COGNITIVE EFFECTS
Avoidance of Alcohol-Related Stimuli Increases During the Early Stage of Abstinence in Alcohol-Dependent Patients

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Abstract — Aims: The aim of this study was to analyse initial orienting processes as well as maintenance of attention towards alcohol cues in recently detoxified alcoholics and light social drinkers. Furthermore, we investigated the influence of pre-treatment alcohol consumption and abstinence duration onto alcohol-related attentional bias. Methods: We used an alcohol-visual-dot-probe-task with two different stimulus onset asynchronies (SOA) to examine processes of initial orienting and maintenance of attention separately (50 and 500 ms SOA). Results: With short SOA, we found a positive attentional bias towards alcohol cues in alcohol-dependent patients and light social drinkers that was positively associated with pre-treatment alcohol consumption in alcoholics. Using a longer SOA, a negative attentional bias was found in light social drinkers and in patients abstenent for more than 2 weeks indicating alcohol stimuli avoidance. In patients, we found a negative correlation between attentional bias and duration of abstinence. Conclusions: After initial visual orienting towards alcohol-related stimuli, light social drinkers as well as longer abstinent alcohol-dependent patients disengage their attention. In patients, this disengagement increased during the first 3 weeks after detoxification indicating assimilation to the attentional bias pattern of light social drinkers.

INTRODUCTION

Attentional bias phenomena have been found in a number of studies, mainly in the anxiety disorder domain (for a review see Lonigan et al. (2004)). Recent theories in the field of addiction research consider biases in implicit cognitive processing of drug-related stimuli as an important factor of drug cue reactivity that is related to maintenance of drug addiction, craving and relapse (for reviews, see Franken (2003) and Field and Cox (2008)).

Due to classical conditioning, primarily neutral stimuli (like drug utensils, environments or advertisements) become associated with drug consumption after repeated pairing and are able to evoke drug-associated effects by themselves (Drummond et al., 2000). These reactions appear on subjective (e.g. drug craving), physiological (e.g. changes in heart rate or neural activations) or behavioural (e.g. relapse, amount of consumption) levels. Drug stimuli become high motivationally salient and the nature of their perception changes during the development of addiction due to a sensitization of the mesolimbic dopamine system (Robinson and Berridge, 2001). According to an extension of the incentive-sensitization theory, drug-using individuals become responsive to drug-related cues in terms of their attention-grabbing properties leading to an attentional bias towards these stimuli (Franken, 2003). Furthermore, Franken and several other authors state a strong bi-directional relationship between subjective craving and attentional bias (Sayette et al., 2000; McCusker, 2001; Ryan, 2002b). Hyper attention to a specific class of material is thought to be a result of increased priority in cognitive processing when individuals pursue a goal. In addiction, this goal is obtaining and self-administering of the specific class of material is thought to be a result of increased priority in cognitive processing when individuals pursue a goal. In addiction, this goal is obtaining and self-administering of the substance that leads to strong subjective craving for the substance (Robinson and Berridge, 2001). Pursuit of the goal to use the drug causes dependent individuals to respond selectively and automatically to addiction-related stimuli and to be easily distracted by these cues (Cox et al., 2006).

Attentional bias towards drug-related cues can be measured with various paradigms. Indirect procedures like the modified visual dot probe task (Lubman et al., 2000) or the addiction stroop task (Cox et al., 2006) make use of the limited attentional resources of the brain. Individuals whose focus of attention is towards drug-related cues can easily be distracted by such cues when conducting a primary task due to less available cognitive capacity. There are two versions of the visual dot probe task. In the probe detection task, subjects have to detect a probe’s position, whereas the probe classification task asks for the type of a probe. For anxiety-related stimuli, it has been shown that results of both tasks are comparable (Mogg and Bradley, 1999). More direct measures of attentional bias can be acquired with eye-movement monitoring (Mogg et al., 2003) or the flicker-induced change blindness paradigm (Jones et al., 2006).

