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To: Science Editor

*Journal of Visual Experiments*

Dear Dr. Myers,

We are grateful to you, Dr. Cao, and the reviewers for all the thoughtful and constructive comments and suggestions. We have addressed them here below and have included the corresponding changes in the manuscript which has, we believe, improved significantly.

The questions and concerns are listed below point by point in regular font and are followed by replies in *italics*. All modifications in the revised manuscript are visibly marked to facilitate review.

**Editorial comments:**

2. Please provide an email address for each author.

*This information has been added to the manuscript.*

3. Please shorten the Long Abstract to 150-300 words.

*The Long Abstract has been shortened to the specified length.*

4. Please revise the protocol to contain only action items that direct the reader to do something (e.g., “Do this,” “Ensure that,” etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as “could be,” “should be,” and “would be” throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a “Note.” Please include all safety procedures and use of hoods, etc. However, notes should be used sparingly and actions should be described in the imperative tense wherever possible.

*The protocol has been revised to the imperative mood with any text that does not fall under these guidelines classified as a “Note”.*

5. Step 2, etc.: The Protocol should contain only action items that direct the reader to do something. Please move the discussion about the protocol to the Discussion.

*Please see above under 4. On several occasions, we have included a brief note to clarify the reason for a particular step or an imperative instruction. For instance, in 3.5.1. we clarify the need to position the participants correctly with the following note: “head position can affect activity estimates in significant ways because the magnetic field gradients decrease with the cube of the distance between the sensors and the brain sources”.*

6. Please add more details to your protocol steps. There should be enough detail in each step to supplement the actions seen in the video so that viewers can easily replicate the protocol. Please ensure you answer the “how” question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action. Some examples:

*Additional detail has been added to the protocol. For the examples below, the new description has been copied below along with the line numbers. Additional changes have been made within the text to clarify each action.*

3.1.2: Please describe how to carry out a brief mock recording run and administer the task practice.

*Carry out an initial recording in the MEG scanner following the protocol described below in sections 3.2, 3.3 and 3.5. Do not provide any beverage. Run the practice version of the task allowing participants to get familiarized with it beforehand.*

3.2.1: How to run a brief test scan? Please specify.

*Upon their arrival to the MEG lab, run a brief test scan by putting the participant in the scanner and checking the channels for possible magnetization.*

3.4.2: Please specify for how many times BAC is measured.

*Check the participants' BrAC with the breathalyzer starting at ~15 min after drinking and then every 5 min until they enter the shielded room. Since electronic devices cannot be used in the shielded room, use a saliva alcohol test (Q.E.D., OraSure Technologies), which consists of a q-tip that is saturated in saliva and is inserted into a receptacle that provides a readout.*

3.5.6: What does “the empty room” refer to?

*When the participant has exited the scanner, acquire approximately two minutes of data from the empty room as a measure of instrumental noise.*

4.3: Please specify how.

*Use the inner skull surface derived from the segmented structural MRI images to generate a boundary element model of the volume conductor, which is used to provide a model for the forward solution that is consistent with each individual’s brain anatomy (Gramfort et al., 2010; Kybic et al., 2005).*

7. 5.1-5.8: Software must have a GUI (graphical user interface) and software steps must be more explicitly explained ('click', 'select', etc.). Please add more specific details (e.g. button clicks for software actions, numerical values for settings, etc.) to your protocol steps. There should be enough detail in each step to supplement the actions seen in the video so that viewers can easily replicate the protocol.

*As suggested, we have included specific functions/commands along with the relevant parameters that need to be run to accomplish such basic processing/analysis tasks, as well as more details on how to visualize results of the various analyses with GUI-based platforms by specifying "clicking" or "selecting" actions.*

*Please note, however, that the actual analyses carried out by many/most software platforms that handle imaging data at this level of complexity are not run via GUIs but with commands/functions. For example, filtering is accomplished by defining filtering parameters in the filter command itself - no GUI is used for that purpose.*

8. Please include single-line spaces between all paragraphs, headings, steps, etc.

*These formatting changes have been added.*

9. After you have made all the recommended changes to your protocol (listed above), please highlight 2.75 pages or less of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol.

