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Investigating biases of attention and memory for alcohol-related and negative words in alcohol-dependents with and without major depression after day-clinic treatment



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ABSTRACT

This study aimed to investigate attentional and memory biases in alcohol-dependents with and without major depression compared to healthy controls. We assumed that both groups of alcohol-dependents would show attentional and memory biases for alcohol-related words. For the alcohol-dependents with depression, we additionally expected both types of biases for negative words. Alcohol-dependents without co-morbidity (Alc) and alcohol-dependents with major depression (D-Alc) as well as control participants with a moderate consumption of alcohol (Con) completed an alcohol Stroop task and a directed forgetting paradigm using word stimuli from three categories: neutral, negative, and alcohol-related. Stroop effects showed that not only alcohol-dependents but also control participants were more distracted by alcohol-related than by negative words. In the directed forgetting procedure, all participants showed a significant effect for each word-category, including alcohol-related and negative words. The D-Alc-group memorized more alcohol-related than negative to-be-remembered words. The results do not corroborate the hypothesis of more pronounced attentional and memory biases in alcohol-dependents. However, in alcohol-dependents with depression a memory bias for alcohol-related material was found, suggesting that this group may be more pre-occupied with alcohol than patients without such co-morbidity.

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1. Introduction

Alcohol use disorders are essentially characterized by compulsive uncontrolled alcohol use despite adverse physical, psychological, or social consequences due to a “strong desire to use alcohol” and/or “unsuccessful efforts to cut down alcohol use” (Development of Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition, DSM-V; American Psychiatric Association). For instance, Lubman et al. (2004, p. 1491) postulate that in chronic alcohol-dependents, maladaptive, uncontrolled behaviors and high relapse rates might be “compulsive in nature as result of dysfunction within inhibitory brain circuitry”. To take a closer look at cognitive control processes, Friedman and Miyake (2004) propose to distinguish between the inhibition of prepotent response and the resistance to proactive interference. The ability

to inhibit prepotent responses or appetitive tendencies (such as impulsive alcohol use) is often measured via the attentional bias with attentional bias referring to the observation that motivationally relevant cues can grab or hold attention, and this is related to individual differences in appetitive and aversive motivation. By contrast, proactive interference as assessed via the memory bias is defined as the ability to resist memory intrusions from information that was previously relevant to the task but has become irrelevant. Thus, the memory bias refers to an enhanced recall of motivationally relevant (but task irrelevant) cues.

In alcohol use disorders, both types of cognitive processing biases are of great importance. To date, most studies in alcohol-dependents focused on problems caused by attentional bias toward alcohol-related information i.e., in the alcohol Stroop test (for review see Cox et al., 2006; Field and Cox, 2008). Less is known regarding the extent to which alcohol-dependents have problems caused by memory biases such as difficulty suppressing repetitive thoughts about drinking and drinking expectations as measured for instance in the directed forgetting paradigm (Todor, 2007). Growing evidence shows that both types of impaired cognitive control may

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lead to stronger craving and preoccupation with alcohol, intensifying the urge to drink, and thereby causing a vicious circle of withdrawal and relapse in alcohol-dependents (Cox et al., 2002; Wiers et al., 2002; May et al., 2004). Moreover, the experience of recurring relapses weakens the alcohol-dependents' confidence in their ability to control their addictive behavior (Cox et al., 2006; Wiers et al., 2006; Fadardi and Ziaee, 2010).

In order to assess alcohol-related attentional bias, Stetter et al. (1995) applied both, the classical Stroop task, as well as the "alcohol Stroop test" to alcohol-dependents and healthy controls. They found an alcohol-specific interference effect for alcohol-dependent patients, which was independent of neuropsychological deficits. Various authors confirmed the alcohol-specific attentional bias in alcohol-dependents (Johnson et al., 1994; Stormark et al., 2000; Sharma et al., 2001; Lusher et al., 2004; Fadardi and Cox, 2009; Field et al., 2013), although some studies – including our own previous investigation (Fridrici et al., 2013) – failed to replicate these findings (Cox et al., 1999; Duka et al., 2002; Ryan, 2002; Cox et al., 2003).

Up to now, only two studies investigated directed forgetting in alcohol-dependents in order to assess memory biases (Todor, 2007; Noel et al., 2009). Directed forgetting experiments demonstrate that, in general, the explicit instruction to forget some and to memorize other stimuli is reflected by a better recall of the to-be-remembered-items (R-items) compared to the to-be-forgotten-items (F-items). According to recent investigations by Hauswald et al. (2011) and Zwissler et al. (2011), the successful performance of directed forgetting is based on two cognitive processes: 1. selective rehearsal of the R-items and, 2. controlled inhibition of the F-items. Consequently, a low performance in directed forgetting (i.e., equivalent recall of R- and F-items) would reflect impaired ability to inhibit the F-items or reduced selective rehearsal of the R-items. Noel et al. (2009) found that alcohol-dependents performed worse in a letter trigram-based directed forgetting procedure than controls. They had more difficulties in forgetting the, presumably motivationally neutral, trigram stimuli than controls (no comparison to alcohol-related stimuli included) and this impairment was correlated with the duration of alcohol addiction. Todor (2007) applied alcohol-related and neutral words and found that healthy controls demonstrated a directed forgetting effect for both word categories. By contrast, alcohol-dependents did neither show directed forgetting effects for alcohol-related or neutral words. Taking a closer look at the results, the alcohol-dependents showed selective rehearsal by remembering more alcohol-related R-words and reduced controlled inhibition by remembering more alcohol-related F-words. However, for neutral words, they performed well in forgetting the F-items, but, comparatively, not in remembering the R-items – with both ways leading to the disappearance of the directed forgetting effect. Thus, for alcohol-dependents it seems to be difficult to attenuate the influence of alcohol-related memories by intentionally forgetting such memories and rendering them inaccessible to their immediate focus of attention.