In this study, we examined attentional bias in abstinent alcohol-dependent patients with the visual dot probe detection task, because we aimed to examine not only maintenance of attention but also initial orienting. With the alcohol stroop task and the flicker-induced change blindness paradigm, this would have not been possible since in both tasks the presentation durations of the alcohol stimuli cannot be manipulated. In contrast, some studies using the visual dot probe detection task varied the presentation duration of the pictorial stimuli yielding different results in alcohol-dependent patients (Field et al., 2004b; Field et al., 2005; Noel et al., 2006) demonstrating that different cognitive processes are assessed with shorter versus longer presentation durations. Because the time between the onset of the stimulus and the appearance of the target equals the presentation duration of the stimulus (see the Methods section), we refer to presentation duration of the stimulus as ‘stimulus onset asynchrony’ (SOA) in this paper. With shorter SOAs (up
to 200 ms), biases in initial orienting can be measured because a shift of attention from the stimulus to which the attention was allocated in the first place to another stimulus is not possible during this time frame (Noel et al., 2006; Field and Cox, 2008). When using longer SOAs, subsequent maintenance or disengagement processes can be measured, because individuals are able to make one or more attention shifts between two stimuli.

With respect to alcohol, an attentional bias towards alcohol cues has been found in heavy drinkers compared to light social drinkers with a SOA of 500 ms (Townshend and Duka, 2001; Field et al., 2004b) and with 2000 ms (Field et al., 2004b). With 50 ms SOA, an attentional bias was found in abstinent alcohol-dependent patients compared to light social drinkers (Noel et al., 2006) whereas with 500 ms SOA, a negative attentional bias was found in alcohol-dependent patients that can be interpreted as an avoidance of alcohol-related stimuli (Townshend and Duka, 2007). An attentional bias towards alcohol cues was also found in light social drinkers with 500 ms SOA (Noel et al., 2006) and in high craving light social drinkers (Field et al., 2005). Using other paradigms, an attentional bias could be demonstrated in alcohol-dependent patients compared to light social drinkers with the flicker-induced change blindness paradigm (Jones et al., 2006) and the alcohol stroop task (Fadardi and Cox, 2006). Using the alcohol stroop task, there are also some studies that have found an attentional bias towards alcohol cues in alcohol-dependent patients and in light social drinkers (Stetter et al., 1994; Bauer and Cox, 1998; Ryan, 2002a).

Townshend and Duka (2007) propose that alcohol-dependent patients undergoing treatment have established active avoiding strategies and thus are able to disengage their attention from alcohol cues. Hence, we hypothesize that this disengagement increases during the early stage of abstinence during which patients are undergoing treatment. To our knowledge, there is no study examining the effects of duration of abstinence during the early stage after detoxification on the attentional bias measured with the visual dot probe paradigm. In this study, we measured attentional bias in abstinent alcohol-dependent patients during the early stage of abstinence (at most 21 days after the last drink). Light social drinkers served as the control group. To analyse processes of initial orienting as well as maintenance of attention, the visual dot probe task was administered with two different SOAs of the stimuli (50 and 500 ms, respectively). Furthermore, we examined the influence of pre-treatment alcohol consumption, number of previous detoxifications and age on attentional bias scores in alcohol-dependent patients using the correlational analysis.

