Original Paper

Acute alcohol effects on explicit and implicit motivation to drink alcohol in socially drinking adolescents

Journal of Psychopharmacology
2017, Vol. 31(7) 893–905

DOI: 10.1177/0269881117691454
journals.sagepub.com/home/jop

Elisabeth Jünger[1], Amir-Homayoun Javadi[2], Corinde E Wiers[3], Christian Sommer[1], Maria Garbusow[4], Nadine Bernhardt[1], Sören Kuitunen-Paul[5], Michael N Smolka[1] and Ulrich S Zimmermann[1]

Abstract

Alcohol-related cues can evoke explicit and implicit motivation to drink alcohol. Concerning the links between explicit and implicit motivation, there are mixed findings. Therefore, we investigated both concepts in 51 healthy 18- to 19-year-old males, who are less affected by neuropsychological deficits in decision-making that are attributed to previous alcohol exposure than older participants. In a randomized crossover design, adolescents were infused with either alcohol or placebo. Self-ratings of alcohol desire, thirst, well-being and alcohol effects comprised our explicit measures of motivation. To measure implicit motivation, we used money and drink stimuli in a Pavlovian conditioning (Pc) task and an Approach-Avoidance Task (AAT). Alcohol administration increased explicit motivation to drink alcohol, reduced Pc choices of alcoholic drink-conditioned stimuli, but had no effect on the AAT. This combination of results might be explained by differences between goal-directed and habitual behavior or a temporary reduction in rewarding outcome expectancies. Further, there was no association between our measures of motivation to drink alcohol, indicating that both self-reported motivation to drink and implicit approach tendencies may independently contribute to adolescents' actual alcohol intake. Correlations between Alcohol Use Disorders Identification Test (AUDIT) scores and our measures of motivation to drink alcohol suggest that interventions should target high-risk adolescents after alcohol intake.

Clinical trials: Project 4: Acute Effects of Alcohol on Learning and Habitization in Healthy Young Adults (LeAD_P4); NCT01858818; **https://clinicaltrials.gov/ct2/show/NCT01858818**

Keywords

Approach bias, Computer-Assisted Infusion System (CAIS), lexical decision task, money and drink stimuli, Pavlovian conditioning

Introduction

Pavlovian learning describes the process by which people learn stimulus–outcome contingencies through simultaneous presence of a neutral cue together with its related rewards or punishments (Bradizza et al., 1994; Daw and O'Doherty, 2014). One example of such a stimulus–outcome contingency might be the repeated association of a beer bottle and the positive or negative aspects of being drunk. By that, the formerly neutral cue 'beer bottle' becomes a conditioned stimulus predicting rewarding or punishing alcohol effects. Later on, such alcohol-related Pavlovian cues can capture attention and elicit explicit as well as implicit motivation to drink alcohol (Field et al., 2009; Roberts and Fillmore, 2015). Although one would expect both aspects of motivation to be positively linked with each other, there are mixed findings about their relationship, which might be explained by different underlying processes. According to Bargh (1994), explicit motivation is based on 'slow', intentional, reflective and controllable cognitive processes, whereas implicit motivation relies on 'fast', unintentional, affective and automatic processes, which are difficult to control. Dual-process models of substance use therefore propose that explicit and implicit motivation independently guide drinking behavior (Ostafin et al., 2008; Stacy and Wiers, 2010). Hence, occasionally, explicit intentions to abstain may be overridden by implicit affective responses to alcohol-related cues, resulting in seemingly paradoxical behavior (Stacy and Wiers, 2010; Watson et al., 2012).

Explicit motivation to drink alcohol is typically measured via self-report, such as ratings of craving or desire to drink. Previous studies reported increased craving or desire to drink after alcohol intake (Amlung et al., 2015; de Wit, 1996; Roberts and Fillmore, 2015; Schoenmakers et al., 2008; Schoenmakers and Wiers, 2010) and placebo drinks (Christiansen et al., 2013). Hence,

[1]Department of Psychiatry and Psychotherapy, Technische Universität Dresden, Dresden, Germany
[2]School of Psychology, University of Kent, Canterbury, UK
[3]National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, MD, USA
[4]Department of Psychiatry and Psychotherapy, Charité Universitätsmedizin Berlin, Berlin, Germany
[5]Institute of Clinical Psychology and Psychotherapy, Technische Universität Dresden, Dresden, Germany

Corresponding author:
Ulrich S Zimmermann, Department of Psychiatry and Psychotherapy, University Hospital Carl Gustav Carus at Technische Universität Dresden, Fetscherstraße 74, 01307 Dresden, Germany.
Email: UlrichS.Zimmermann@uniklinikum-dresden.de

explicit motivation to drink is sensitive to both acute alcohol administration and the expectancy to receive alcohol.