10. Please highlight complete sentences (not parts of sentences). Please ensure that the highlighted part of the step includes at least one action that is written in imperative tense.  
11. Please include all relevant details that are required to perform the step in the highlighting. For example: If step 2.5 is highlighted for filming and the details of how to perform the step are given in steps 2.5.1 and 2.5.2, then the sub-steps where the details are provided must be highlighted.

*The steps appropriate for visualization have now been highlighted.*

12. Please obtain explicit copyright permission to reuse any figures from a previous publication. Explicit permission can be expressed in the form of a letter from the editor or a link to the editorial policy that allows re-prints. Please upload this information as a .doc or .docx file to your Editorial Manager account. The Figure must be cited appropriately in the Figure Legend, i.e. “This figure has been modified from [citation].”

*Our figures have been modified from our publication in PLoS ONE, which uses the Creative Commons Attribution (CC BY) license. Under this license, authors retain ownership of the copyright for their content, but they allow anyone to download, reuse, reprint, modify, distribute and/or copy the content as long as the original authors and source are cited.*

13. Figure 2 legend: Should the unit for 4-7 be Hz instead of H?

*Apologies for this inadvertent lapsus calami. Yes, this has been corrected to Hz.*

14. Figures 3 and 9: Please include a space between numbers and their corresponding units (i.e., 800 ms, 400 ms).

*The suggested change has been made to the figures.*

15. Lines 288-289 and 296-297: Please convert the reference to a superscripted numbered reference.

*The reference has been converted.*

16. Figure 7 legend: Please define error bars in the figure legend. Please define the two treatments “Plac” and “Alc”.

*The figure legend has been clarified.*

17. Please renumber the videos as movie 1, movie 2, etc. Please number video 8a and 8b as separate movies.

*The videos have been renamed to Movie 1 (from figure 5) and Movie 2 (from figure 8). Please note that the two videos previously numbered 8a and 8b are meant to be shown simultaneously to show both the medial and lateral sides of the right hemisphere. They are the same length & timing. We have numbered them as such to suggest that they are part of the same figure. Given this information, if we should still rename them in separate numbers we are happy to do so.*

18. JoVE articles are focused on the methods and the protocol, thus the discussion should be similarly focused. Please revise the Discussion to explicitly cover the following in detail in 3-6 paragraphs with citations:  
a) Critical steps within the protocol  
b) Any modifications and troubleshooting of the technique  
c) Any limitations of the technique  
d) The significance with respect to existing methods  
e) Any future applications of the technique

