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Cognitive control in young heavy drinkers: An ERP study

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\section{Introduction}

Many studies show that substance use disorders (SUD) are characterized by problems with cognitive control (e.g., Garavan and Weinerstall, 2012; Luijten et al., 2014; Noel et al., 2013; Wiers et al., 2013). In particular two aspects of cognitive control have been studied in SUD patients: error-processing and response inhibition (see for a review, Luijten et al., 2014).

Inhibitory control and error-processing can be regarded as two core components of cognitive control that are both associated with specific neural networks and are both crucial to control substance use. More specifically, inhibitory control is the process of inhibiting inappropriate and automatic behavior, whereas error-processing refers to the monitoring of performance errors and ongoing behavior to prevent future mistakes (Ridderinkhof et al., 2004). Deficits in either inhibitory control or error-processing may respectively result in the inability to inhibit substance use intake, and an apparent failure to adaptively learn from previous harmful behavior thereby hampering the ability to prevent excessive substance or alcohol use (Franken et al., 2007).

The GoNogo task is one of the most commonly used tasks to measure inhibitory control (Chambers et al., 2009). In this task, participants have to respond as quickly as possible to frequent ‘Go’ stimuli, and inhibit the responses to infrequent ‘Nogo’ stimuli thereby requiring inhibitory control to overcome automatic response tendencies. Two ERP components have been reported to reflect changes in brain activity related to inhibitory control (Kok et al., 2004). The Nogo-N2 is a negative-going wave visible 200–300 ms after stimulus presentation and is thought to index a top-down mechanism necessary to inhibit the automatic tendency to respond (Falkenstein, 2006). The Nogo-N2 has also been related to early-stage conflict detection during the inhibition process (Nieuwenhuis et al., 2003). The Nogo-P3 is a positive-going wave visible 300–500 ms after stimulus onset. The Nogo-P3 arises from motor and pre-motor cortices (Huster et al., 2010). Hence, Nogo-P3 amplitudes likely reflect a later stage of the inhibitory process when actual inhibition of the motor system in the premotor cortex takes place (Band and Van Boxtel, 1999).

Several studies among alcohol dependent patients showed reduced response inhibition using behavioral indices (e.g., Lawrence et al., 2009; Noel et al., 2007; Rubio et al., 2008), which was confirmed in a recent meta-analyses clearly showing that substance use disorders, including alcohol dependence, are associated with impairments in inhibitory control on the behavioral level (Smith et al., 2014). At the...
neural level, some studies suggest Nogo-P3 deficits in individuals with alcohol dependence during inhibition-related task performance (see Luijten et al., 2014 for a systematic review).

For error-processing, the most commonly used paradigm is the Eriksen Flanker task. In a typical version of the Eriksen Flanker task (Eriksen and Eriksen, 1974), participants are exposed to series of letters and participants are asked to identify the middle letter. In the incongruent condition the middle letter differs from the other letters (e.g., SSHSS/HHSSH) as opposed to the congruent condition (HHHHH/SSSSS). The high stimulus conflict situation in the incongruent condition usually results in performance errors, making it possible to measure the brain’s response to mistakes.

On the electrophysiological level, two independent error-related ERPs consistently emerge after performance errors, i.e., the error-related negativity (ERN) and the error-positivity (Pe) (Overbeek et al., 2005). The ERN arises 50–80 milliseconds after an error and reflects initial and automatic error detection with the anterior cingulate cortex as the neural generator (Bernstein et al., 1995). In contrast, the Pe is a positive EEG peak, emerging approximately 300 ms after incorrect responses with a centro-parietal distribution (Falkenstein et al., 2000). Conceptually, the Pe appears to be associated with the more conscious evaluation of errors, error-awareness (Overbeek et al., 2005), and the motivational significance attributed to an error (Ridderinkhof et al., 2009).

Previous studies consistently showed reduced ERN and Pe amplitudes in various addicted populations, including cocaine dependent patients, smokers as well as behavioral addictions such as food addiction and gaming (Franken et al., in press; Luijten et al., 2014). In contrast to the other addicted populations alcohol dependent patients showed increased ERN amplitudes, which could be explained by enhanced anxiety levels observed in this sample of alcohol dependent patients (Schellekens et al., 2010).

