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Detrimental effects of a high-dose alcohol intoxication on sequential cognitive flexibility are attenuated by practice

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ABSTRACT

It is well-known that alcohol impairs behavioral control and motor response inhibition, but it has remained rather unclear whether it also impairs cognitive inhibition. As automatized behavior is less vulnerable towards the detrimental effects of alcohol than cognitive control processes, potential cognitive inhibition deficits might however improve with training.

We investigated the effect of an acute, binge-like alcohol intoxication in a balanced within-subjects design, asking n = 32 healthy young males to perform a backward inhibition paradigm once sober and once while intoxicated (~1.1 ‰). To identify the underlying neurophysiological mechanisms, we analyzed stimulus- and response selection-related processes in neurophysiological data after Residue Iteration Decomposition (RIDE).

Alcohol generally impaired behavioral task performance (accuracy and response times) during task switching. This was associated with impaired attentional processing of the task-relevant cue (reflected by reduced P1 and N1 amplitudes), which likely resulted in a larger need for reactive control at the later stage of response selection and control (reflected by increased fronto-central theta power). Without prior practice (~30 minutes), the intoxicated participants further struggled to overcome the cognitive inhibition of a previously relevant task set (reflected by a larger backward inhibition effect). This was linked to reduced posterior theta power, which reflects alcohol-induced impairments in working memory capacity and task set-relevant memory retrieval. As individuals with ~30 min task practice did not show the same alcohol-related deficit, it may be deduced that (partial) task set automatization via stimulus-response associations may help to reduce the detrimental effects of alcohol on cognitive inhibition during task switching.

1. Introduction

Binge drinking is a prevalent problem, especially in western countries (Montgomery et al., 2012). Occasional binge drinkers seem to have a much higher risk of developing alcohol dependence or abuse compared to the non-heavy episodic drinkers (Knight et al., 2002). Regular binge drinking may furthermore be associated with slight to moderate long-term decreases in cognitive functioning, but studies investigating this aspect have so far yielded rather mixed results (Montgomery et al., 2012). By comparison, findings on the acute detrimental effects of binge-like high dose alcohol (i.e. ethanol) intoxications on cognition are much more consistent, but also quite specific (Montgomery et al., 2012; Stock and Beste, 2014): While executive functions and other top-down cognitive control processes are usually strongly affected by an acute alcohol intoxication, processes which do not require conscious control (like automatic processes or implicit learning) seem to be less impaired, if not even resistant to high-dose alcohol intoxication (Balodis et al., 2007; Beaton et al., 2018; Lister et al., 1991). In this context, the executive function of inhibitory control has been demonstrated to be particularly vulnerable to the effects of alcohol (Beaton et al., 2018; Stock et al., 2016a, 2016b; Wolff et al., 2018b). As it may also play a crucial role in the development and maintenance of substance abuse (Aragues et al., 2011; Smith et al., 2014; Stock, 2017), there are many studies focusing on response inhibition deficits during acute alcohol intoxication (e.g. Stock et al., 2014; Wolff et al., 2018b). Other forms of inhibitory control, like cognitive inhibition (of inappropriate thoughts, action plans and task sets, which are incongruent with an individual's intentions or goals, see Diamond, 2013), could also be critical to the persistence of alcohol abuse, but have received much less attention. Deficits in this cognitive faculty may impede cognitive flexibility, i.e.

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efficient switching to new appropriate patterns of thought or behavior in adaption to changes in environmental conditions, action outcomes, or goals (Everitt and Robbins, 2005; Stalnaker et al., 2009). Impairments in cognitive inhibition and the resulting changes in cognitive flexibility might also aggravate alcohol abuse or addiction. Yet, the effects alcohol on cognitive inhibition/inhibitory control during task switching have remained largely unknown.

We therefore set out to experimentally investigate the effects of an acute, binge-like alcohol intoxication on cognitive inhibition during task switching using a backward inhibition (BI) paradigm. In order to efficiently switch between different tasks, it is usually not sufficient to merely activate the appropriate task set, as the task set of the previous (i.e. now irrelevant) task needs to be inhibited in order to avoid or at least minimize the conflict between the currently active and the previously relevant task set (Dajani and Uddin, 2015; Mayr and Keele, 2000). The BI effect is measured by assessing the time cost of overcoming the inhibition of a recently abandoned task set that has just become relevant again (Mayr and Keele, 2000). For this, BI paradigms compare the behavioral performance in task sequences in which a given task is repeated from n - 2 trials (BI condition), to when that particular task has no n – 2 trial sequence history and thus re-occurred only after at least two different trials in between (BASE condition). As the BI effect reflects the cost to overcome the previous inhibition of a task set, a larger BI effect is commonly thought to indicate a larger (cognitive) inhibition of the previous task. With respect to alcohol, it could however also reflect larger difficulties in overcoming the inhibition of a previous task. Given that the BI effect has been reported to strongly depend on attentional selection mechanisms (Sinai et al., 2007; Zhang et al., 2017, 2016a, 2016b), which can be impaired by an acute alcohol intoxication (Stock et al., 2017a), it may be more difficult to reactivate the recently suppressed task rules and to overcome the BI when intoxicated. We therefore expected that alcohol increases the BI effect, as compared to the sober state.

