

ALCOHOL CUE-REACTIVITY IN HEAVY AND LIGHT SOCIAL DRINKERS AS REVEALED BY EVENT-RELATED POTENTIALS

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Abstract — An elevated cue-reactivity evoked by alcohol-related stimuli (cues) in alcohol-dependent patients has been described for different physiological variables, including electrophysiological measures, such as event-related potentials (ERPs). Cue-reactivity has, however, also been reported for social drinkers. The aim of this study is to assess the effect of the drinking behaviours of social drinkers on cue-reactivity as measured with ERPs. Forty alcohol-related and 40 neutral pictures were presented to 15 heavy and 15 light drinkers (all males). ERPs were recorded using 21 scalp electrodes. Stimuli were presented for 500 ms with an inter-stimulus interval of 2000 ms. Heavy social drinkers displayed a cue-reactivity of significantly higher amplitude at the frontal electrode location Fz, elicited by alcohol-related, as compared to neutral, pictures. This effect was not found in light social drinkers. The results indicate that the cue-reactivity previously found in alcohol-dependent patients is also present in social drinkers, and that electrophysiological cue-reactivity is associated with alcohol consumption.

INTRODUCTION

Exposure to alcohol-related cues leads to an increased urge to drink (Cooney *et al.*, 1987; Staiger and White, 1991; Payne *et al.*, 1992; Wiesbeck *et al.*, 2000), to increased anxiety and tension (Eriksen and Goettestam, 1984), and to changes in several physiological measures, such as heart rate (Kaplan *et al.*, 1985; Turkkan *et al.*, 1989; Payne *et al.*, 1992), skin-conductance level (Kaplan *et al.*, 1985; Turkkan *et al.*, 1989) and intense salivation (Pomerleau *et al.*, 1983) in alcohol-dependent patients. Previous research has demonstrated an electrophysiological cue-reactivity of significantly higher amplitude in the event-related potentials (ERPs) in alcohol-dependent patients, elicited by alcohol-related, as compared to neutral, stimuli (Herrmann *et al.*, 2000). Alcohol-related cues did not in general have this effect in the control group in this study, except in certain subjects who were social drinkers.

This finding is in line with other studies investigating cue-reactivity in social drinkers. These studies have consistently revealed that social drinkers respond to the presentation of alcohol cues, as compared to neutral stimuli, with an increased desire for alcohol (Cooney *et al.*, 1987; Walitzer and Sher, 1990). When the drinking behaviours of control participants were examined, it was found that heavy drinkers were characterized by an increased urge to drink after exposure to alcohol cues, compared to light drinkers (Greeley *et al.*, 1993). Furthermore, heavy drinkers (Cox *et al.*, 1999), similar to alcohol-dependent patients (Wetterling *et al.*, 1992; Drobles *et al.*, 1994; Sayette *et al.*, 1994), display decreased performance whilst exposed to alcohol cues. The current investigation postulates that heavy drinkers display a higher cue-reactivity than light drinkers in an electrophysiological paradigm, particularly in the P300 time segment.

MATERIALS AND METHODS

Participants

A total of 30 healthy male participants took part in this investigation. Twenty participants were employees of the hospital, and 10 were recruited by means of advertising and received a small monetary payment. The participants were not selected according to the amount of alcohol they habitually consumed. Exclusion criteria included an actual or former psychiatric or neurological disorder. All participants had normal or corrected to normal vision and were native German speakers. Formal consent was obtained from participants who met the requirements of the study. In order to exclude problematic drinking behaviour, the CAGE questionnaire (Mayfield *et al.*, 1974) was administered. This questionnaire consists of four items and has been shown to screen for alcoholism in German samples (Wetterling, 1999). A cut-off point of 1 was applied. Furthermore, participants were asked about the quantity and frequency of their drinking habits as well as their family history of alcohol dependency according to the items of the German version of the Semi-Structured Assessment of Genetics of Alcoholism (SSAGA; Buchholz *et al.*, 1994). The mean age (\pm SD) of the participants was 36.6 ± 8.5 years. All participants were males and right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). The experimental group was divided into heavy and light drinkers according to the median [27 standard drinks (216 g of pure alcohol) per month] of the given monthly drink consumption. The ages and the drinking characteristics of the sample are summarized in Table 1.