…

19. References: Please do not abbreviate journal titles.

**Reviewers' comments:**

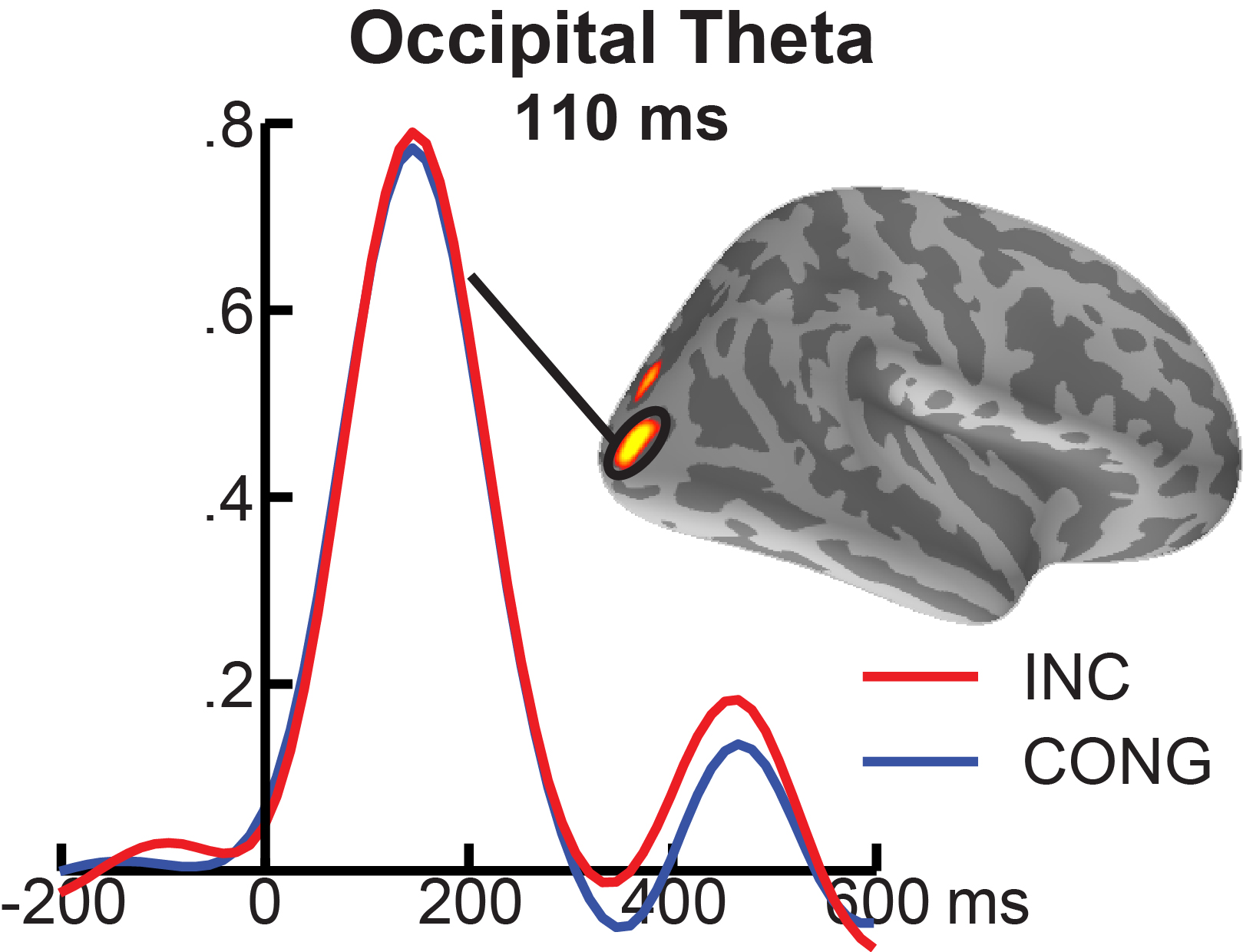
*We would like to thank all three reviewers for their careful reading of the manuscript and for sharing their expertise as reflected in thoughtful and constructive comments and suggestions.*

**Reviewer #1:**

Manuscript Summary:  
The MS explores whether the MEG event-related theta oscillations in theta freq band changes the brain dynamics during a higher cognitive demand (i.e. incongruent condition) in two specific regions of brain (ACC and latPFC). The authors conclude that ACC theta oscillatory power increases during incongruent condition about 100 ms in ACC, and about 100-200 ms later in latPFC. Alcohol condition changes this theta increase during incongruent condition. The authors comment this finding in favor of the effect of alcohol in top-down regulation by means of theta oscillatory responses.

Major Concerns:

1. The visual modality is chosen for the cognitive task, however the changes in primary or association visual cortices were not included to the study. How are the ROI ACC and latPFC was chosen solely? Please provide the rationale for choosing these two areas in more detail.