To our knowledge, only one recently published study (Noel et al., 2013) examined the ability to suppress automatic or prepotent responses compared to the ability to control interference from memory among alcohol-dependents. The ability to suppress automatic responses was assessed by the anti-saccade task, the Stroop task and the Hayling task, whereas the ability to control interference from memory was measured by the Peterson Brown task and the cued recall. Their findings suggest that alcohol-dependence is mainly associated with an impaired ability to suppress automatic responses (seen in a higher attentional bias), whereas the ability to control interference from memory was preserved (no memory bias).

Alcohol-related cognitive biases seem to be malleable. Franken et al. (2003) found a positive correlation between memory bias

and craving in alcohol dependents. With respect to the alcohol-related attentional bias, recent studies found this bias to be positively correlated with craving (Field et al., 2013), quantity and frequency of substance use (Field et al., 2004), relapse risk (Cox et al., 2002) as well as alcohol priming by smelling alcoholic beverages (Cox et al., 2003), expectancy of substance availability (Field and Cox, 2008) and experienced stress level (Field and Powell, 2007; Garland et al., 2012). In addition, efficient treatment appears to reduce alcohol-related attentional bias (Flaudias et al., 2013). However, as most studies focused on untreated alcohol-dependents or patients at an early stage of treatment, little is known about the presence of alcohol-related cognitive biases in successfully treated alcohol-dependents who – nevertheless – show a high risk of relapse (Boothby and Doering, 2005). To our knowledge, the alcohol-related attentional bias and the alcohol-related memory bias have never been comparatively investigated in alcohol-dependents after completing a day-clinic rehabilitation program.

Depression is the most frequent co-morbid disorder in alcohol-addiction (Driessen et al., 1998). Various investigations found impaired performance in the Stroop task (Schatzberg et al., 2000; Harvey et al., 2005) as well as in the directed forgetting procedure (Power et al., 2000; Cottencin et al., 2008) in patients with major depression. However, some studies did not find an attentional bias in depressed patients (Murphy et al., 1999; Markela-Lerenc et al., 2006; Wong and Moulds, 2008). According to Lau et al. (2007) inhibitory dysfunction in patients with major depression is most likely valence-specific – most pronounced for negatively valenced stimuli. This attentional bias toward negatively valenced information may lead to an enhanced memory for negatively valenced emotional material in patients with major depression (Leppanen, 2006) and decreased memory performance if negatively valenced distractors are present (Beblo et al., 2010). All in all, as Sinclair et al. (2010) pointed out, despite high prevalence of co-morbid depression among alcohol-dependents and its acknowledged impact on etiology, presentation and outcome, still little is known about its impact on cognitive biases in alcohol use disorders.

In the present investigation, alcohol-dependents without depressive symptoms (Alc) were compared with alcohol-dependents suffering from co-morbid depression (D-Alc) and healthy controls (Con) by means of the alcohol Stroop task and the directed forgetting paradigm. First, it was assumed that both groups of alcohol-dependents are more distracted by alcohol-related words than by negative words shown by a higher Stroop interference effect as well as a smaller directed forgetting effect for alcohol-related words. Second, we expected alcohol-dependents with co-morbid major depression to be more distracted by negative words than the other two study samples.

2. Methods

2.1. Subjects

Three groups of subjects participated in the investigation. Alcohol-dependent patients without co-morbid diagnoses (Alc, $n=28$), alcohol-dependent patients with co-morbid major depression (D-Alc, $n=28$) and healthy control participants (Con, $n=28$). The three groups were matched for age, gender and educational level (see Table 1).

The alcohol-dependent patients were recruited during a rehabilitation program at a day-clinic of the Clinic of Psychiatry and Psychotherapy Bethel, Ev. Hospital Bielefeld, Germany. They were tested between 15 and 45 days after drinking cessation at the end of their treatment – the D-Alc-group after 26 days on average which differed significantly from the Alc-group without depression (20 days on average, see Table 1). All patients were free of any withdrawal symptoms and detoxification medication for at least 10 days. All alcohol-dependents were routinely checked for substance abuse during their treatment. We can be reasonably sure that there was no use of substances during the entire period of

Table 1

Demographic, clinical and neurocognitive variables (M ± S.D.) for the alcohol-dependents without (Alc, n=28) and with depression (D-Alc, n=28) compared to control participants (Con, n=28).

