Gender Effects in Inhibition in Patients with Alcohol Use Disorder

Preliminary Results

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Background

- Current neuroscientific theories postulate deficits in inhibition as a significant factor in the development and maintenance of alcohol use disorders (AUD) [e.g. 1].
- Preclinical behavioral studies indicate that deficits in context-unspecific inhibition are more pronounced in women than in men [e.g. 2].
- Neurophysiological findings show alterations in the N2- and P3-components (EEG) in AUD patients [3, 4].
- Only one preclinical EEG-study investigated gender effects. No neurophysiological effects were observed [5].
- Studies investigating gender effects in (alcohol-specific) inhibition in clinical samples are missing.

Methods

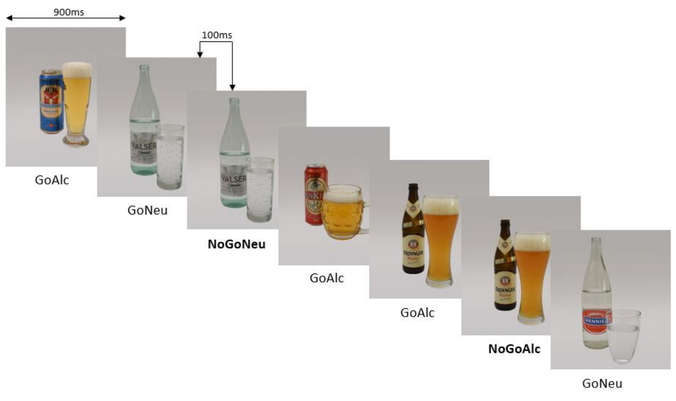


Figure 1: Go-NoGo Task with neutral and alcohol-related context

A total of 31 abstinent in-patients with AUD, attending a specialized treatment program (Clinic Südhang or Forel Clinic) were measured with a 64-channel EEG. All subjects completed a Go-NoGo Task (with 75/25 ratio) to assess inhibition in alcohol-related (alcoholic beverages) and neutral context (mineral water).

After preprocessing (i.e. artefact removal), all data was re-referenced to average reference and four ERPs were obtained for each subject over all correct trials using *BrainVision Analyzer*: Alcohol-related (alcNoGo) and neutral NoGo (neuNoGo) as well as alcohol-related (alcGo) and neutral Go (neuGo). Finally, the ERPs were filtered (1-20Hz, 50Hz notch).

All further analyses were performed with *Ragu*. After identifying data outliers (n=1), the time windows for N2- and P3-components were defined using microstates. They were defined according to the minimal onset and maximal offset times of the identified microstates in the four ERPs: N2a (150-220ms), N2b (220-330ms) and P3 (330-550ms).

Furthermore, differences in map topography and map strength were examined in these microstates: First, a 2x2x2 TANOVA (not normalized) with the between-factor **gender** (male, female) and the within-factors **response-type** (Go, NoGo) and **stimulus-type** (alcohol, neutral) was performed for the time windows of the N2- and P3 microstates to test for interactions. Second, GFP analyses were performed for the same interactions.

Descriptives

Men and women did not differ regarding age, education (years) and severity of AUD (number of DSM-5 criteria / standard drinks (SD) in the last 90 days before detoxification).

	♀ (n = 13)	♂ (n = 17)
Age	42.62 (±9.11)	42.76 (±10.62)
Education	14.62 (±3.10)	13.94 (±2.59)
Severity of AUD DSM SD/90d	 9.23 (±1.30) 809.22 (± 600.83)	 8.18 (±2.53) 1192.97 (±709.88)

Results

The TANOVA the with the factors gender, response- and stimulus-type in the time windows (N2a, N2b, P3) showed the following results:

- For N2a and N2b, no significant interactions were found.
- A significant gender by stimulus-type interaction occurred in the P3 microstate (p=0.01): Women showed an extended fronto-parietal positivity compared to men, which seems to be more extended towards the back during processing of neutral compared to alcohol-related stimuli (see figure 2a). Corresponding to this, differences (alcohol vs. neutral stimuli) for men did not vary significantly (p=0.44), whereas the maps for women showed a significant difference (p=0.02).