From the abovementioned studies, it can be concluded that there are behavioral and electrophysiological indications that alcohol dependence is associated with deficits in both inhibitory control and error-processing. However, it is not clear whether these deficits are specific for patient populations or whether these deficits might also be observed in high-risk populations. One important high-risk population is the group of young heavy drinkers (i.e., adolescents and young adults). It is known that heavy drinking in adolescence and young adulthood is associated with substance use disorders (SUDs) in adulthood (DeWit et al., 2000). Besides this risk, heavy drinking among students is related to a series of negative alcohol-related consequences and psychosocial problems (Perkins, 2002; Turrisi et al., 2006; Wechsler et al., 1998). In addition, there is growing literature on the relation between binge-drinking, particularly among college-aged populations, showing that an intermittent-but-high alcohol use pattern is associated with less inhibitory control (see a review by Lopez-Caneda et al., 2014), and a range of ERP indices of aspects of cognitive control (see a review by Petit et al., 2014). More specifically, several studies provide indications that heavy drinking during adolescence and young adulthood might indeed be associated with electrophysiological and behavioral indices of reduced cognitive control discussed above (i.e., error-processing and response inhibition measured using the GoNogo task). For example, Smith and Mattick (2013) found evidence for deficits in response inhibition and error processing in young female heavy drinkers. However, that sample size was relatively small (13 heavy drinkers), in inhibition and error processing in young female heavy drinkers.

2. Methods

2.1. Participants

Participants were recruited by written and verbal advertisement on the university campus. The educational level for all subjects was equal for both groups as we recruited only subjects following higher education. Both groups (i.e., light and heavy drinkers) were selected from a larger population that was screened on alcohol use using the Quantity-Frequency-Variability index (QFV; Bongers et al., 1997; Lemmens et al., 1992). The QFV measures alcohol consumption by four questions: “Which alcoholic drinks do you usually drink when you drink?”; “How many days a month do you drink on average?”; “If you drink alcohol, how many glasses do you drink on average?”; “Have you ever drunk six or more glasses at one day in the past six months?” Based on this QFV, participants were categorized either as light drinkers or as heavy drinkers (i.e., the joined categories “very excessive” and “excessive” drinkers; see Table 1).1 The QFV was assessed also in the week of testing. If the person did not fill the criteria anymore, he or she was not invited to participate in the study.

The resulting group of participants consisted of 49 light drinkers and 48 heavy alcohol drinkers. Mean age of the heavy drinkers was 23.4 years (SD = 10.0) and mean age of the light drinkers was 22.9 (SD = 8.5). The groups were matched on gender, age and education. No differences between these variables were observed (see Table 2, all p’s > .75).

For the ERN/Pe EEG analyses ten participants (4 heavy drinkers and 6 light drinkers) were excluded from the analyses because they either

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1 If all persons (n=23) who fulfill the criteria of having a (albeit infrequent) binge drink were removed from the light drinking group (i.e., by excluding persons who drink > 3 glasses on average per drinking day), the analysis yield the same results, except for the Pe difference, which becomes non-significant (probably due to reduced power).
had fewer than 8 artifact-free incorrect response EEG epochs (n = 9; see Rietdijk et al., 2014) or too many errors (i.e., > 50% incorrect; n = 1). For the behavioral analyses, responses of six subjects were missing due to recording problems (3 in each group). The study was conducted in accordance with the Declaration of Helsinki and all procedures were carried out with the adequate understanding and written informed consent of the subjects. This study was performed according to local ethical guidelines of the Department of Psychology, Education and Child Studies at the Erasmus University Rotterdam.

2.2. Task and procedure

Upon arrival, subjects were instructed about the procedure and informed consent was obtained. Subsequently, participants filled out a short demographic questionnaire. After this, participants were seated on a comfortable chair in a light and sound-attenuated room. First subjects performed the GoNogo task (Littel et al., 2012). Participants were presented with a GoNogo paradigm, consisting of four blocks of 159 letters (636 in total) that appeared one after one on the screen (e.g., A B C D). In total, 74 letters (11.6%) were repetitions of the previously presented letter (e.g., A B C C). Participants had to press a button with the right index finger for all letters (Go trials) but withhold their response for repeated letters (Nogo trials). Letters were presented for 700 milliseconds, each preceded by a fixation cross, which was displayed for 300 milliseconds. Nogo trials were presented unpredictably by introducing jitter in the number of intermitted Go trials. Nogo trials were never presented in succession. Between blocks, participants received breaks of 60 s.