Demographic variables	Alc	D-Alc	Con	Statistics
Age	45.9 ± 7.3	46.6 ± 9.4	44.4 ± 8.6	F(2, 81)=0.50
Gender	22m, 6f	15m, 13f	16m, 12f	$\chi^2(2, N=84)=4.40$
Mean years of school education	10.1 ± 1.9	9.6 ± 2.0	10.6 ± 1.8	F(2, 80)=2.04
Clinical variables				
General Depression Scale	9.3 ± 5.8 ^{ab}	19.1 ± 9.0 ^{ab}	5.2 ± 3.5	F(2, 78)=32.87
State-Trait-Anxiety Inventory	41.5 ± 10.4 ^{ab}	54.0 ± 10.0 ^{ab}	33.4 ± 7.9	F(2, 78)=32.85
Barrett Impulsiveness Scale	63.4 ± 9.0	65.7 ± 11.1 ^a	58.7 ± 8.5	F(2, 78)=3.73
European Addiction Severity Index				
Medical condition	1.0 ± 1.8	2.1 ± 2.6	–	t(54)=1.814
Employment	2.6 ± 2.6	2.7 ± 2.6	–	t(54)=0.000
Alcohol use	6.6 ± 1.8	6.6 ± 1.4	–	t(54)= – 0.052
Legal status	1.3 ± 2.5	0.4 ± 1.7	–	t(48.222)= – 1.625
Family and social relationships	2.0 ± 2.3 ^b	4.2 ± 2.6 ^b	–	t(54)=3.379
Psychiatric condition	2.3 ± 2.6 ^b	6.1 ± 1.9 ^b	–	t(54)=6.245
Duration of alcohol addiction (years)	11.4 ± 4.1	13.3 ± 5.1	–	t(54)=1.535
Duration of abstinence (days)	20.4 ± 6.6 ^b	26.2 ± 11.2 ^b	–	t(43.835)=2.366
Mean number of drinking days (per month)	19.9 ± 9.9 ^a	19.4 ± 9.9 ^a	8.2 ± 8.5	F(2, 78)=13.09
Daily amount of alcohol (g)	205.3 ± 121.3 ^a	147.0 ± 94.5 ^a	23.9 ± 16.1	F(2, 78)=28.97
Obsessive Compulsive Drinking Scale	19.0 ± 8.2 ^a	19.2 ± 7.8 ^a	0.6 ± 1.8	F(2, 75)=71.29
Alcohol Abstinence Self-Efficacy Scale				
Self-efficacy	80.8 ± 23.9 ^a	69.5 ± 17.4 ^a	96.2 ± 17.3	F(2, 72)=11.89
Temptation	44.9 ± 18.6	55.7 ± 17.3 ^a	35.7 ± 19.3	F(2, 75)=7.64
Neurocognitive variables				
Pre-morbid verbal IQ	105.9 ± 13.8	102.4 ± 10.5	109.6 ± 11.2	F(2, 81)=2.59
Trail making test A	36.7 ± 12.1	37.2 ± 13.3	32.0 ± 10.4	F(2, 81)=1.57
Trail making test B	82.5 ± 35.6	91.3 ± 53.2	74.6 ± 27.9	F(2, 81)=1.20

Note: Post-hoc comparisons using Bonferroni ($P < .05$).^a Significantly different from the control group.^b Significantly different from the related alcohol-group.

abstinence. After providing written informed consent, patients underwent a clinical interview according to DSM-IV criteria (American Psychiatric Association, 1994) by a trained psychologist. Inclusion criterion was the diagnosis of alcohol-dependence. The consumption of other addictive substances, severe medical conditions, neurological impairments, the relapse during stay and mental disorders (except depression) led to exclusion. In the co-morbid depressed alcohol-dependents, the medication consisted of tricyclic and tetracyclic antidepressants ($n=8$), as well as serotonergic antidepressants and selective serotonin- and noradrenalin-re-uptake inhibitors ($n=10$) and atypical neuroleptic drugs for sedation purposes ($n=3$).

The control participants were recruited by advertisement, as well as by word-of-mouth. Exclusion criteria were psychiatric diagnosis, a history of serious medical illness, substance abuse or medication with central nervous system side-effects. The control participants received a financial compensation of 10€. All participants were native German-speakers who gave their informed written consent. The current study was approved by the local ethics committee.

2.2. Procedure and methods

Data collection was performed on two separate mornings within one week – each session lasted about 100 min and was conducted by a trained psychologist. All participants completed all interviews, questionnaires and neuropsychological tasks in the same order. After signing an informed consent document on assessment day 1, participants' current clinical status was rated using the General Depression Scale (ADS-k; Hautzinger and Bailer, 1993) and the State-Trait-Anxiety Inventory (sub-scale Trait-Anxiety; Laux et al., 1981). The short version of the Barrett Impulsiveness Scale (BIS-11; Barratt, 1994) was conducted in order to assess self-reported cognitive control problems in everyday life. Moreover, the Obsessive Compulsive Drinking Scale (OCDS; Anton et al., 1996) and the Alcohol Abstinence Self-Efficacy Scale (AASE; DiClemente et al., 1994) were used to compare both alcohol-dependent groups with regard to alcohol craving, temptation and self-efficacy. For all questionnaires the sum scores are presented in Table 1. Information on recent alcohol consumption was obtained via the Form 30 Interview (Miller, 1996), and a clinical interview assessing mental disorders according to DSM-IV (American Psychiatric Association, 1994) was conducted by a psychologist trained in clinical interviewing. Moreover, the same psychologist undertook a semi-structured interview, called the European Addiction Severity Index (EuropASI; Gsellhofer et al., 1994), to generate an addiction severity profile referring to seven independent problem areas: medical condition, employment, alcohol use, drug use (exclusion criterion, not mentioned in Table 1), legal status, family and social relationships, and psychiatric condition. The severity ratings are interviewer estimates on a

9 point scale indicating the need for further treatment (0–1: no problem, no treatment required up to 8–9: major problem, treatment absolutely necessary).