*While the stimulus modality is indeed visual, no differences in theta power estimated to the visual cortex were detected between task conditions, as demonstrated in this figure. Indeed, previous studies from our lab using word stimuli have found no differences in early activation of the visual cortices using time-domain analyses 1-5. This is due, in part, to carefully balancing stimulus sensory parameters such as word length, size, or color, as the early processing in the visual cortex is not expected to be sensitive to word meaning.*

*Extensive evidence points to the anterior cingulate cortex (ACC) as a central node in a predominantly frontal cortical network subserving cognitive control 6-10, referring to the capacity to inhibit automatic responses in favor of relevant, but non-habitual responses 11-13. As described in the introduction, Conflict Monitoring theory 6,7 proposes that the ACC monitors for conflict between competing representations and that it engages latPFC to maintain performance. However, since this account is primarily based on temporally imprecise BOLD-fMRI, the presumed interplay between the medial and lateral prefrontal cortex has not been verified adequately 14. The anatomically-constrained MEG method described here can test this basic tenet by examining the nature and the extent of the theta oscillatory synchrony between the ACC and latPFC. Indeed, theta oscillations may represent the fundamental mechanism of integrating task-relative information across different cortical domains 15-20. We hypothesize that increased cognitive demands are associated with greater functional synchrony and that alcohol-induced dysregulation of synchronous activity of the medial and lateral prefrontal cortices underlies impairments of cognitive control.*

2. How the authors reached the conclusion that processes start from posterior and extends to anterior? Please explain more explicitly and discuss it with relevant literature.

*One of the principle advantages of the aMEG methodology is the ability to observe the spread of cortical activity in time and space. As seen in the “brain movies,” (Movie 2a-b), the earliest visual stimulus-locked signal arises in the visual cortex. It is followed by activity that progresses anteriorly toward the supramodal (or sensory-nonspecific) areas in the pre-supplementary motor area, the ACC, and latPFC which is more prominent on incongruous trials. Simultaneous activation of these distributed areas presumably underlies cognitive processing, before the primary motor cortex activation signals the subject’s response and the end of the trial. Taken together this pattern of activation demonstrates an overall posterior-to-anterior sequence of visual processing which is consistent with anatomical, functional, and developmental evidence from animal models 21,22, as well as intracranial EEG in humans 23,24, and MEG recordings 1-5,25-27.*

Minor Concerns:

On the page 26 and 27 catalogue numbers are placed out of page margins.  
*We will ensure that the manuscript is formatted properly.*

**Reviewer #2:**

Manuscript Summary:

The paper describes a protocol to study the effects of alcohol intoxication on oscillatory brain activity in humans using anatomically-constrained MEG. The protocol is useful for characterizing brain networks associated with cognitive control and their sensitivity to pharmacological challenge.

Major Concerns:

None.

Minor Concerns:

The methods are clearly described and motivated. I have the following minor comments:

- line 276: Figure 3 should show axes with appropriate scales for the Morlet wavelet.

*We agree with the reviewer that the Figure should describe the Morlet wavelet with appropriate scaling parameters. The new version of the Figure contains the suggested change.*

- line 278-281: The caption for Fig. 4 refers to "group averages of theta power" and "sulcal estimates", but those are not shown in the Figure. Please clarify.

*The purpose of the figure is to illustrate inflated cortical surface used as an anatomical constraint for MEG source estimates but we agree that the caption may be confusing without activity estimates.*

*The caption now reads:*

***Figure 4: Cortical reconstruction and inflation.*** *Individual cortical surfaces are reconstructed using FreeSurfer and are used to constrain estimated source power. Here shown is an average cortical surface which is inflated to enhance visibility of the sources estimated to cortical sulci.*

- line 287: "arbitrary units" is neither correct nor acceptable. Since these are noise-normalized values, it appears that there are no units.

*As the reviewer correctly points out, there are indeed no units associated with noise-normalized values so “arbitrary units” is not uncommon for dimensionless quantities. However, figure captions now describe it as “source power”.*

*We would be glad to consider alternative labels that the reviewer may care to suggest*

- line 299: In Fig. 8 (and similarly in Fig. 9) please show the color scale and explain what is the measure shown (and preferably re-format the numbers to 0.72, 0.79, etc.)