Experimental stimuli

To construct a set of picture stimuli, we started with 80 words. Each word was rated for its specificity to alcohol and emotionality by a group of 11 alcohol-dependent patients not taking part in this electrophysiological investigation. These patients were required to estimate the relatedness of each item to their alcohol-drinking habits (specificity of the items) and state the current pleasantness or unpleasantness of the item described (emotionality of the items). The specificity scale

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Table 1. Age and drinking characteristics of heavy and light drinkers

	Light	Heavy	<i>t</i> (df = 28)
Age (years)	36.5 ± 12.1	36.5 ± 13.9	0.0
Drinking days/week = frequency	1.0 ± 1.1	3.9 ± 2.0	-5.0***
Drinks#/days = quantity	2.2 ± 2.0	4.0 ± 1.2	-3.0**
Drinks/month	11.1 ± 9.8	61.2 ± 36.8	-5.1***

Values are mean ± SD.

*One drink = 8 g alcohol.

P* < 0.01; *P* < 0.001.

ranged from 0 ('not at all') to 4 ('extremely'). The emotionality scale ranged from -2 ('very unpleasant') to 2 ('very pleasant'). Based on the results of these ratings, the eight words with the highest specificity were chosen as alcohol-related stimuli and the eight words with the lowest specificity were selected as neutral stimuli (Herrmann *et al.*, 2000). The alcohol-related words were the German terms for 'bottle', 'tin', 'brandy', 'booze', and four words for beer that are specific to the German language. The neutral words included the German terms for 'juice', 'water', 'coffee', 'chips', 'apple', 'bread', 'banana', and 'lemonade'. Each word was translated into five different coloured pictures resulting in 40 alcohol-relevant and 40 neutral pictures. The pictures were presented on a neutral background.

EEG recordings

The electroencephalogram (EEG) was recorded at 21 scalp sites positioned according to the international 10–20 system using gold-cup electrodes (Nicolet, 3 mm diameter). Linked mastoids with compensating resistors of 10 kΩ were used as reference electrodes. Three additional electrodes were placed on the outer canthi of both eyes and below the right eye to monitor eye blinks. The band pass was set to 0.1–70 Hz and the EEG was sampled continuously at a rate of 256 Hz. Impedance values were kept at ≤5 kΩ. A 32-channel DC amplifier (Brain-Star-System) and acquisition software (Neuroscan) were used to record results.

Procedure

Prior to the EEG recording, participants were required to respond to a list of adjectives in order to measure their current mood (EWL-60-S; Janke and Debus, 1996). The subscales of the EWL-60 are activity-related activation, general deactivation, extraversion and introversion, general positive feeling, emotional petulance and anxiety, and depression. During the electrophysiological investigation, participants were seated in a comfortable chair in a light and sound-attenuated, electrically shielded room. They received instructions to avoid movement during the test and to open their mouth slightly.

The task itself consisted of 80 pictures, 40 alcohol-related and 40 neutral slides. Eight different objects were presented in five slightly modified versions for both stimulus categories. The stimuli were presented in a pseudo-randomized order in the centre of a computer monitor placed 100 cm from the participants' eyes, with a visual horizontal angle of ~8.0° and a vertical angle of ~5.7°. Each stimulus was displayed for 500 ms with a constant inter-stimulus interval of 2000 ms. To control for attentional influences, the participants were asked

to name the last object displayed on the screen after presentation of 8–10 stimuli. Following the EEG recording, participants rated the pleasantness (emotionality rating) and the relatedness of the stimuli to their personal alcohol drinking habits (specificity rating).

Data analysis

Trials affected by artefacts were automatically identified, highlighted by the software employed, and rejected from all further analyses (based on an artefact criterion of >98 µV voltages in any one of the 24 channels (21 scalp electrodes and three EOG leads) at any point within the first 500 ms following stimulus presentation). The artefact-free trials were averaged separately offline for each participant for alcohol-related and neutral stimuli. The peak amplitudes for the electrode locations Fz, Cz and Pz were calculated for each time segment.