On the second assessment day, 1–5 days after the first assessment, the alcohol Stroop task and the directed forgetting paradigm were administered. To control for intelligence, we applied the Mehrfachwahl-Wortschatztest (MWT-B; Schmidt and Metzler, 1992). The MWT-B is a German test to assess pre-morbid verbal intelligence. Moreover, we administered the Trail Making Test (TMT; Reitan, 1958) to assess further executive functions (TMT-B).

2.2.1. Word stimuli

In order to assess attentional and memory biases neutral and negative words were selected on the basis of emotionality, familiarity and statistical frequency in German (Borsutzky et al., Unpublished Manuscript). Alcohol-related words were selected from a list of 100 alcohol-related words rated by 30 alcohol-dependent patients and 30 control participants in a pilot study as being closely associated with alcohol consumption.

2.2.2. Alcohol Stroop

We adopted the design of the alcohol Stroop task of our preliminary studies (Wingenfeld et al., 2006, 2007; Fridrici et al., 2013). Parts of the data sets of the alcohol-dependents (15 participants) and the healthy controls (25 participants) have already been included in a previous investigation of Fridrici et al. (2013) – the D-Alc-group was newly added to the present study. Twelve different words were chosen with four words per category (neutral, negative, and alcohol-related words, see Appendix A). The participants were instructed to identify the ink-color of a word presented on a computer-screen by using the middle and forefingers of both hands to press the corresponding button on a keyboard as fast as possible, regardless of the word's meaning. The four colors were presented in a fixed random order, so that the same key was pressed for the same color for every participant. The test session comprised of 192 words divided into six category-specific blocks of 32 words each. Each block included the four words of one word category, which were repeated eight times in pseudo-randomized order to ensure that neither the same word nor the same color was presented in direct sequence. The presentation of a word-stimulus lasted 1500 ms, followed by an inter-stimulus interval of 350 ms. Between two blocks, participants had a resting period of 30 s during which a white cross appeared on the black screen. The presentation of the blocks was pseudo-randomized. Before testing, three training trials were conducted to rehearse dexterity to minimize error variance.

2.2.3. Directed forgetting (DF)

Our version of the DF task closely paralleled that used by Korfine and Hooley (2000). Participants performed the DF task as free recall test. Overall, 42 words were presented on a computer screen; 14 for each of three word categories (neutral, negative, and alcohol-related, see Appendix A). Each word appeared for 2000 ms and was replaced by a cue instructing the participants either to remember (seven words of each category) or to forget (seven words of each category) the word (either RRRR or FFFF). The instruction cues were shown for 3000 ms followed by an inter-stimulus-interval of 350 ms. Immediately after presenting these 42 words, the participants were asked to name as many words as possible in the free recall test, regardless of the previous instructions to forget or remember.

2.2.4. Apparatus

Word stimuli were presented on a 14-in. monitor of a laptop computer using the software Presentation® (Neurobehavioral Systems Inc., SF, California).

2.3. Statistical analyses

Statistical analyses were performed using SPSS, Version 20. Demographic, clinical and cognitive data were analyzed using univariate analyses of variance or Chi²-tests. According to the results of a recent study by Flaudias et al. (2013) the duration of treatment affected alcohol-related attentional bias. To control for treatment-duration, we correlated the duration of abstinence as result of day-clinical treatment with the neuropsychological parameters for both groups of alcohol-dependents, separately. The calculations of all conducted ANOVAs were Huynh-Feldt corrected. The mean reaction times of the alcohol Stroop in alcohol-dependents with or without depression compared to control participants were analyzed by means of a three-by-three ANOVA with repeated measures of word category (alcohol, negative and neutral) and group (Alc, D-Alc, Con). To further analyze the attentional bias as reflected by the Stroop interference the average reaction time to neutral words was subtracted from the average reaction time to negative words or to alcohol-related words tested with a two-(word category differences) by three-(group) ANOVA.

For analyzing the directed forgetting (DF) effect, we calculated a two-by-three-by-three ANOVA with repeated measures of instruction cue (remember vs. forget), word category (alcohol, negative, neutral) and group (Alc, D-Alc, Con). In order to specify the impact of categorical valence of the specific DF effect we subtracted the F-words (to-be-forgotten) from the R-words (to-be-remembered) for each category. In a second step we subtracted the "R – F-difference-score" of the neutral category from the "R – F-difference-scores" of the negative and the alcohol-related word category, respectively. Thereby, we got a difference score depicting the specific DF effect for negative and alcohol-related words each corrected for the neutral word DF bias. These specific DF effects were statistically evaluated via a two-(word category "R – F-difference-scores": negative and alcohol) by three-(group) repeated-measures ANOVA. Subsequent two-tailed *t*-tests using Bonferroni correction were performed, if necessary.

3. Results

3.1. Subject, clinical and neurocognitive variables

Demographic, clinical and neurocognitive data of the three groups are presented in Table 1. No significant differences were found with respect to demographic and neurocognitive variables. The analyses of the clinical questionnaire and interview scores revealed significant group differences (see Table 1).

3.2. Correlational analyses

In both groups of alcohol-dependents no significant correlations were found between the duration of abstinence and the neuropsychological parameters.