**METHODS**

**Subjects**

Seventeen abstinent alcohol-dependent patients (age 42.06 ± 10.13 years, 11 male) and 17 light social drinkers (age 35.94 ± 9.23 years, 11 male) were recruited (age difference n.s., P = 0.075). Subjects were all in good physical health and provided informed consent according to the Declaration of Helsinki. Patients were recruited in the day clinic of the Department of Addictive Behavior and Addiction Medicine at the Central Institute of Mental Health in Mannheim (Germany) after detoxification had been completed. They were alcohol dependent according to DSM-IV criteria, drank 1412 ± 740 g of alcohol per week before admission (range 700–2940 g/week), were abstinent from alcohol for 12.65 ± 7.28 days (range 1–21 days) and underwent 3.41 ± 4.45 previous detoxifications (range 0–15). Patients had no severe physical diseases. One patient abused in addition to alcohol tetrahydrocannabinol and one benzodiazepines; however, both patients were completely detoxified and abstinent at the date of the experiment. All patients were free from withdrawal medications and antiepileptics. For subsequent analysis, we conducted a median split regarding the duration of abstinence (median: 12 days) yielding one group with a shorter duration of abstinence (SDA, N = 9, abstinence: 6.78 ± 4.49 days, range 1–12 days) and one group with a longer duration of abstinence (LDA, N = 8, abstinence: 19.25 ± 1.98 days, range 15–21 days). Differences between these two groups in age, pre-treatment alcohol-intake or number of previous detoxifications were not significant. Healthy control subjects (HC) were contacted either personally by one of the authors or by a letter from our institute (addresses drawn from the registration office). Exclusion criteria for control subjects were axis I psychiatric disorders in the last 6 months assessed with the structured clinical interview I (First et al., 2001), consumption of illegal drugs in the past 4 weeks, alcohol abuse, binge-drinking and an alcohol consumption >20 g/day (females) or 40 g/day (males) in the last 2 months as well as lifetime alcohol dependence. The mean weekly alcohol intake was 49 ± 38 g in healthy controls (range 5–140 g/week).

**Task**

To measure attentional bias, we used a dotprobe paradigm using the same setting and also the same pictorial stimuli as described by Townshend and Duka (2007). Participants were seated in front of a notebook with a 15.4-inch display and screen resolution of 800 × 600 pixels and were told that their reaction time was measured. They were instructed to press as quickly as possible one of two touchpad buttons to indicate on which side a dot probe had appeared after the presentation of a picture pair. In each trial, a picture pair was presented for 50 ms (paradigm 1) or 500 ms (paradigm 2), respectively. Immediately after the offset of the picture pair, a dot probe (50 pt size) appeared in either the location of the left picture [i.e. position (x,y) = (200 px, −300 px)] or the right one (x,y) = (600 px, −300 px)]. The dot probe remained until the subject performed the response. Subjects had to press the left button with the left index finger if the dot probe appeared on the left side of the screen; otherwise, they had to press the right button with the right index finger. The intertrial interval lasted for 1500 ms during which a fixation cross was presented. The pictorial stimuli consisted of 20 colour photographs of alcohol-related scenes (e.g. a picture of a hand holding a glass of wine). Each was paired with a picture of another scene showing office equipment (e.g. a picture of a hand holding a phone) matched as closely as possible for complexity of the picture design and for colours. Additionally, we selected 20 pairs of filler pictures from the International Affective Picture System (Lang et al., 2008) under considerations of low arousal and neutral valence. Each stimulus pair was presented four times, counterbalancing all possible combinations of picture location and dot probe location, yielding a total number of 160 trials. Pictures had a resolution of...
Data analysis

Congruent trials were defined as trials in which the dot probe was in the same location as the alcohol-related cue. In incongruent trials, dot probe and alcohol cue were in different locations. Reaction time data from filler trials and from trials where subjects made errors were discarded. To eliminate outliers, reaction times were excluded if they were <100 ms or >1000 ms according to Townshend and Duka (Townshend and Duka, 2007). An attentional bias score was calculated for each subject by subtracting the mean response time (ms) in congruent trials from the mean response time (ms) in incongruent trials (Lubman et al., 2000).

Statistical analysis

One-sample t-tests were conducted in the patient as well as in the control group, separately for the different SOAs, to test whether attentional bias scores were different from zero. For the 500 ms experiment, we additionally applied one-sample t-tests in the SDA and LDA groups to assess attentional bias scores (see the Results section regarding the purpose of this analysis). In the whole group of alcohol-dependent patients, pairwise correlations were performed to assess the association between attentional bias scores and duration of abstinence and pre-treatment alcohol intake as well as between number of detoxifications and age. Partial correlations controlled for age were calculated between number of previous detoxifications and attentional bias scores, amount of alcohol intake and reaction times. For control subjects, we assessed correlations between attentional bias scores and weekly alcohol consumption. For all subjects, pairwise correlations between age and mean reaction times were conducted.

