

Brain connectivity between networks implied in inhibition and cue-reactivity in alcohol use disorder

Summary

Even if an imbalance between enhanced cue-reactivity and impaired opposing control processes is at the center of most neuroscientific conceptualizations of alcohol use disorder (AUD), these two processes are still rarely investigated in direct interaction.

Attempting to target both processes in one design, initial studies reported enhanced brain activation in anterior cingulate cortex (ACC) and ventrolateral prefrontal cortex (vlPFC), when control processes had to be carried out in the context of alcohol-related cues, and linked this altered brain activation to relapse risk. As a **first objective**, the proposed study will for the first time take advantage of the higher spatial resolution and signal-to-noise ratio of a 7 Tesla fMRI scanner to investigate more subtle effects and the involvement of subregions of vlPFC and ACC during alcohol-related inhibition.

Of special interest, particularly when it comes to explaining an imbalance between brain systems related to cue-reactivity and inhibitory control, are concurrent measures of functional brain connectivity. Aberrant resting-state functional connectivity in networks involved in reward prediction, motivation, salience attribution and executive control have been reported in AUD. Also, altered task-related connectivity was observed during cue-reactivity as well as during executive control. However, functional connectivity measures during a task combining both aspects are still missing. Hence, as a **second objective**, the planned study will examine the mutual interplay between cue-responsive regions and opposing inhibitory control networks. To this aim, task-related functional connectivity will be measured in a specifically tailored experimental design allowing for the assessment of effects related to cue-reactivity, inhibition, as well as their interaction.

Research has shown that task-related brain activation patterns (measured with BOLD) as well as resting-state connectivity change with clinical parameters, such as the level of craving and the duration of abstinence during recovery, and are related to drinking outcome. As a **third objective**, the planned study will extend this research to task-related functional connectivity, particularly to interaction effects of cue-reactivity and inhibitory control. We will assess whether these interaction effects on task-related functional connectivity vary with craving, changes with prolonged abstinence and predicts drinking outcome.

Taken together, the proposed study will deepen our understanding of the interplay between neuronal networks central to AUD, cue-reactivity and inhibitory control. The (im)balance between these processes is crucial for recently abstinent patients striving to control drinking habits and urges in an environment infused with alcohol-related cues. As such, markers capturing the interaction between these processes are of high conceptual and clinical relevance and might pave the way towards a potential biomarker indicating enhanced relapse risk.