3.3. Alcohol Stroop

The average mean reaction time (RT) of the three word categories (neutral, negative, alcohol) is presented in Fig. 1 and Table 2. A three-(word category: neutral, negative, alcohol) by three (group: Alc, D-Alc, Con) ANOVA with repeated measures revealed a main effect of word category ($F(2, 142)=12.668; P<0.001$) indicating the slowest RTs for alcohol words and the fastest for neutral words. According to post-hoc paired sample *t*-tests (Bonferroni-adjusted significance level of

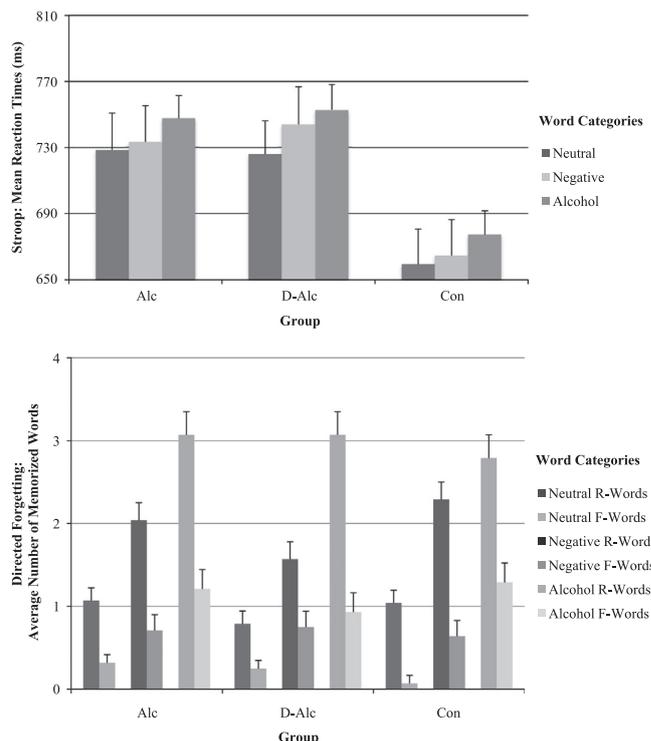


Fig. 1. Stroop mean reaction times: for neutral, negative and alcohol-related words (means and standard errors) and directed forgetting: average number of memorized R(to-be-remembered)- and F(to-be-forgotten)-words of neutral, negative and alcohol-related categories (means and standard errors) for alcohol-dependents (Alc, n=28), depressive alcohol-dependents (D-Alc, n=28) and controls (Con, n=28).

$P=0.0167$, analogous for the following paired sample *t*-tests) the RTs of the alcohol category were significantly slower than the RTs of the negative category ($t(73)=-2.730; P=0.008$), whereas the mean RTs between the negative and the neutral category did not show significant differences ($t(73)=-2.267; P=0.026$). Both alcohol-dependent groups showed significantly slower RTs in all three word categories compared to the control group (main effect group: $F(2, 74)=6.332; P=0.003$), but not between each other ($P=0.730$). There was no group \times word category interaction effect ($F(4, 148)=0.791; P=0.533$).

A two-(word category differences) by three (group) ANOVA with repeated measures was used to evaluate interference effects. The Stroop interference values (mean RT to neutral words subtracted from the RTs of the other two word-categories) are presented in Fig. 2.

The only significant main effect of word category ($F(1, 71)=7.244; P=0.009$) revealed a stronger interference effect for the alcohol words in comparison to the negative words. This was true for all groups seen in the post-hoc paired sample *t*-test ($t(73)=-2.730; P=0.008$). The groups did not show significantly different interference effects (main effect group: $F(2, 71)=1.019; P=0.366$) and the interaction effect group \times word category was not significant, either ($F(2, 71)=0.133; P=0.876$).

3.4. Directed forgetting (DF)

Table 2 shows the number of words recalled per category (neutral, negative and alcohol-related) and initial instruction (to be remembered or to be forgotten).

The three-(word-category: neutral, negative, alcohol) by three-(group: Alc, D-Alc, Con) by two-(cue: Remember, Forget) repeated-measures ANOVA revealed a DF effect with significantly more R-words than F-words that were recalled (main effect of instruction cue: $F(1, 81)=151.161; P<0.001$). The significant main effect of word

Table 2

Stroop task: average reaction times in milliseconds with means and standard deviations and Directed Forgetting: average number of memorized R-(to-be-remembered) and F-(to-be-forgotten) words in the Alc ($n=28$), D-Alc ($n=28$) and Con-groups ($n=28$).