*We agree with the reviewer that the color scale for these figures should be explained. The new figures and figure legends contain the suggested changes.*

*Please note that the movies have been streamlined and now show the timing. The color scale is described in the figure caption.*

- line 303: The caption says "after ~250" but in the video the activity occurs only at ~350 ms. Please check the consistency of the latencies.

*The suggested change has been made.*

- line 308: Was zero-lag excluded in the evaluation of the PLV measure? This seems important for reducing spurious connectivity due to the spatial spreading of the estimated source power.

*We concur with the reviewer on the importance of considering potential confounds resulting from field spread. Schoffelen and Gross 28 have provided an excellent review of this problem. Their paper includes a simulation of connectivity analysis based on a 248-channel 4D neuroimaging magnetometer system and a realistic head model. However, it is important to note that this particular system seems to use magnetometers which are sensitive to magnetic flux at some distance from the source. In contrast, the largest signal detected by planar gradiometers that were used in the present study (Neuromag Elekta) is above the source as they measure the rate of change in flux between two coils 29,30. Direct comparisons between the two types of sensors indicate that planar gradiometers have better spatial sensitivity 31 which has been borne out by comparisons based on real data 32.*

*Ultimately, this is a question of localization uncertainty which is influenced by a variety of factors including the spread of the signal from the generator to the sensors, the limited sampling of the field (even with a very large number of sensors), and the overlap of activity from different sources at each sensor, all within the context of a particular inverse procedure. Liu and colleagues 33 estimated localization uncertainty with the same inverse approach used here 34 and concluded that the values of the estimated point-spread extent average around 20 mm based on the 122 MEG sensor locations and on single-subject solutions. Since the estimated localization accuracy improves with increasing the number of sensors and multiple subjects, it is reasonable to assume that the spatial resolution obtained in the current study is appreciably better.*

*While zero-lag contributions to PLV were not excluded this study, the inter-ROI distance is certainly greater than 20 mm, mitigating these concerns.*

- line 319 (and similarly 361) : "By optimally combining.." It is not clear what is being optimized here. Perhaps the word "optimal" can simply be deleted.

*We agree that “optimal” is vague and unquantified in this context and it has been omitted from the text.*

*The discussion has been expanded and it now summarizes how this methodology combines the complementary features of each technique.*

**Reviewer #3:**  
Manuscript Summary:  
The authors describe a protocol for anatomically-constrained MEG (aMEG) modelling of functional brain activity during a Stroop task under two within-subject conditions: alcohol and placebo. The purpose of the study is to measure response interference during the task, and how that is altered by alcohol consumption. The main measures of interest were frontal theta (3-7 Hz) power in the anterior cingulate cortex (ACC) and lateral prefrontal cortex (latPFC). In addition, the authors describe a method for measuring co-oscillations in the theta frequency band across these two sources using a Phase-Locking Value (PLV). The authors found increased frontal theta power in both sources for incongruous trials over congruous trials, in both conditions. In addition, the increase in theta power over baseline and PLV were reduced in the alcohol condition. They conclude that these findings support the role of the ACC in monitoring for conflict in processing stages, that intoxicated individuals exhibit deficient self-control, that the aMEG method provides a temporally-sensitive insight into functional brain activity, which can serve as biomarkers of individual vulnerability to pharmacological effects.

Major Concerns:

1. It appears that the time-locked power changes (evoked response) is not subtracted from the raw data prior to computing low frequency theta activity. As a result what is labeled theta power following the stimulus could contain an ERN-like evoked response, originating from the ACC and latPFC.