Figure 2: TANOVA (not normalized) for P3

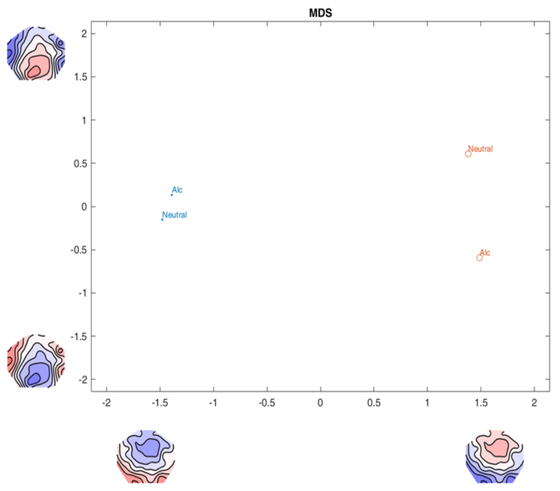
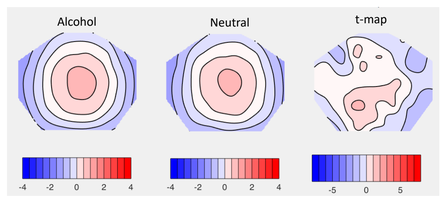
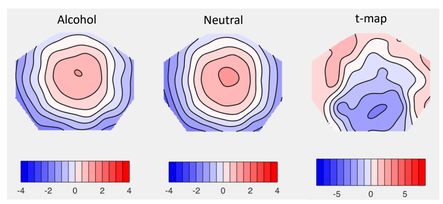


Figure 2a: Multi-Dimensional Scaling (arbitrary values)



2b: t-map for men



2c: t-map for women

GFP analyses with the same factors in the same microstates showed:

- In N2a and P3 no significant interactions.
- For the N2b microstate, a trend to a significant three-fold interaction was found (p=0.06): Women had higher GFP in neutral NoGos than men (see figure 3).

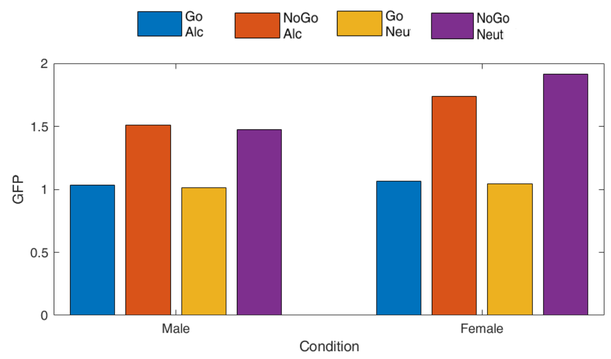


Figure 3: GFP for N2b

Discussion

This study examines neurophysiological gender effects of (context-specific) inhibition in AUD patients for the first time. Preliminary GFP-analyses revealed a trend for the threefold interaction with the factors gender, response- and stimulus-type in late N2. This indicates that female patients have a higher N2b in NoGos, a difference that is even more enhanced in neutral NoGos. As the N2 component reflects the monitoring of a response conflict [6], females thus tend to have a greater conflict in neutral inhibition. Thus, inhibition (of neutral stimuli) could be more difficult for women than for men as it was shown in behavioral studies [2, 5].

During P3 microstate, women differed between alcohol-related and neutral stimuli whereas men did not.

Further, analyses are needed to elaborate the underlying processes in inhibition. Especially the comparison of the (full) patient sample to healthy controls, the inclusion of other inhibition-tasks (SST) and the analyses of errors of commissions (EOC) will help to understand the gender-specific effects in patients with AUD.

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südhang

Registration

ClinicalTrials.gov (NCT02968537)

References

[1] Volkow ND, Baler RD: Addiction science: Uncovering neurobiological complexity. *Neuropharmacolog*, *76*(0):235-349.

[2] Nederkoorn, C., Baltus, M., Guerrieri, R., & Wiers, R. W. (2009). Heavy drinking is associated with deficient response inhibition in women but not in men. *Pharmacology Biochemistry and Behavior, 93(3*), 331-336.

[3] Petit, G., Kornreich, C., Noël, X., Verbanck, P., & S. Campanella (2012). Alcohol-related context modulates performance of social drinkers in a visual Go/No-Go task: a preliminary assessment of event-related potentials. *PLoS One*, *7*(5): e37466.

[4] Stein, M., Fey, W., König, T., Oehy, K., & F. Moggi (2018). Context-specific inhibition is related to craving in alcoholuse disorders: a dangerous imbalance. *Alcohol Clin Exp Res*, *42*(1):69–80.

[5] Smith, J. L., & R. P. Mattick (2013). Evidence of deficits in behavioural inhibition and performance monitoring in young female heavy drinkers. *Drug & Alcohol Dependence, 133*(2), 398-404.

[6] Nieuwenhuis, S., Yeung, N., Van Den Wildenberg, W., & Ridderinkhof, K. R. (2003). Electrophysiological correlates of anterior cingulate function in a go/no-go task: effects of response conflict and trial type frequency. *Cognitive, Affective, & Behavioral Neuroscience*, *3*(1), 17-26.