RESULTS

The mean reaction times in alcohol-dependent subjects (508.35 ± 92.94 ms) did not differ significantly from healthy controls’ reaction times (464.77 ± 72.39 ms, t(1, 32) = 1.670, P = 0.105). In both groups, reaction times in the 500 ms experiment were greater compared to the 50 ms paradigm (alcohol-dependent patients: t(16) = 3.097, P = 0.018, healthy controls: t(16) = 2.647, P = 0.007), see Table 1. During the 50 ms condition, alcohol-dependent subjects showed an attentional bias towards alcohol stimuli that differed significantly from zero (i.e. greater reaction times in incongruent trials compared to congruent trials, t(16) = 2.225, P = 0.041). In contrast, with 500 ms SOA, patients directed their attention away from the alcohol stimuli (i.e. shorter reaction times in incongruent trials), but this effect was not significant (t(16) = −1.414, P = 0.177). Control subjects showed an attentional bias towards alcohol-related cues in the 50 ms experiment (t(16) = 2.747, P = 0.014) and an attentional bias towards neutral cues when stimuli were shown for 500 ms (t(16) = −2.854, P = 0.011), see Fig. 1a. However, in the direct comparison, attentional bias scores between alcohol-dependent patients and light social drinkers did not differ significantly neither in the 50 ms condition (t(1, 32) = 0.611, P = 0.546) nor in the 500 ms condition (t(1, 32) = 1.158, P = 0.255). The mean reaction times of the congruent and incongruent trials as well as overall reaction times are shown in Table 1.

Table 1. Mean reaction times (ms) in the 50 and the 500 ms experiment in patients (N = 17) and healthy controls (N = 17)

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<thead>
<tr>
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<th>Alcohol-dependent patients</th>
<th>Light social drinkers</th>
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<tr>
<td></td>
<td>Congruent trials</td>
<td>Incongruent trials</td>
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<tr>
<td>50 ms</td>
<td>479.22 ± 82.10</td>
<td>487.45 ± 79.41</td>
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<tr>
<td>500 ms</td>
<td>537.81 ± 103.58</td>
<td>528.89 ± 98.24</td>
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325 × 325 pixels with 72 dpi. The presentation order of the categories alcohol/neutral and neutral/neutral was pseudorandomized, whereas the stimulus order was randomized for each subject. Subjects conducted the two paradigms with a break of 5 min in between. The 50 ms paradigm was always presented first to avoid recognition effects as far as possible, because we used the same stimulus set in both paradigms. Showing the 500 ms paradigm at first would have enhanced memorizing the stimuli because of longer SOA. Furthermore, it has been shown that priming by consciously available cues could affect attentional bias by strategic coping processes (Luecken et al., 2004). Before the task, subjects underwent a training session to get familiar with the challenge. Task presentation and recording of the behavioural responses were performed using Presentation® software (Version 9.9, Neurobehavioral Systems, Inc., Albany, CA, USA).

The partial correlations controlling for age did not yield different results than the bivariate correlations. Therefore, we report only the bivariate results.

A negative correlation between the attentional bias score and the duration of abstinence was found in the 500 ms condition, which could be the reason for undetected differences between social drinkers and subgroups of alcohol-dependent patients due to changes in early abstinence. Therefore, we conducted a median split into the LDA and the SDA group (see...
Fig. 1. (a) Attentional bias scores separated for 50 and 500 ms SOA in light social drinkers (N = 17, 11.67 ± 17.52 ms in the 50 ms condition and −19.77 ± 28.56 ms in the 500 ms condition) and alcohol-dependent patients (N = 17, 8.23 ± 15.25 ms in the 50 ms condition and −8.92 ± 26.02 in the 500 ms condition). (b) Attentional bias scores for 500 ms SOA in light social drinkers (HC, N = 17, −19.77 ± 28.56 ms) and in alcohol-dependent patients with a longer duration of abstinence (LDA, N = 8, −18.44 ± 19.69 ms) and patients with a shorter duration of abstinence (SDA, N = 9, −0.46 ± 29.04 ms).

Fig. 2. Negative association between duration of abstinence and attentional bias score in the 500 ms experiment in alcohol-dependent patients (N = 17, r = −0.534, P = 0.027).