*The reviewer correctly notes that we did not remove the evoked response prior to computing the event-related theta activity. However, it has been demonstrated*  *{Cohen, 2011 #7894} that for conflict-related activity specifically, removing the ERP component does not markedly change the effect size of theta band modulation. More broadly, the practice of subtracting the evoked responses is based on the assumption that the two processes are independent. However, evidence indicates that the stimulus resets the phase and modulates the amplitude of the ongoing oscillations during cognitive processing, suggesting a single underlying process 35* *16* *36. This may not hold true, however, for short latency, high frequency responses characteristic of sensory processing, but that was not of primary interest in the current study.*

2. There is no mention or description of statistical methods as they apply to the reliability of the results.

*We regret this unfortunate omission.*

*This information has been added to the text and it reads as follows:*

* + 1. *Extract time windows of interest from each ROI time course and perform ANOVAs with beverage (alcohol, placebo) and trial type (CONG, INC) as within subject factors. Use a nonparametric cluster-based permutation test 37 to examine beverage and condition comparisons of event-related theta power as well as PLVs.*

*In addition, results of statistical analyses and their respective significance values have been provided in the representative results section and figure captions, where appropriate.*

3. For the Stroop task - how many trials are there and what proportion of trials are congruent?

*Details on this particular version have been added to the text: the CONG and INC conditions were equiprobable and were presented on 16.7% trials each out of 576 trials total.*

4. What are participants told about this experiment? Are they made aware that one condition is placebo? And is their awareness tested in some way?

*The Reviewer raises an important issue concerning alcohol administration and possible effects of expectancies. In a series of studies, we have employed a within-subject design in which participants serve as their own controls. All participants imbibe both alcohol and placebo in a counterbalanced manner so that alcohol is presented in the first session for half the sample and in the second session for the other half. This design controls for neurophysiological idiosyncrasies, resulting in less error variance and has indeed been used in a great majority of neuroimaging studies of acute intoxication 38-46.*

*Participants are told that in each session they will consume a beverage that may or may not contain a moderate dose of alcohol. The dose is calculated based on each subject's gender and weight to adjust for the body mass index difference 47. The beverages are administered cold and do not markedly differ in taste given a strong taste of natural orange juice. However, all of our participants have had experience with drinking mixed alcoholic beverages and they all drink regularly in social situations. They are familiar with the timeline of alcohol metabolic process and how it affects them and are able to easily discern the beverage content based on a variety of sensations. At the end of each experimental session the participants are queried about their estimated intoxication levels, beverage contents, and the estimated number of “drinks” contained in the beverage. The results in all of our studies indicate that participants are aware of the beverage content.*

*The essential question is whether this knowledge (i.e. expectancy) could influence their brain activity. Balanced placebo design makes it theoretically possible to dissociate the pharmacological effects of alcohol from the effects of instructions as to the beverage content by fully crossing the factor of beverage (given alcohol or given placebo) and the factor of instructions, "expectancy" (told alcohol or told placebo). This means that subjects participate in four sessions of the balanced placebo design in a random order. They undergo the same procedure each time except for the consumed beverage and information concerning the alcohol content. In two sessions they are told the correct beverage content (i.e. given and told juice and given and told alcohol). In the other two sessions they are given inaccurate information regarding the beverage content (i.e. given juice/told alcohol and given alcohol/told juice). The beverage administration in all sessions includes the cues (e.g. vodka bottle) appropriate to the instructional expectancy condition procedure 48. For example, in the given juice/ told alcohol condition, strong olfactory cues are provided by a small piece of vodka-saturated gauze placed in the cap of the bottle with water, unbeknownst to the participants. In an effort to parse out the "expectancy" effects from the pharmacological effects of alcohol, some of our previous studies employed the balanced placebo design in a within-subject setting and with a lower alcohol dose, 0.4 g/kg for men 49-51. We observed only pharmacological effects of alcohol on physiological and behavioral measures during cognitive tasks. Expectancy did not affect the ERP or autonomic measures in those studies. However, this design has its own problems as it is difficult to implement all the cells of the balanced placebo design with equal success, even at rather low doses 52-54. For example, if an alcoholic beverage is given, it is virtually impossible to convince participants that they drank only juice. Crucially, however, even when subjects are successfully tricked into believing that the beverage contains some alcohol, this expectancy has no effect on any of the physiological measures and only the actual administration of (moderately low dose of) alcohol results in observable changes 49-51.*

Minor Concerns:

Intro:

-[line 65] "multifaceted role in integrating modulatory effects within a goal-directed context" -> The meaning of this statement is unclear.