Alcohol Stroop		Alc	D-Alc	Con	Statistics
I: Neutral		728.6 ± 107.5	726.0 ± 107.5	659.4 ± 73.0	3 × 3 ANOVA Stroop mean reaction times
II: Negative		733.5 ± 94.7	744.1 ± 111.1	664.8 ± 80.9	Word category: $F(2, 142)=12.668^{***}$ Group: $F(1, 71)=5.260^{**}$ Group × category: $F(4, 142)=0.542$
III: Alcohol		747.8 ± 100.1	752.9 ± 105.8	677.3 ± 76.0	
II-I		4.9 ± 46.5	18.2 ± 30.4	5.4 ± 29.2	2 × 3 ANOVA Stroop interference
III-I		19.2 ± 33.9	26.9 ± 42.6	17.9 ± 30.4	Word category: $F(1, 71)=7.244^*$ Group: $F(2, 71)=1.019$ Group × category: $F(2, 71)=0.133$
Directed forgetting					
I: Neutral	R-words	1.1 ± 0.8	0.8 ± 0.9	1.0 ± 1.0	2 × 3 × 3 ANOVA Directed forgetting
	F-words	0.3 ± 0.6	0.3 ± 0.5	0.1 ± 0.3	Instruction: $F(1, 81)=151.161^{***}$ Word category: $F(2, 162)=101.980^{***}$ Group: $F(2, 81)=0.623$
II: Negative	R-words	2.0 ± 1.2	1.6 ± 1.4	2.3 ± 1.1	Instruction × category: $F(2, 162)=14.081$ Instruction × group: $F(2, 81)=0.332$ Group × category: $F(4, 162)=0.428$ Instruction × category × group: $F(4, 162)=2.306$
	F-words	0.7 ± 1.0	0.8 ± 1.0	0.6 ± 0.9	
III: Alcohol	R-words	3.1 ± 1.5	3.1 ± 1.7	2.8 ± 1.2	
	F-words	1.2 ± 1.3	0.9 ± 1.0	1.3 ± 1.2	
II(R-F)-I(R-F)		0.6 ± 1.7	0.3 ± 1.4	0.7 ± 1.6	2 × 3 ANOVA Specific directed forgetting
III(R-F)-I(R-F)		1.1 ± 1.8	1.6 ± 1.8	0.5 ± 2.1	Word category: $F(1, 81)=6.263^*$ Group: $F(2, 81)=0.439$ Group × category: $F(2, 81)=3.378^*$

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

category ($F(2, 162)=101.980$; $P < 0.001$) revealed in post-hoc paired sample t -tests that most remembered words belonged to the alcohol-related word category followed by negative and neutral word categories (all $P < 0.002$). However, the three groups did not differ significantly from each other (no significant main-effect of group; $F(2, 81)=0.623$; $P=0.539$).

The number of recalled words varied significantly depending on word category and instruction seen in the significant interaction effect ($F(2, 162)=14.081$; $P < 0.001$). In post-hoc paired sample t -tests comparing the R- and the F-words for each word category separately, the discrepancies between R- and F-words were significant for all word categories (all $P < 0.001$, with the biggest difference value for the alcohol category with $M=1.8$, S.D.=1.7; followed by the negative category with $M=1.3$, S.D.=1.5; and the neutral category with $M=0.8$, S.D.=1.0). No significant interactions of group and word category ($F(4, 162)=0.428$; $P=0.788$) or group and instruction cue ($F(2, 81)=0.332$; $P=0.719$) were found. The three-way interaction of word-category, instruction and group was approaching significance ($F(4, 162)=2.306$; $P=0.064$).

In order to take a closer look at the impact of alcohol-related words in comparison to negatively valenced words in the DF procedure, we calculated the specific DF effects (analogous to the Stroop interference effects). In a first step, we subtracted the average number of recalled F-words from the average number of R-words recalled for each word category to get the “R–F-difference-score” indicating the simple DF effect. In a second step we focused on the impact of categorical valence by subtracting the “R–F-difference-score” of alcohol-related words from the “R–F-difference-score” of neutral words to get the alcohol-specific

DF effect and the same difference score was calculated for negative words.

The specific DF effects corrected for the magnitude of DF for neutral words as baseline was statistically assessed via a two-(DF “R–F-difference-score” of negative or alcohol-related words subtracted from the DF “R–F-difference-score” of neutral words) by three (group) repeated-measures ANOVA is presented in Fig. 2 and Table 2. All participants showed a significantly higher alcohol-specific DF effect (main effect of word category: $F(1, 81)=6.163$; $P=0.015$), seen in the post-hoc paired sample t -test between alcohol-related and negative words ($t(83)=2.414$; $P=0.018$). The groups did not differ significantly from each other (no main effect group: $F(2, 81)=0.439$; $P=0.646$). However, the word category × group interaction effect was significant ($F(2, 81)=3.378$, $P=0.039$). Post-hoc paired sample t -tests (Bonferroni-adjusted significance level of $P=0.01667$) revealed one significantly higher alcohol-related specific DF effect compared to the negative specific DF effect for the D-Alc-group only ($t(27)=3.092$; $P=0.005$; Alc: $t(27)=1.350$; $P=0.188$; Con: $t(27)=-0.386$; $P=0.702$). To take a closer look at the origin of this discrepancy between the alcohol-related and negative specific DF effect, we conducted post-hoc paired sample t -tests (Bonferroni-adjusted significance level of $P=0.008$) within the D-Alc-group to test whether this effect can rather be attributed to a better remembering of the R-words or a stronger forgetting of the F-words between both categories. On this basic level, we found that the D-Alc-group memorized significantly more R-words from the alcohol-related compared to the negative category ($t(27)=4.762$; $P < 0.001$), whereas the forgetting of the F-words did not differ between both categories ($t(27)=0.867$; $P=0.394$).