After the GoNogo task subjects performed an Eriksen Flanker task (Eriksen and Eriksen, 1974; see for details Franken et al., 2010), while ERPs were measured. Four different letter strings (SSSSSS, HHSS, HHISH, HHHH) were presented on the computer screen and subjects were instructed to press a button with the right index finger of the central letter was an H and with the left if the central letter was an S. Response times from onset stimulus to button press on congruent (SSSSSS, HHHHHH; n = 200) and incongruent trials (SSSSH, HHISHH; n = 200) were recorded. Trials started with a 150 ms cue (”) where the central letter of the letter strings would appear. Letter strings were presented for 50 ms. Responses were followed 700 ms later by a feedback symbol (duration = 500 ms) about correctness of the response (+ or -). When no response was made within 700 ms, participants received a feedback stimulus informing them their answer was not fast enough.

2.3. Electroencephalographic (EEG) recording and signal processing

The EEG was recorded using Biosemi Active-Two amplifier system from 32 scalp sites (10–20 system) with Ag/AgCl electrodes (acta electrodes) mounted in an elastic cap.

Furthermore, six additional electrodes were attached to left and right mastoids, two outer canthi of both eyes (HEOG), and infraorbital and supraorbital regions of the eye (VEOG). All signals were digitized with a sample rate of 512 Hz and 24-bit A/D conversion. Data were offline re-referenced to computed linked mastoids. Off-line, EEG and EOG activity was filtered with a bandpass of 0.1–35 Hz (phase shift-free Butterworth filters; 24 dB/octave slope).

For both tasks, data were segmented in epochs of 900 ms: 100 ms before and 800 ms after response (Eriksen Flanker task) or stimulus onset (GoNogo task). After ocular correction (Gratton et al., 1983), epochs including an EEG signal exceeding ± 75 μV were excluded from the average. The mean 100 ms pre-response period served as baseline. The ERN was defined as the as the mean value in the 25–75 ms time segment after onset of the response.

The Pe was defined as the mean value in the 200–400 ms time segment after onset of the response. For the ERN we studied the midline electrodes Fz, FCz and Cz, for the more posterior Pe component we studied the Cz, CPz and Pz electrodes. Because the number analyzable error-epochs in the Eriksen Flanker tasks is depending on performance, we analyzed the number of available epochs. The ERN and Pe were based on a mean number of 26.0 (SD = 28.0) analyzable error-epochs in the light drinking group and 25.2 epochs (SD = 21.0) in the heavy drinking group. The mean number of available error-epochs did not differ between groups, t(95) = .16, p = .87.

Concerning the inhibition related ERPs, we defined the N2 as the mean value in the 220–320 range and the P3 as the mean value in the 320–500 range (Littel et al., 2012). Both N2 and P3 were studied on the Pz, Cz and Pz electrodes.

2.4. Data analysis

For the behavioral accuracy in the GoNogo task we employed a t-test with group (heavy vs. light drinkers) as the independent variable to test the differences in inhibition (errors on the Nogo trials/commission errors). For the behavioral reaction time (RT) data, we employed a t-test to test for overall RT differences (over all trials). For the N2 and P3 we conducted a $2 \times 2 \times 3$ ANOVA with group (heavy vs. light drinkers) as between subjects factor, and condition (Go, Nogo) and Region (Fz, Cz, Pz) as within subjects factor.

For the behavioral accuracy in the Eriksen Flanker task we employed 2 × 2 ANOVAs (Group X Congruency). For the behavioral reaction time (RT) data, we employed a t-test for overall RT differences (over all trials). For the N2 and P3 we conducted a $2 \times 2 \times 3$ ANOVA with group (heavy vs. light drinkers) as between subjects factor, and correctness (incorrect, correct), and Region (Fz, FCz, Cz and Cz, CPz, and Pz, respectively) as within subjects factor. Follow up t-tests on the incorrect minus correct ERP difference scores were employed if the interactions were significant. For repeated measurement ANOVAs Greenhouse-Geisser adjusted p-values were used. Significant ANOVA interaction effects were further analyzed using Bonferroni-corrected post-hoc t-tests. For all analyses, the .05 level of significance was employed.