Segmentation

In order to determine the time segments for the analyses in a data-driven manner, the grand mean time course of the ERPs was calculated for all participants, in both conditions and at the three electrode localizations. This curve revealed three maxima and three minima located within the first 500 ms (Fig. 1). The minima (maxima, respectively) preceding and following each of the three maxima (minima, respectively) were set as the limits of the respective segment, resulting in time windows of 62.5–101.6 ms for the first negative component (N100), 74.2–125.0 ms for the first positive component (P100), 101.6–187.5 ms for the second negative component (N200), 125.0–250.0 ms for the second positive component (P200), 187.5–347.7 ms for the third negative component (N300), and 250.0–429.7 ms for the third positive component (P300).

Statistical analyses

Cue-reactivity is defined as the peak amplitude elicited by alcohol-related stimuli minus the peak amplitude elicited by neutral stimuli, for every component. Group differences in cue-reactivity and current mood ratings were tested with the non-parametric Mann–Whitney test (values were not normally distributed). Spearman correlations were calculated between the cue-reactivity and the amount of alcohol habitually consumed. *t*-Tests for independent measures were carried out on the emotionality and specificity ratings in order to assess group differences; *t*-tests for dependent measures were applied to assess differences in stimulus categories within each group. Spearman correlations for the emotional states according to the subscales of the EWL-60 and stimuli ratings were calculated for components in which the electrophysiological cue-reactivity differed significantly between groups.

RESULTS

Cue-reactivity

Figure 2 shows the grand mean curves elicited by alcohol-related and neutral cues for heavy and light drinkers. Analyses of the group differences in cue-reactivity revealed a significant effect for the late positive component P300 at the frontal electrode position Fz ($Z = -2.2$, $P < 0.05$) and a significant effect for the early negative component N100, peaking at the central

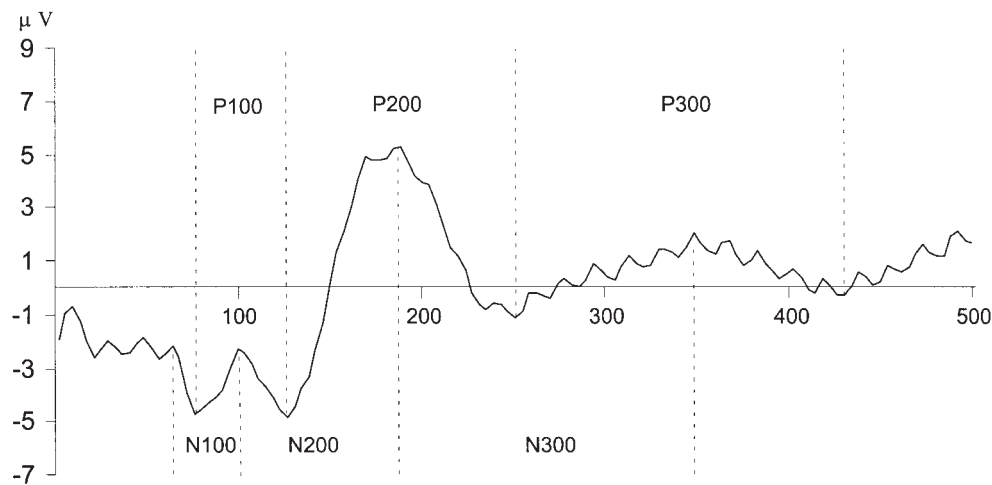


Fig. 1. Grand mean amplitude curve.

Grand mean event-related potential curve for all participants and both stimulus categories over three electrode positions (Fz, Cz, Pz) are shown. Vertical lines indicate segment borders for the negative (N100, N200, N300) and positive (P100, P200, P300) components.