-[line 66] Gap in lit: "However, the nature of the involvement of the ACC and the ways it exerts top-down influences on response selection, inhibition, and execution are not clear." This is not clear and rather vague.

*These two sentences have been replaced with:*

*While the abundant anatomical connectivity between the ACC and lateral frontal cortices is well-described 55,56, the functional characteristics of communication between these regions during cognitive control, response selection and execution, are poorly understood.*

-[line 76] "slower" -> quantify

*It has been well established that the individual postsynaptic currents, which in aggregate form MEG/EEG signal have durations in ms 57 and are, for that reason, sampled at 1000 Hz in this experiment. Within one trial, the entire sequence of cortical activations presented here, from early visual system to motor response, occurs over several hundred ms. In contrast, the hemodynamic response that forms the basis of the BOLD, peaks at 4-6 sec after stimulus onset and, following a post stimulus undershoot, levels approximately 20 sec after stimulus onset 58.*

*Therefore, the wording has been modified as follows:*

*As a result, the BOLD signal changes unfold on a much slower time scale (in seconds) than the underlying neural events (in msec) 58.*

-[line 104] "to measure…in real time" -> Acquisition is in real time, measurement (i.e. analysis of oscillatory activity and synchrony) are not.

*The wording has been changed to “high temporal precision”.*

Protocol:

-[line 114] how many females?

*This information has been added to the text. Eight women and twelve men participated in this experiment.*

-[line 115] "no alcohol- or drug-related problems" -> please explain

*All potential participants are screened for possible alcohol or drug dependence. The description now reads as follows:*

*twenty young, healthy individuals (mean ± SD age = 25.3 ± 4.4 years, 8 women) were recruited who drink in moderation, who have never been in treatment or arrested for drug or alcohol related offenses, who report no alcoholism-related symptoms on the Short Michigan Alcoholism Screening Test 59 who do not smoke nor use illegal substances, who do not have a history of neuropsychiatric disorders or any current health problems, who are medication free, and have no internal ferromagnetic objects or implants.*

-[line 124] is 1 of these a placebo?

*Step 2.1. now clarifies the experimental design as follows:*

*Scan each participant four times, including three MEG sessions (a no-beverage introductory session and two experimental beverage sessions in which alcohol and placebo are administered in a counterbalanced manner), and one structural MRI scan.*

-[line 128] any examples or further descriptions of typical questionnaires?

*We thank the reviewer for pointing out this omission.*

*The description now reads as follows:*

*During the initial introductory session, administer questionnaires to obtain more information about the participants' medical history, their drinking patterns and severity of alcoholism-related symptoms 60**59, family history of alcoholism 61, and personality traits including impulsivity 62,63.*

-[line 143] I suppose these values for food and alcohol deprivation are based on previous work? Ref.

*It is known that food influences BrAC as it delays absorption 64. Therefore, in our studies of acute intoxication we request that participants do not eat 3 hrs prior to the experiment 49 50 51,65 26,66 67 68 69 5,70,71 72.*

-[line 145] "multi-drug test panel" - source?

*This information has been added to the text as follows:*

*Collect urine samples for a multi-drug test panel (American Screening, LLC) from all participants and exclude those who test positive for any drug.*

-[line 163] This single reference to EEG seems inappropriate

*Should the experimenter be interested in collecting simultaneous EEG, this is the step of the protocol during which the experimenter should affix the EEG cap or electrodes to the head.*

-[line 165] Note this procedure is specific to Neuromag systems only.