Although it was not a main goal of the present study, but given the fact that in a previous study only female subjects were included (Smith and Mattick, 2013) or deficits were only found in females (Smith et al., 2015), we included gender as additional factor in all analyses. However, no significant gender nor gender x group interactions were found (all ps > .08), therefore gender effects are not reported.

3. Results

3.1. Behavioral data

From Table 3 it can be seen that on the Go-Nogo task, light and heavy drinkers exhibited similar performances concerning behavioral inhibition. No significant behavioral differences between the heavy and light drinkers were observed in terms of inhibition errors, t(91) = .08; p = .94, and reaction times, t(91) = .55; p = .59. Also on the Eriksen Flanker task no group differences (nor group interaction) on performance measures were found (see Table 3, all p’s > .78). However, an effect of Congruency (i.e., the classical flunker effect) was observed: we found over both groups more errors F(1,90) = 146.6; p < .001 and slower reaction times F(1,90) = 603.6; p < .001 on the incongruent
Inhibition

For the N2 (see Fig. 1), the main effect of Condition (Go vs. Nogo) just failed to reach significance (F(1,91) = 3.4; p = .07, with Nogo trials having larger N2s than Go trials. Further, no effect of group nor an interaction with group were observed (all p’s > .09) showing that heavy drinkers and light drinkers did not differ on the inhibition associated N2 amplitude.

For the P3, a main effect of condition was found on the Go versus Nogo trials, F(1,91) = 143.4, p < .001. As expected, the P3 was larger for Nogo than Go trials, confirming that the P3 is indeed associated with behavioral inhibition. However, no Group or Group interaction effects were observed (all p’s > .27). These findings show that heavy drinkers did not differ on the Nogo-P3 from light drinkers.

Error processing

For the ERN (see Fig. 2), a Condition effect was observed, F(1,85) = 136.6, p < .001, with higher (i.e., more negative) amplitudes on the incorrect trials as compared to correct trials. No main or interaction effect of Group was observed (all p’s > .37).

If we employed an N2 peak measure as done by several authors, a main effect of condition (Go vs. Nogo) was significant (F(1,91) = 28.0; p < .001), with Nogo trials having larger N2s than Go trials. However, consistent with the area measure results, no effects of Group nor Group interaction effects were observed (all p’s > .08) if a peak measure was used.

For the Pe, we also observed a significant effect of Condition (F(1,85) = 269.5, p < .001, with enhanced Pe amplitudes on the incorrect trials as compared to correct trials. In addition, the Group × Condition effect approached significance F(1,85) = 3.6, p = .06. Importantly, there was a significant Group × Condition × Electrode effect F(1,85) = 3.7, p < .02. Follow-up tests on difference waves (incorrect minus correct) showed an Electrode × Group effect, F(2,170) = 4.8, (p < .02) with a group difference at Pz (p = .01), but not at Cz (p = .26) and CPz (p = .06). Heavy drinkers demonstrated reduced error-related Pe amplitudes on Pz as compared to light drinkers.

4. Discussion

In the present study, we examined the presence of problems with cognitive control by employing both behavioral and psychophysiological indexes of response inhibition and error-processing in a sample of young heavy drinkers.

