drinking prevalence and. Yet, the CORE questions are not neutral, but slightly biased by moralizing and judgmental undertones commonly found in US campus drug politics,
and the test mainly assesses consumption within the past 12 months. Given that the available literature on long-term use often reports on the effects of much longer time intervals, and further given that the students who were included in the current study are unlikely to have started their substance consumption within the 12 months prior to testing, I would suggest to either clearly define long-term use as pertaining to this 12-month time interval, or use different term (like "consumption habits", or the like). In summary, I would recommend that the authors would need to EITHER rectify their hypotheses to what is actually assessed by the AUDIT, OR explicitly define long-term use as a 12 month period and then focus on the CORE, OR recollect data with a more detailed and appropriate questionnaire.

Author response:
We are grateful to the reviewer for bringing up these valuable comments and suggestions. First, wording such as lifetime and long-term alcohol use have been replaced by past year alcohol use.

Second, we did not administer the long version of CORE and only know in the past year and past month on how many occasions the participants used a certain kind of substance. Therefore, we prefer to continue using the AUDIT score and rephrase the research question and conclusions achieved from it:
- the hypothesis of study 1
p. 5 "we tested the hypothesis that higher AUDIT scores (i.e., increase in problematic alcohol use) were associated with prolonged SSRTs"
- discussion of study

1 p. 12 "In the first experiment, past-year increase in risky drinking showed no relationship with any of the inhibition-related tasks and questionnaires." In addition, the first three items in AUDIT (also known as AUDIT-C) assess alcohol consumption. We, therefore, replicated our analysis with AUDIT-C. p. 9 footnotes: "In addition, we replicated these analyses by replacing AUDIT total score by AUDIT-C (the first three items of AUDIT)."

p.12 "Results were very similar when AUDIT-C was used (see Supplementary Materials)."
Accordingly, in the Supplementary Materials, all those results were reported.

Reviewer reply:
p. 5 please state that "higher AUDIT scores (i.e., more risky alcohol use within the past 12 months) were associated with prolonged SSRTs"

Also, please try to briefly explain in your footnote on page 9 that the first three items of the AUDIT are not limited to the past 12 months, as not all readers might be aware of this.

Q3:

Initial Review comment:
Against this background, I also found some of the current conclusions to be only partly justified (e.g. "it's time to ask whether the stimulus-driven inhibition deficit is a real finding among drinkers"). These should be specified or toned down a bit.

Author response:
Yes, we agree with the reviewer, this statement may be a bit strong. We now rephrased it into p. 12 "It's time to re-assess the connection between recreational moderate alcohol use and stimulus-driven inhibition impairment."

p. 12 "Relatedly, in our recent individual-level mega-analysis, very limited evidence supporting such deteriorating relationship was found across a broad range of substances (see Liu et al., 2019). As only a small proportion of the participants are diagnosed with SUD, the conclusions cannot be applied to SUD."

Reviewer reply:

p. 12 it does not have to be this absolute. How about "As only a small proportion of the participants are diagnosed with SUD, it is still unclear whether these conclusions would also apply to SUD."

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?
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