To investigate this, we employed a balanced intra-individual study design, where each participant performed the BI task once while intoxicated and once in a sober state. This means that half of the participants were intoxicated during their first appointment and sober during their second appointment, while the other half of the participants were sober during their first appointment and intoxicated during their second appointment. Importantly, balancing the order of appointments in this manner does not only reduce variability between the two investigated states, but also allows to test for potential training effects: Executive functions, including cognitive flexibility, have repeatedly been shown to improve with training on the task and it has been suggested that within-task practice may even help to alleviate performance impairments and raise behavioral performance to an “unimpaired” level in some groups that normally display executive deficits (Sabah et al., 2018). One of the main reasons why training might help to conceal executive performance deficits on the behavioral level is that it establishes rather automated stimulus-response (S-R) mappings, which reduces the strain on limited cognitive control capacities. In the context of our study, it is furthermore important to note that the degree of (task) automaticity may modulate the effects of binge drinking (Stock et al., 2016a), as automated processes and implicit learning seem to remain relatively intact even during high-dose intoxications (Balodis et al., 2007; Beaton et al., 2018; Lister et al., 1991; Stock et al., 2016a). Training and the resulting automaticity may hence diminish or at least reduce the detrimental effects of high-dose ethanol intoxication on executive functions, including BI. We hence hypothesized that extended practice (as defined by already having performed the task for ~30 minutes) increases the automatization of response selection and may therefore reduce the strain on working memory capacity and other cognitive control functions of intoxicated participants. We therefore expected to find smaller intoxication effects (i.e. a smaller increase in BI effect size) in those who were intoxicated during the second of their two identical study appointments, as compared to those who were intoxicated during their first appointment.

To be able to identify the cognitive sub-processes underlying the expected behavioral effects, we recorded an EEG during task performance.

In order to deal with the alcohol-induced increase in response variability and to further be better able to dissociate stimulus- and response-selection associated processes in the neurophysiological data, we ran a residue iteration decomposition (RIDE) (Ouyang et al., 2011, 2015a; Verleger et al., 2014) before quantifying all neurophysiological measures (for details, please refer to the methods section). In short, RIDE decomposes EEG data into several component clusters (Mückschel et al., 2017; Ouyang et al., 2011): The S-cluster reflects stimulus-related processes like perception and attention, while the C-cluster depicts intermediate processes between stimulus and response like response selection and the R-cluster depicts response-related processes including motor preparation and execution (Ouyang et al., 2011). Previous studies had shown that the size of the BI effect seems to strongly depend on early attentional stimulus processing and attentional selection processes (Wolff et al., 2018a; Zhang et al., 2016b, 2017), as reflected by the visual P1 and N1 event-related potentials (ERPs) (Luck et al., 2000). As several other studies with comparable intoxication levels (but other experimental paradigms) have shown that alcohol may decrease attentional processing as reflected by smaller amplitudes in one or both ERPs (Stock et al., 2017a; Wolff et al., 2018b) and impair the top-down allocation of attention (Stock et al., 2017b), we expected alcohol-related changes in the size of the BI effect to be reflected by decreases in the P1 and/or N1 amplitude in the S-cluster. In contrast to this, (the size of) the BI effect has usually not been found to be associated with modulations of the fronto-central N2, which is thought to reflect conflict monitoring and cognitive effort (Larson et al., 2014), or the parietal P3 found in this paradigm, which is commonly believed to reflect the process of linking stimuli to appropriate responses/response selection (Polich, 2007; Verleger et al., 2005). Due to the lack of BI effects on those response selection-associated components (Zhang et al., 2016c), we did not expect these C-cluster ERPs to reflect alcohol-associated or any other changes of BI size. As detrimental effect of an acute alcohol intoxication on various cognitive control functions, including motor response inhibition, have however repeatedly been associated with decreases in N2 and P3 ERPs (e.g. Rohrbaugh et al., 1987; Stock et al., 2017a, 2016b, 2014), we nevertheless decided to also quantify and analyze the N2 and P3 ERPs in the C-cluster in order to provide a more complete picture.

Another neurophysiological measure, which has repeatedly been linked to cognitive control and shown to reflect modulations of (response) inhibition, are theta frequency band oscillations (Beste et al., 2011; Cavanagh and Frank, 2014; Dippel et al., 2016; Mückschel et al., 2017). Both stimulus- and response-related aspects of inhibitory control can be found in theta frequency oscillations (Beste et al., 2011; Dippel et al., 2016; Mückschel et al., 2017): Response-related theta frequency oscillations are mainly observed over frontal areas (Beste et al., 2011; Cavanagh and Frank, 2014; Dippel et al., 2016; Mückschel et al., 2017), closely associated with the N2 and N450 ERPs (Larson et al., 2014), and thought to reflect rather “reactive” aspects of cognitive control such as conflict detection and monitoring or cognitive effort (Botvinick et al., 2001; Cavanagh and Frank, 2014; Cooper et al., 2017). Stimulus-related theta is however more often observed over posterior regions (Freunberger et al., 2007; Gladwin and de Jong, 2005; Sauseng et al., 2006) and thought to reflect more “proactive” aspects of cognitive control (Cooper et al., 2017). Posterior theta has been found at parietal and/or occipital electrodes during task switching (Freunberger et al., 2007; Gladwin and de Jong, 2005) and is supposed to reflect top-down regulation processes in recalling the task set memory, as its power is enhanced when the previous irrelevant visual task must be reactivated (Freunberger et al., 2007; Gladwin and de Jong, 2005). Likewise, posterior theta has been reported to increase when cognitive content needs to be suppressed (Depue et al., 2013). Further matching this, (Cooper