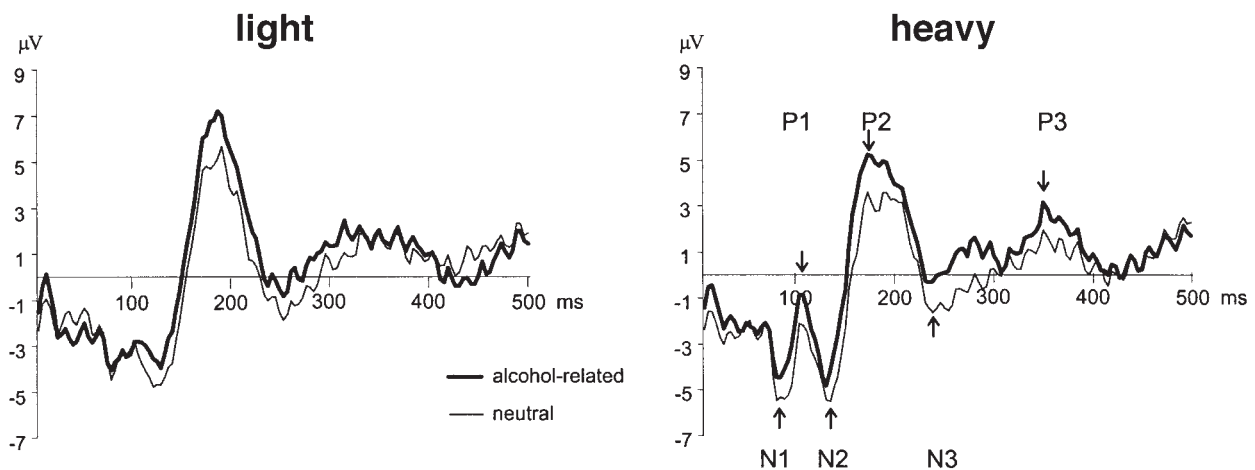


Fig. 2. Grand mean amplitude curves for heavy and light drinkers in response to alcohol-related and neutral stimulus categories.

Grand mean event-related potential curve for all participants and both stimulus categories over three electrode positions (Fz, Cz, Pz) divided into alcohol-related (bold lines) and neutral stimulus categories (thin lines) are given.

electrode position Cz ($Z = -2.1$, $P < 0.05$) (Table 2). The P300 cue-reactivity correlated significantly with the amount of habitually consumed alcohol at Fz ($r = 0.39$, $P < 0.05$) and showed a tendential correlation at Cz ($r = 0.35$, $P < 0.10$). N1 cue-reactivity only indicated tendential effects at Fz ($r = 0.35$,

$P < 0.10$) and Cz ($r = 0.34$, $P < 0.10$). These results indicate that heavy drinkers display decreased N100 and increased P300 amplitudes to alcohol relevant stimuli in relation to neutral stimuli. These effects were not observed in light drinkers.

Stimuli ratings

The stimuli ratings of the heavy and light drinkers for the stimuli presented are given in Table 3. Both the light ($t = 2.29$; $P < 0.05$) and the heavy ($t = 3.97$; $P < 0.01$) drinkers rated the alcohol-related stimuli as more specific to their drinking habits than neutral stimuli. Furthermore, the neutral stimuli were rated as more pleasant than the alcohol-related stimuli by light ($t = -7.81$; $P < 0.000$) and heavy ($t = -9.17$; $P < 0.000$) drinkers. Heavy drinkers rated the alcohol-related stimuli as more pleasant than did the light drinkers ($t = -2.14$; $P < 0.05$).

Spearman correlations were calculated for the electro-physiological cue-reactivity and the cue-reactivity of the

Table 2. Cue reactivity

	N100	P100	N200	P200	N300	P300
Fz	-1.7**	-1.3	-0.7	-0.6	-0.7	-2.2*
Cz	-2.1*	-1.7**	-0.0	-0.8	-0.2	-1.3
Pz	-1.8**	-0.9	-1.0	-0.9	-0.6	-1.0

Z-values for group differences between light and heavy drinkers for cue reactivity (alcohol-related minus neutral). N100, N2, N3 are the negative, P1, P2, P300 are the positive components of the ERP. Electrode position is abbreviated with Fz (frontal), Cz (central), and Pz (parietal) at midline.

* $P < 0.05$; ** $P < 0.10$.

Table 3. Stimuli ratings for specificity and emotionality

Ratings	Stimuli	Light (n = 15)	Heavy (n = 15)	t (df = 28)
Specificity	Alcohol-related	0.99 ± 0.66	1.29 ± 0.43	-1.44
	Neutral	0.55 ± 0.61	0.66 ± 0.67	-0.44
	t	2.29*	3.97**	
Emotionality	Alcohol-related	1.48 ± 0.61	1.87 ± 0.29	-2.14*
	Neutral	3.11 ± 0.57	2.88 ± 0.46	1.21
	t	-7.81***	-9.17***	

Means, SD and *t*-tests, two-tailed, for independent measures between the light and heavy drinkers, paired *t*-tests between stimulus categories alcohol-related and neutral within both groups for specificity and emotionality ratings.