DISCUSSION

In light social drinkers and alcohol-dependent patients who were abstinent for longer than 2 weeks (LDA subgroup), we found similar patterns of attentional bias towards alcohol stimuli. With a short SOA, attention was focused towards alcohol stimuli, whereas with 500 ms SOA, a disengagement of attention from alcohol stimuli was found.

In line with a study of Noel et al. (2006), we found a significant attentional bias in alcohol-dependent patients when stimuli were presented for a short time (50 ms). During the early stages of selective visual attention, alcohol-dependent patients’ attentional bias seems to be unaffected by attentional avoidance strategies whereas these cognitive strategies seem to be successful when pictorial stimuli are shown long enough. Light social drinkers also showed an attentional bias towards alcohol-related stimuli, which at first sight sounds surprising. However, taking into account that alcohol cues are also associated with pleasant situations in social drinkers and may be more interesting than pictures of office equipment, it appears plausible that these cues also draw attention in light social drinkers. Furthermore, we already found an alcohol-related attentional bias in both alcoholics and healthy controls in a previous study using the alcohol stroop task (Stetter et al., 1994). Other studies also demonstrated an alcohol-related attentional bias in light social drinkers (Bauer and Cox, 1998; Ryan, 2002a). Moreover, in social drinkers, cue-reactivity in response to alcohol cues has also been shown, measured with fMRI (George et al., 2001; Tapert et al., 2004) or EEG (Herrmann et al., 2001), which is in line with the attentional bias also found in social drinkers.

Avoidance of alcohol-related stimuli in light social drinkers as seen in our study using the 500 ms SOA is in line with a study of Field and colleagues who found similar patterns with 500 and 2000 ms SOA (Field et al., 2004b). The disengagement from alcohol-related stimuli that we found in the LDA group of alcohol-dependent patients is in part in accordance with a recent study of Townshend and Duka who found similar results with the same experimental settings in alcohol-dependent patients who were comparable in duration of abstinence (Townshend and Duka, 2007), whereas they did not find this avoidance in healthy controls. For tobacco dependence, it was shown that substance availability increases subjective craving (Dols et al., 2002) and therefore also could increase attentional bias because of their assumed bi-directional relationship. Our sample of LDA alcohol-dependent patients was abstinent and therefore alcohol was not available, which could be the reason why patients were able to focus their attention away from the alcohol stimuli. In the SDA patient group, the last alcohol consumption and therefore alcohol availability was not as long ago as in the LDA group that could complicate averting the gaze away
from alcohol-associated cues in SDA subjects. The correlation between attentional bias measured with 50 ms SOA and alcohol consumption before admission is in accordance with studies showing a greater attentional bias in heavy compared to light drinkers examined with the visual dot probe task or the stroop paradigm (Townshend and Duka, 2001; Sharma et al., 2001; Cox et al., 2003; Field et al., 2004b) also indicating a relationship between alcohol-related attentional bias and quantity of alcohol intake. In cannabis users, Field et al. found a positive correlation between the amount of cannabis intake and the stroop-measured attentional bias (Field et al., 2004a), whereas to our knowledge no such correlation was demonstrated previously in alcohol dependence. In smokers, results are divergent with some studies showing a positive correlation (Mogg and Bradley, 2002) and other studies finding a negative association (Bradley et al., 2003; Hogarth et al., 2003) between smoking-related attentional bias and amount of tobacco consumption. Mogg and colleagues argued that this could be due to differences between tobacco dependence and other addictions regarding a habitual intake of tobacco in heavy smokers without a need for external triggers like drug-related cues (Mogg et al., 2005). The increasing alcohol-related attentional bias in the 50 ms experiment with increasing alcohol consumption found in our sample of alcohol-dependent patients is consistent with the incentive-sensitization model of Robinson and Berridge (2001) that postulates that drug-related stimuli are perceived as particularly salient and individuals become responsive to the attention-grabbing properties of drug-related cues with increases in drug consumption.

