Neurophysiological Correlates of Context-Dependent Inhibition in Alcohol Use Disorder – Findings from Event-Related Potentials and fMRI

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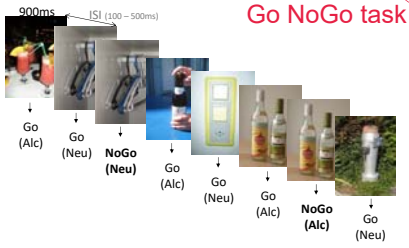
Background and Objective

Alcohol use disorder (AUD) is characterized by both impaired inhibitory control and enhanced cue reactivity, including cue-induced drinking urges and craving [1]. Therefore, inhibitory functions have to be assessed not only in neutral contexts but also in the presence of alcohol-related cues, which may induce craving. The present study investigates in patients with AUD how the neurophysiological correlates of inhibition change in response to exposure to alcohol-related cues depending on individual levels of craving.

Go NoGo task



Patients have to press a button at display of each picture (Go; 75% of trials), unless it is repeated (NoGo; 25% of trials)

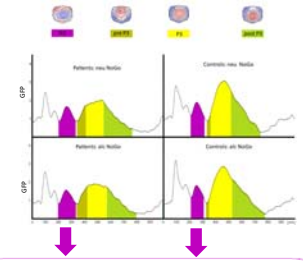
Methods

- At two separate occasions, functional magnetic resonance imaging (fMRI) and 72-channel EEG was recorded from 15 AUD patients and 15 healthy controls [*1)].
- During neurophysiological measurement, participants performed a Go/NoGo task, which incorporated alcohol-related and neutral stimuli.
- Two reaction types: **Go** (reaction) and **NoGo** (no reaction). Two contexts (defined by stimulus type): Alcohol (**Alc**) and Neutral (**Neu**) → Four conditions (**GoAlc, GoNeu, NoGoAlc, NoGoNeu**)
- **EEG**: average reference, preprocessed, filtered (0.5 – 18Hz; 50Hz notch). **Event related potentials (ERPs)** computed for 4 conditions, and analyzed for differences in topography (TANOVA) and global field power (GFP) in N2 and P3 components.
- **fMRI**: whole brain analysis of alcohol-specific inhibition [(NoGoAlc>GoAlc) > (NoGoNeu>GoNeu)] in patients and controls. Significance level: p<0.05, FWE corrected (peak level) after SVC (8mm).
- **Craving**: Assessed with German version of Obsessive compulsive drinking scale (OCDS) and included in analyses as a between-factor.

Results

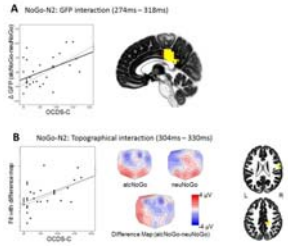
Event-related potentials

Microstate analysis identified time windows for N2 and P3 components. Maps shown above, time windows color-coded under Global Field Power curve of ERPs:



N2: Significant interaction

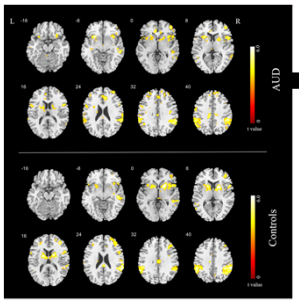
context × craving for map strength **(A)** and topography **(B)**: Difference between alcohol-related and neutral NoGO-trials increases with higher craving



Both effects localized in the PCC with sLORETA source analysis, topographic interaction additionally in pre-SMA [2].

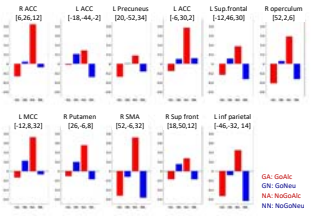
fMRI

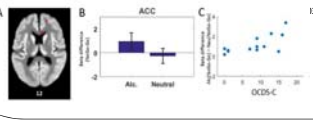
The **inhibitory control** network as revealed by contrast **NoGo>Go:**



In **patients only**, alcohol-specific inhibition evoked higher activation than neutral inhibition [(NoGoAlc>GoAlc) > (NoGoNeu>GoNeu)]

Activated areas	MNI peak coordinate	Cluster size	*t*	*p* value
L Superior frontal gyrus (med.)	-12 46 30	16	4.19	0.006
R Superior frontal gyrus (med.)	18 50 12	6	3.69	0.023
R Precentral gyrus	52 -6 32	16	3.74	0.020
L Anterior cingulate cortex	-18 44 -2	31	4.52	0.003
R Anterior cingulate cortex	6 26 12	25	5.14	<0.001
L Anterior cingulate cortex	-6 30 2	33	4.38	0.004
R Putamen	26 -6 8	9	3.79	0.018
L inferior parietal cortex	-46 -32 14	7	3.68	0.023
L Middle cingulate gyrus*	-12 8 32	17	4.04	0.010
R rolandic operculum*	52 2 6	9	4.10	0.008

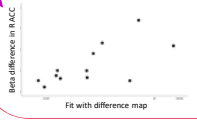




[3] In right ACC, activation differences between alcohol-specific and neutral inhibition increased with craving.

ERPs & fMRI

Interestingly, activation differences in right **ACC** correlated with size of topography effect in the **N2**.



Errors of commission (EOCs)

No differences in errors of commission between groups or contexts.

Discussion and Outlook

- EEG: N2 thought to indicate conflict between the impulse to react to a stimuli and the required inhibition. Difference between alcohol-related and neutral N2 increases with craving, maybe as a sign of enhanced conflict.
- fMRI: For patients only, alcohol-specific inhibition recruits enhanced neuronal resources. In right ACC, this difference increases with craving.
- Effects from ERP and fMRI correlate. Differences in localization between ERPs and fMRI due to different parts of neurophysiological signal picked up by different methods?
- Particularly for patients with high craving, neurophysiological correlates of inhibitory control functions differ in response to the respective context and should therefore be assessed – and eventually changed by training - in alcohol-related contexts in AUD.

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Footnotes:

[*1)] 2 AUD patients and 1 healthy control had to be excluded from analysis of the fMRI data due to too many errors on Go trials (1) and technical problems during fMRI scanning (2),

References:

[1] Volkow & Baler (2014). Addiction science: Uncovering neurobiological complexity. Neuropharmacology 76:235-249
[2] Stein, Fey, Koenig, Oehy, Moggi (2018). Context-Specific inhibition is related to craving in alcohol use diesorders: a dangerous imbalance. Alcoholism: Clinical and Experiment Research , 42(1).