Overall, we did not observe differences in several behavioral and psychophysiological indexes of cognitive control between young light and heavy drinkers. Specifically, no behavioral differences were observed on an Eriksen Flanker task and a GoNogo task suggesting an intact behavioral inhibition in heavy drinkers. In addition, electrophysiological differences between the groups were limited to a reduced Pe for the heavy drinkers during error processing, but no differences were observed on the ERN and no differences on electrophysiological indexes of response inhibition (i.e., inhibition-related N2 and P3 components related to the GoNogo task). The present findings suggest that cognitive control in young heavy drinkers is generally unaffected as compared to light drinkers. This is consistent with recent reviews (Wiers et al., 2015) and a recent large scale epidemiological study (Boelema et al., 2015) showing that, in contrast to patient populations, such as alcohol use disorder patients, young heavy drinkers do not display major neurocognitive deficits associated with cognitive control. In the present study, one exception was found: the Pe amplitude on the Pz electrode was reduced in heavy drinkers as compared to light drinkers. Since the Pe reflects a motivational component, (i.e., the salience attributed to the making of errors; see Overbeek et al., 2005; Ridderinkhof et al., 2009), rather than a basic cognitive process, it can be concluded that heavy drinking in this population is not associated with major impaired cognitive control, but rather with impairments that are associated with aberrant attribution of salience to the making of errors. We measured several EEG and behavioral measures, but only found evidence for a difference between the groups on this Pe component that most likely represents a motivational process. Although this is a relatively minor finding, we don’t have any information on whether or how this will result in impairments in real life. The present design of the study prohibits making causal statements. The aberrant attribution of salience in this population might be the result of alcohol drinking or the heavy alcohol drinking could be the result of the aberrant attribution of salience. Longitudinal research is needed to clarify this issue.

Importantly, several recent studies suggest that reduced cognitive control (i.e., response inhibition and performance monitoring) is specifically observed in female heavy drinkers (Nederkoorn et al., 2009; Smith and Mattick, 2013; Smith et al., 2015). We additionally conducted specific analyses on gender, but these analyses did not yield any significant (interaction) effects for gender, suggesting that we are not able to confirm the previous findings that cognitive control deficits are only present in female heavy drinkers.

One possible interpretation of the present findings is that it might be important to attend more closely to the pattern of use, rather than just to the overall level of alcohol use. For example, Maurage et al. (2012) report significant reductions in ERP amplitudes specifically for binge-drinkers. Therefore, it might well be that a specific binge drinking pattern is more associated with reduced control-related ERPs than alcohol consumption per se.

The present study has a number of limitations. One limitation is the sample size. With the present sample size we were not able to detect small effects, so we cannot exclude the possibility that heavy drinking is associated with subtle impairments in cognitive control, particularly in subgroups such as female heavy drinkers. Having said this, the present sample size is larger than most studies using EEG measures in this area (Smith and Mattick, 2013; Smith et al., 2015). Clearly, larger studies using physiological measures are needed to resolve this issue. Another limitation is that we did not collect data on the number of years of drinking and on the use of other substances than alcohol in our sample. In future studies it would be interesting to investigate whether the duration of heavy drinking is associated with cognitive problems. Also the influence of binge drinking vs. “steady but not-binging drinking” could be addressed in future studies. In addition, the distribution of other substance use could be different in the two groups. However, it is
expected that if anything, the heavy drinkers display more substance use (other than alcohol). Previous studies show that the likelihood that one has tried a greater number of substances is related to a higher amount of alcohol use (O’Grady et al., 2008). Therefore, it is unlikely that the use of other drugs could explain the fact that no differences on ERN and P3 were found. However, it could explain the Pe differences between the groups. An additional limitation is that we don’t have information about the abstinence rate of the participants during the EEG measurements (e.g., hangover effects) and smoking status. Although this theoretically could have influenced the results, it is not likely that it would explain the fact that we did not observe major differences between light and heavy drinkers since it is more likely that, if anything, heavy drinkers would have higher hangover rates and are known to have higher smoking rates. Further, the present study is not longitudinal, so we can’t say anything about the development of impairments of cognitive control over time. In the present study we are not able to investigate the long term consequences of heavy drinking and can therefore not rule out the possibility that heavy drinking could have consequences on cognitive control later in life. Finally, we only included persons with higher education. We don’t know whether the present results generalize to persons with lower education.

From the present study it can be concluded that heavy drinking in young adults is not associated with a major impairment in cognitive control.
control, but might be associated with rather motivational impairments that are associated with aberrant attribution of salience to the making of errors.

Contributors

Ingmar Franken: Designed the study, conducted the analyses, wrote the first draft of the paper Maartje Luijten: Contributed to the article preparation.
Jan van Strien: Contributed to the article preparation.
Freddy van der Veen: Contributed to the article preparation.
All authors participated in the research and article preparation. All authors have approved the final article.

Role of funding

Nothing declared.

Conflict of interest

No conflict declared.

Acknowledgement

None.

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