With the 500 ms paradigm, we found a positive association between avoidance of alcohol-related stimuli and duration of abstinence in the early stage (i.e. 3 weeks) after detoxification. This could be the result of the development of an active avoiding strategy (Townshend and Duka, 2007) in abstinent alcohol-dependent patients who are currently in the early stage of treatment. In the present literature, alcohol-dependent subjects are mainly examined after 2 or 3 weeks of abstinence (Stormark et al., 1997; Noel et al., 2006; Townshend and Duka, 2007), maybe at a point of time where active avoiding strategies are already established. Therefore, alcohol-dependent patients during the early stage of abstinence are underrepresented in studies examining alcohol-related attentional bias that could be the reason why a negative correlation between duration of abstinence and attentional bias towards alcohol-stimuli has not been reported previously. The avoidance of alcohol stimuli was also seen in our group of light social drinkers that indicates that alcohol-dependent patients who are longer abstinent have assimilated their alcohol-related attentional bias to that of healthy controls.

The pattern of a positive attentional bias towards alcohol cues when stimuli were presented shortly (50 ms) and a disengagement from alcohol cues in the 500 ms interval of cue presentation indicate that after an initial visual orienting towards alcohol cues individuals tend to direct their attention away from alcohol stimuli. This pattern could be found in light social drinkers and alcohol-dependent patients, who were abstinent for >2 weeks. Regarding abstinent alcohol-dependent patients, evidence for this visual approach–disengagement pattern was shown before in two studies (Stormark et al., 1997; Noel et al., 2006). Furthermore, we propose that measuring the attentional bias towards alcohol cues with the 50 ms version of the visual dotprobe paradigm yields a trait measure because in our sample it is correlated with individual drinking patterns (measured by amount of alcohol) and it does not change during the early stage of abstinence. This would also be in line with findings of Noel and colleagues (2006) who found a positive correlation between the initial orienting attentional bias and severity of dependence. In contrast, we suggest the 500 ms version of the dotprobe task to be a tool to measure state because in our study, it changes rapidly during the first weeks of abstinence.

Because light social drinkers and also alcohol-dependent patients who are abstinent for longer than 2 weeks show an avoidance of alcohol-related stimuli when they are presented for 500 ms and there is a lot of evidence that heavy drinkers show the opposite behaviour with this SOA, i.e. an attentional bias towards alcohol stimuli (Townshend and Duka, 2001; Field et al., 2004b), we propose an inverted-U function as a model for attentional bias in this experiment depending on whether subjects are consuming low or high amounts of alcohol or are abstinent alcohol-dependent patients. Studies with heavy drinkers usually include students or non-treatment-seeking heavy drinkers (Townshend and Duka, 2001; Field et al., 2004b). Both groups probably do not regard their alcohol consumption as problematic and therefore may be not trying to suppress their subjective craving or to disengage their attention from alcohol stimuli that could be the reason why in this group an alcohol-related attentional bias was found in a number of studies instead of an avoidance of alcohol cues. Furthermore, they could have had more difficulties to divert attention away from the alcohol stimuli. It could be possible that light social drinkers as well as longer abstinent alcohol-dependent patients apply active avoiding strategies leading to a disengagement from alcohol stimuli, maybe due to social desirability. Another explanation for this disengagement after initial orientation to alcohol stimuli in light social drinkers could be a loss of interest at longer presentation times.

Because we did not examine heavy drinkers, we cannot provide more evidence for the suggested inverted-U function model of the attentional bias dependent on drinking status. Nevertheless, our experiment was identical to that of Townshend and Duka (2001), who found a positive attentional bias in heavy drinkers, because we have used the same pictorial stimulus set and also the same timing parameters (SOA and inter-trial interval). Recently detoxified patients (SDA) are probably located between the active drinking heavy drinkers and the alcohol-dependent patients who are abstinent for more than 2 weeks (LDA) because active avoiding strategies are not yet established in the SDA group.

In summary, the present study provides evidence for a disengagement of visual attention from alcohol stimuli subsequent to an initial orienting towards these stimuli in both longer abstinent alcohol-dependent patients as well as healthy controls. In alcohol-dependent patients, this temporal attentional bias pattern seems to assimilate during the early stage of abstinence to the pattern seen in light social drinkers.

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