P* < 0.05; *P* < 0.01; ****P* < 0.001.

emotionality and specificity ratings (mean rating given to alcohol-related stimuli minus rating given to neutral stimuli). The emotional cue-reactivity correlated significantly with the electrophysiological cue-reactivity at the electrode positions Fz (*r* = 0.40; *P* < 0.05) and Cz (*r* = 0.50; *P* < 0.01), and with the N100 cue-reactivity at Fz (*r* = 0.37; *P* < 0.05). Separate analyses of heavy and light drinkers did not replicate the significant correlations mentioned above. No significant correlations between the specificity cue-reactivity and the electrophysiological cue-reactivity were found.

Emotional state

Heavy and light drinkers did not differ on their scores on any of the subscales of the EWL-60 used to measure their emotional state before the EEG recording. The cue-reactivity of the N100 component at the electrode positions Cz (*r* = -0.45; *P* < 0.01) and Pz (*r* = -0.45; *P* < 0.01) correlated significantly with the subscale of the EWL-60 'Performance Oriented Activity', and the cue-reactivity of the N100 component at the electrode position Pz correlated with 'extraversion' (*r* = -0.39; *P* < 0.05) according to Spearman rank correlations. No significant correlations were found for the cue-reactivity of the P300 component and the emotional state according to the EWL-60.

Family history

In each group, ~12% of the participants had a close relative with a history of alcoholism.

DISCUSSION

A significantly enhanced N100 and P300 cue-reactivity was found in heavy drinkers, as compared to light drinkers. This result is in line with other studies indicating cue-reactivity for non-dependent social drinkers (Cooney *et al.*, 1987; Walitzer and Sher, 1990) as well as a stronger cue-reactivity for heavy drinkers, compared to light drinkers (Greeley *et al.*, 1993). Furthermore, this view is supported by a previous study in which increased electrophysiological cue-reactivity in alcohol-dependent patients, as compared to healthy controls, was shown (Herrmann *et al.*, 2000). However, a direct comparison of these two studies is not possible, as the first used words as stimuli, whereas the present study used pictures as stimuli.

Since the groups, heavy and light drinkers, do not differ in their family histories of alcoholism, it seems unlikely that the observed differences in ERP amplitudes are the result of differential genetic loading.

The relatively small sample size and the exploratory nature of the experimental proceedings are weaknesses of the present study and should be taken into consideration in interpretation of the results.

P300 component

Three basic processes regarding the P300 component need to be considered. These are effects of attention, of emotional content, and of memory. The P300 component is usually elicited with the instruction to focus attention on the stimuli. Therefore, a higher P300 component for alcohol-related cues, as compared to neutral stimuli, could be the result of a shift in attention. Indeed, Stetter *et al.* (1995) found significantly longer reaction times for alcohol-related words as compared to neutral cues, in a modified Stroop task in alcohol-dependent patients, which could not be found for healthy controls. This result can be interpreted as a shift in attention toward alcohol-related stimuli in alcohol-dependent patients. Stormark *et al.* (1997) investigated shifts in attention with a dot-probe paradigm for two time points, 100 and 500 ms after stimulus presentation (Posner *et al.*, 1982). Their results showed a shift toward alcohol-related stimuli after 100 ms, but a shift away from alcohol-related stimuli after 500 ms, in alcohol-dependent patients. In contrast, the higher P300 amplitudes in heavy drinkers elicited by alcohol-related cues, as compared to neutral stimuli, in this study showed a shift of attention toward alcohol-related stimuli.

This attentional modulation of the P300 component should be considered separately from the finding in alcohol dependence of generally reduced P300 in a classical oddball paradigm (Begleiter and Porjesz, 1990), which has also been found in those at high risk of alcoholism before it has developed (Hill *et al.*, 1988). It has been proposed that this reduced P300 amplitude is a genetic marker for alcoholism and is the consequence of disturbed frontal brain activity. The psychological correlate is a reduced ability to direct attention to certain stimuli, which is reflected by a diminished P300 amplitude. In contrast, the participants of our study did not receive instructions to focus their attention on one category of stimuli. Our data imply that heavy drinkers pay more attention to alcohol-related stimuli than light drinkers, independently of whether general ability to focus attention on certain stimuli is comparable.