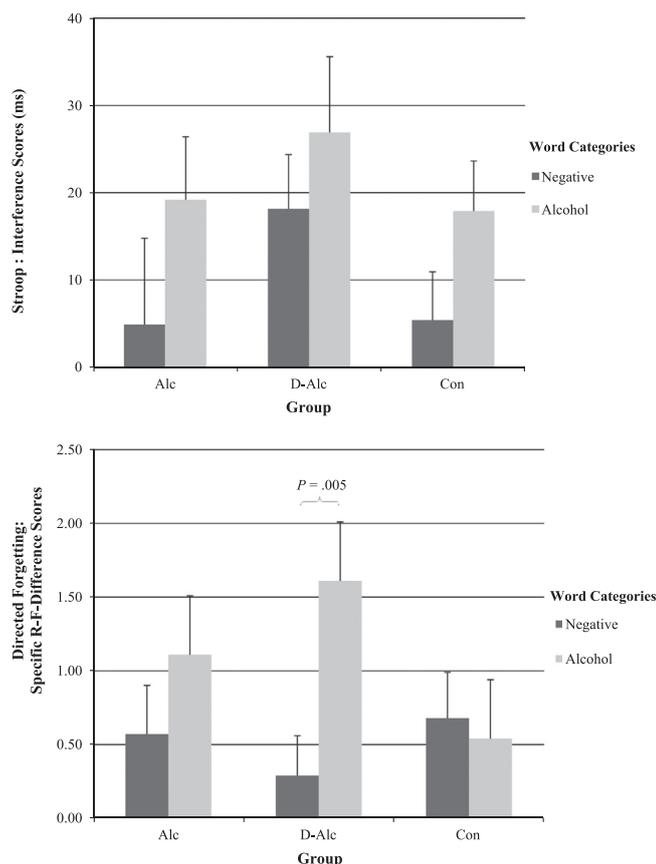


Fig. 2. Stroop interference effect: mean reaction time (ms, means and standard errors) of neutral word category subtracted from negative and alcohol categories and specific directed forgetting effect: word scores for negative and alcohol-words (neutral word difference (R–F) subtracted from negative and alcohol word differences (R–F, means and standard errors) for alcohol-dependents (Alc, $n=28$), depressive alcohol-dependents (D-Alc, $n=28$) and controls (Con, $n=28$).

4. Discussion

Cognitive control plays a key role in alcohol use disorders as impaired cognitive control contributes to the development and maintenance of addictive behavior and addictive behavior may – vice versa – deteriorate impairments of cognitive control (e.g. Lubman et al., 2004; Euser and Franken, 2012; Noel et al., 2013). To gain a better understanding of nature of these impairments, we investigated two aspects of cognitive control, namely susceptibility to either attentional or memory biases. Contradictory to our hypothesis, our main finding was that alcohol-dependents with and without depression did not show more pronounced attentional and memory biases to alcohol-related words compared to healthy controls.

In the alcohol Stroop task alcohol-dependents with and without depression and the healthy controls were notably slower to color-name alcohol-related words than negative or neutral words. This slowing is in line with previous studies (Bauer and Cox, 1998; Cox et al., 1999; Ryan, 2002; Cox et al., 2003; Field et al., 2007). Thus, we did not find an increased alcohol-related attentional bias that is specific for alcohol-dependents. This finding might be due to a high degree of intrinsic salience of alcohol-related words in general, being inherently more “attention-grabbing” to people regardless of whether or not they are problem drinkers (Bauer and Cox, 1998). Furthermore, Cox et al. (1999, 2003) suggest that allocating attentional resources disproportionately to alcohol-related stimuli also occurs in non-dependent drinkers under certain circumstances (e.g. relatively high

consumption of alcohol, exposition to alcoholic beverages prior to the Stroop task). In our previous investigation (Fridrici et al., 2013) we even found that our presumption of an increased attentional bias caused by personally relevant alcohol-related words did not apply to alcohol-dependents but to the control participants only. However, there are also conflicting results. Two representative studies by Field et al. (2013) and Stetter et al. (1995) found an alcohol-related attentional bias in alcohol-dependents indicated by slower RTs for alcohol-related words relative to neutral words in comparison to control participants. Both of those investigations took place at an early stage of a detoxification program (during the first week of an abstinence oriented day-treatment program or between 10 and 20 days after admission to an inpatient detoxification and motivation program). By contrast, the alcohol-dependent patients in the present study had participated for at least three weeks in a day-clinic rehabilitation program. In agreement with this argumentation, Flaudias et al. (2013) showed that four weeks of an inpatient treatment reduced the attentional bias in alcohol-dependents. In detail, our program consists of various cognitive behavioral therapeutic interventions, elements of motivational interviewing, interpersonal and alcohol rejection skills trainings and the transfer of relapse-prevention strategies. Therefore, the alcohol-dependents of our study have been continuously encouraged to deal and cope with alcohol-related thoughts during treatment.

Two mechanisms may explain why the more extensive treatment program that was completed by the patients of the present study (compared to the patients of the Field et al. and the Stetter et al. studies) may have led to the absence of the attentional bias: first Klein (2007) found that alcohol-dependents who were encouraged to freely experience any alcohol-related thoughts showed no increased interference for the word “alcohol”. By contrast, alcohol-dependents who were instructed to suppress their thoughts about alcohol showed color-naming interference. Thus, attempts of thought suppression might have been reduced in our patient sample. Second, habituation toward alcohol-related stimuli as consequence of treatment could be another possible result of a more extensive treatment program (Wingenfeld et al., 2007).