*Thank you for pointing this out. It has been noted in the text.*

-[line 171] formula for calculating BAC of 0.06%?

*This has been clarified as follows in step 3.4.1.:*

*Prepare alcohol beverage by mixing premium quality vodka with chilled orange juice (25% v/v), based on each participant’s gender and weight (0.60 g/kg alcohol for men, 0.55 g/kg alcohol for women), targeting a BrAC of 0.06% 47.*

-[line 172] placebo with voka on rim - an estimate of BAC for this condition?

*This minuscule amount is not detectable and the BrAC is zero.*

-[line 174] breathalyzer source?

*The breathalyzer maker (Dräger, Inc.) is now specified in the text in 3.2.1.*

-[line 176] saliva alcohol test - description and source?

*This information has been added to the text in 3.4.2.: Q.E.D.®, OraSure Technologies*

-[line 219] what is the baseline? What is the timing and duration of the event-relate theta power?

*Baseline is the period immediately preceding stimulus onset and it serves as a reference to the change in theta power after stimulus onset. Theta power is calculated as event-related theta power and is commonly expressed as percent signal change relative to baseline.*

*Theta power and duration vary as a function of the stage of processing (shorter during sensory processing, longer during cognitive integration and in more difficult tasks).*

-[line 223] Are the ROIs whole-brain?

*Regions of Interest (ROIs) are selected based on overall group-averaged estimates to incorporate cortical locations with most notable source power. Figure 5 shows the ACC and latPFC ROIs.*

Results:-[line 242] " The ACC is the principal generator of theta oscillations" -> this is not always true, and should be qualified and limited to this particular task

*The wording of this sentence, as well as the movie caption has been changed to reflect that the ACC is the principal generator of theta oscillations during tasks evoking cognitive control.*

-[line 246] "…especially in the prefrontal cortex." -> Reference?

*This statement is now supported by relevant references.*

*As observed here and in previous reports17,26,71,72, theta oscillations increase in power in response to cognitive demands such as overriding prepotent or dominant patterns of behavior, which is primarily subserved by prefrontal cortical regions.*

-[line 247] How is theta power measured? Using max power? AUC? Also, does the relationship for reduced theta power on incongruent trials in the alcohol condition hold across conditions? (i.e. incongruous\_placebo - incongruous\_alcohol)?

*Data analysis is described in greater detail in step 5. MEG Data Analysis. Morlet wavelets are used to calculate complex power spectrum for each trial in 1 Hz increments within theta frequency band (4-7 Hz).*

*As described here and in previous reports* 26,71*, even though acute alcohol intoxication attenuates theta power during cognitive control tasks, the effects are greatest on high conflict (incongruous) trials and in more difficult tasks.*

-[line 252] There is no clear null hypothesis here.

*In this instance, the null hypothesis would indicate that there is no effect of task congruity or beverage on phase locking values between regions.*

-What was done with the questionnaires that were administered?

*Questionnaire data can be used to examine correlations with MEG estimates to enrich and facilitate interpretation of the observed effects.*

*This is now specified in step 5.11.*

Discussion:

-[line 326-328] This relationship equally holds for the congruent condition, that there is greater theta power in the prefrontal cortex compared to the prestimulus baseline.

*The wording had been changed to reflect increased theta to incongruous trials compared to congruous trials.*

-[line 331-332] "… in response preparation and execution" this was not tested or measured in this experiment.

*This sentence has been removed from the discussion.*

-[line 352] how do the PLV results compare to other studies?

*As briefly mentioned in the discussion, the current study extends previous findings indicating that alcohol disrupts synchronized co-oscillations 72,73.*

Please note that the reference list is enclosed here below.

On behalf of all the co-authors, I thank you for your consideration.

Sincerely,



Ksenija Marinković, Ph.D.

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