It has been shown that the P300 component is modulated by the emotional content of the stimuli, resulting in an enhanced P300 amplitude elicited by emotional, as compared to neutral, stimuli (Diedrich *et al.*, 1997; Naumann *et al.*, 1997; Schupp *et al.*, 2000). These latter authors interpreted this effect following presentation of affective pictures as an indication of the intrinsic motivational significance of these pictures. Therefore, one may argue that the higher amplitudes elicited by alcohol-related cues indicate a more emotional evaluation of these stimuli.

Memory effects contribute to enhanced ERP components (Rugg, 1995). Enhanced late positive ERP components were reported for learned, as opposed to new, stimuli in a retrieval memory paradigm. However, this effect is at its maximum at ~600 ms post stimulus at parietal electrode positions (Johnson,

1995), in contrast to which, the observed cue-reactivity in our study was at its maximum at ~350 ms post stimulus at a frontal electrode position. Based on these findings, we assume that the observed P300 cue-reactivity in the present study is affected more by the attentional and emotional impact of the stimuli, than by memory effects.

N100 component

Flor *et al.* (1997) reported that patients with chronic pain have a significantly elevated N100 as a reaction to pain-related words, as compared to neutral words. The current study, however, only showed that heavy drinkers have a diminished N100 in response to alcohol-related pictures, as compared to neutral pictures. As the N100 is assumed to be an indicator of early, still preconscious allocation of attention (Hillyard *et al.*, 1973), a diminished N100 component in response to alcohol-relevant words may be interpreted as an indication of a shift in attention away from alcohol-related stimuli. In contrast to this interpretation, Stormark *et al.* (1997) only found a shift in attention toward alcohol-related stimuli 100 ms after stimulus presentation in alcohol-dependent patients.

Stimuli ratings

This investigation found a significant positive correlation between cue emotionality ratings and N100 and P300 cue-reactivity, which is in line with previous research (Warren and McDonough, 1999; Herrmann *et al.*, 2000). This finding indicates that participants who rate alcohol-related stimuli as pleasant compared to neutral stimuli are characterized by an enhanced cue-reactivity for the N100 and P300 amplitudes. However, this correlation was no longer significant when heavy and light drinkers were analysed separately. As the heavy drinkers rated the alcohol-related stimuli as more pleasant than the light drinkers, the above-mentioned correlation could be due to group differences *per se*. It remains unclear whether a more positive evaluation of alcohol stimuli or higher alcohol consumption is the cause of the differences in cue-reactivity. A speculative explanation is that electrophysiological cue-reactivity indicates an individual's predisposition for alcohol, which leads to a more positive subjective evaluation of alcohol-related stimuli and to higher alcohol consumption.

Current emotional state

The affective state of the participant has been shown to be an important factor influencing individual cue-reactivity (Rees and Heather, 1995). Negative affective states have been found to correlate with an increased subjective desire to drink alcohol under cue-exposure (Cooney *et al.*, 1987; Litt *et al.*, 1990; Greely *et al.*, 1993). By contrast, the present study did not find any significant correlations between P300 cue-reactivity and affective state. Significant negative correlations with 'performance-oriented activity' and 'extraversion' were observed for the N100 component, indicating a lower cue-reactivity in positive emotional states.

In summary, heavy social drinkers display a higher N100 and P300 cue-reactivity to alcohol-related stimuli, than to neutral stimuli. This was, however, not the case for light social drinkers. N100 cue-reactivity, but not P300 cue-reactivity, was positively correlated with a positive current emotional state. Both N100 and P300 cue-reactivities are interpreted as an expression of the attentional and emotional processing of the

stimuli presented. Future studies should aim to replicate and to expand the knowledge on electrophysiological cue-reactivity by analysing attentional processes in more detail. Additionally, the relationship between electrophysiological cue-reactivity, attention and craving requires closer investigation.

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