Regarding the directed forgetting procedure, all participants – including the alcohol-dependents – memorized more to-be-remembered words than to-be-forgotten words of the neutral, negative and alcohol-related word-categories. Moreover, the groups did not differ with respect to the total number of recalled words. Thus, for the alcohol-dependents no memory bias was found so that controlled inhibition of the to-be-forgotten words as well as selective rehearsal of the to-be-remembered words, both seem to be unaffected. In agreement with our results, Noel et al. (2013) showed no differences between alcohol-dependents and control participants in different procedures assessing the capacity to control irrelevant information in working memory (cued recall and Brown–Peterson variant). However, our findings and those of Noel et al. (2013) do not correspond with two studies by Todor (2007) and Noel et al. (2009), both showing that alcohol-dependents remembered more to-be-forgotten-items than control participants in the directing forgetting paradigm indicating reduced controlled inhibition in alcohol-dependents. In both of these studies the participants were tested during detoxification programs – in the case of Noel et al. (2009) the detoxification regimen consisted of administration of B vitamins and a gradual decrease of the doses of sedatives (diazepam). Todor (2007) recruited participants from an out-patient detoxification program, in which the concrete components of therapeutic interventions remain unclear. Analogous to the Stroop-results discussed above, we suppose that the alcohol-dependent sample of our study might have improved their ability to resist alcohol-related memory intrusions during their rehabilitative treatment.

In contrast to our hypotheses we did not find an attentional bias in the Stroop task for negatively valenced words specifically for alcohol-dependents with co-morbid major depression. In line with our results, some previous studies did not find any differences between depressed patients and control participants for the processing of negative items either (Mogg et al., 1993; Schlosser et al., 2011). However, there are also data indicating higher attentional bias for depression-related stimuli in depressive patients (i.e. Dozois and Dobson, 2001). The missing attentional bias for negative words in our study might, at least partly, be due to the self-reported moderate severity of depressive symptoms in our sample (seen in the General Depression Scale, Table 1). In fact, the adverse effects caused by the alcohol-dependence seem to remain the key symptoms in our sample of alcohol-dependents with depression – as they reported significantly more social and family problems and a worse psychiatric condition as a consequence of their alcohol consumption (seen in the European Addiction Severity Index, Table 1). Moreover, only the alcohol-dependents with depression memorized significantly more alcohol-related to-be-remembered words than negative to-be-remembered words in the directed forgetting paradigm – this discrepancy was not found in any other group. In contrast to Leppanen (2006) who postulated that attentional bias toward negatively valenced material may lead to enhanced memory for negatively valenced material in patients with depression, we rather found an attenuated memory for negatively valenced words in alcohol-dependents with depression and a comparatively more pronounced bias towards alcohol-relevant material, perhaps reflecting a stronger tendency to ruminate over alcohol-related material. Rumination is a typical problem in depressed patients (i.e. Watkins and Moulds, 2005; Beblo et al., 2011).

The primary limitation of this study is that we only included alcohol-dependent patients after completing a day-clinic rehabilitation program. The additional investigation of acutely ill patients would have enabled us to investigate the cognitive biases in the course of treatment. Moreover, the inclusion of other variables that are known to influence the cognitive biases (such as alcohol priming by smelling alcoholic beverages, expectancy of substance availability or manipulation of stress level) would have helped to specify our results. Further studies are needed that explore the association between these variables and cognitive biases in alcohol-dependents.

In summary, our findings do not support the hypothesis of more pronounced biases of attention and memory in alcohol-dependents. Cognitive biases were neither found for alcohol-related words in alcohol-dependents without co-morbidity, nor for negative words in alcohol-dependents with co-morbid depression. However, alcohol-dependents with depression showed a memory bias for alcohol-related material, suggesting that this group may be more pre-occupied with alcohol than alcohol-dependents without such co-morbidity. Before final conclusions can be drawn, future studies need to replicate our findings keeping possible treatment effects under control.

Appendix A

The following German words ('English translation') were employed in the Stroop and in the directed forgetting paradigm.

A.1. Stroop

Neutral: Sekunde ('second'), Etikett ('label'), Nummer ('number'), Quadrat ('square').

Negative: Gewalt ('violence'), Morder ('murderer'), Blutbad ('bloodbath'), Folter ('torture').

Alcohol: Alkohol ('alcohol'), Aquavit ('aquavit'), Saufen ('booze'), Whiskey ('whiskey').

A.2. Directed forgetting

Neutral: Abschnitt ('article'), Auffassung ('concept'), Aufkleber ('sticker'), Drehpunkt ('swivel'), Gegenstand ('object'), Geschehen ('event'), Kalender ('calendar'), Kommode ('dresser'), Material ('material'), Programm ('program'), Rechteck ('rectangle'), Schablone ('stencil'), Streifen ('stripes'), Vorgehen ('approach').

Negative: Demütigung ('abusement'), Diktatur ('dictatorship'), Gemetzelt ('butchery'), Malaria ('malaria'), Massaker ('massacre'), Missbrauch ('abuse'), Notigung ('duress'), Quälerei ('cruelty'), Sklaverei ('slavery'), Schmerzen ('pain'), Totschlag ('homicide'), Verachtung ('contempt'), Verbrecher ('criminal'), Verderben ('bane').

Alcohol: Apfelkorn ('Apfelkorn liqueur'), Besäufnis ('bender'), Biergarten ('beer garden'), Brauerei ('brewery'), Cocktail ('cocktail'), Filmriss ('mindlapse'), Martini ('martini'), Nachdurst ('afterthirst'), Ramazotti ('ramazotti'), Rotwein ('red wine'), Sauf tour ('booze'), Suchtdruck ('craving'), Tequila ('tequila'), Vollrausch ('drunken stupor').

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