Implicit motivation to drink alcohol requires more complex methods, such as measuring automatic action tendencies to alcohol-related cues with an Approach-Avoidance Task (AAT; Wiers et al., 2009). The AAT usually requires subjects to push or pull alcohol-related Pavlovian cues (e.g., pictures of alcohol) with a joystick according to their format. The speed difference between these actions is then compared with the actions to neutral cues. Previous studies using the AAT showed that alcohol-dependent patients compared to non-dependent controls exhibit stronger approach tendencies to alcohol-related cues, which is labeled 'alcohol-approach bias' (Ernst et al., 2014; Wiers et al., 2014). Nevertheless, another study failed to find such a difference between patients and controls (Wiers et al., 2016). Besides that, AAT approach and avoidance tendencies were found to predict real-life drinking 12 weeks later in people with alcohol use disorders (Martin Braunstein et al., 2016). Only one study examined alcohol effects on the AAT in healthy subjects and found no differences in alcohol-approach bias scores after alcohol (50 mg%) compared to placebo administration (Korucuoglu et al., 2014).

As highlighted above, previous studies reported mixed findings on the links between explicit and implicit motivation to drink alcohol, which might be explained by different alcohol doses and paradigms. None of these studies used the AAT. One study measured how fast a manikin figure could be moved towards or away from alcohol or neutral pictures (Christiansen et al., 2013). The study found that the expectancy to receive alcohol increased both craving and approach tendencies to alcohol pictures, but there was no difference in alcohol-approach tendencies after alcohol (90 mg%) compared to placebo intake (Christiansen et al., 2013). This null finding, together with the null effect reported in Korucuoglu et al. (2014), suggests that behavioral approach tendencies to Pavlovian alcohol-related cues might be unaffected by acute alcohol administration. Another indicator of motivation to drink alcohol is the attentional bias when examining healthy subjects (Schoenmakers et al., 2008). Three studies examined the attentional bias by measuring response times to cues that were presented locally identical with either alcohol or neutral pictures. In these studies, faster responses to alcohol-related cues indicated a preexisting visual attention allocation to alcohol pictures. All three studies reported alcohol-induced increases in craving or alcohol desire, but the attentional bias to alcohol-related cues was either enhanced (30–40 mg% vs placebo: Schoenmakers et al., 2008), or attenuated (65–80 mg% vs placebo: Roberts and Fillmore, 2015; 0–200 mg% in a field study: Schoenmakers and Wiers, 2010). These findings indicate a dose–response relationship such that lower alcohol doses increase the attentional bias, whereas higher doses decrease it.

The goal of the present study was to examine the impact of a highly standardized ethanol exposure on the links between explicit and implicit motivation to drink alcohol. Participants received either an alcohol or a placebo infusion in order to control for differences in alcohol expectancy. Contrary to previous studies in this field, we used a legally 'intoxicating' dose and produced a stable blood alcohol concentration of 80 mg%. Moreover, we tested 18- to 19-year-old adolescents, who are less affected by neuropsychological deficits in basic decision-making that are attributable to previous exposure to large alcohol doses than older participants. We measured explicit motivation to drink alcohol by self-reports of alcohol desire and thirst. Since the drift diffusion model postulates that current mood states directly affect approach and avoidance tendencies (Trimmer et al., 2013), we also expected actual well-being and positive alcohol effects, including stimulation, to promote approach behavior towards alcoholic drink stimuli. Conversely, negative alcohol effects, including sedation, were expected to motivate avoidance behavior. Numerous studies confirmed that alcohol administration increases both stimulation and sedation (Hendler et al., 2013). In our study, self-reports of subjective alcohol effects and well-being therefore served as further indicators of explicit motivation to drink, besides desire to drink and thirst.

To measure implicit motivation to drink alcohol, we used an AAT as well as a Pavlovian conditioning (Pc) task. The Pc task was introduced, because the interpretation of the approach bias might be complicated by the fact that the AAT involves instrumental learning of pushing or pulling Pavlovian cues according to their format, independent of their emotional value. These actions involve instrumental learning of stimulus (format) – action (approach/avoid) – outcome (feedback) contingencies (Daw and O'Doherty, 2014). A negative result, where the approach bias does not differ between cues, might therefore be interpreted in two ways: either, the cues truly had the potential to affect behavior, but subjects happened to be perfect instrumental learners of the format-related action, who, for that reason, could hardly be distracted by any cue; alternatively, the cues were in fact ineffective to alter behavior even in imperfect instrumental learners. The Pc task should help us to disentangle both possibilities, because it contained the same cues as the AAT, but they were used to produce second-order Conditioned Stimuli (CS). In forced-choice trials, we then measured individual preferences for the CS. Crucially, if there was no preference for any of the CS, it would imply that our Pavlovian cues were inefective to alter behavior, not only in the Pc task, but also in the AAT. Both tasks also contained money stimuli, enabling us to compare approach behavior to alcoholic drink stimuli with other emotionally valenced stimuli (Delgado et al., 2011). Finally, we assessed explicit knowledge of the Pc stimuli to control for general memory impairments.

Alcohol administration might solely impair general decision-making abilities, leading to unspecific effects on our measures of implicit motivation to drink alcohol, such as more random behavior. We therefore used a lexical decision task to control for general alcohol-induced decision-making impairments, because this task efficiently measures simple two-choice decision-making (Ratcliff et al., 2004).

To summarize, the main novel elements of our study are: (a) we examined the effect of a legally 'intoxicating' alcohol dose in (b) a young sample of 18- to 19-year-olds on (c) explicit motivation to drink measured not only by alcohol desire, but also by thirst and subjective alcohol effects. With respect to implicit motivation to drink, (d) we controlled for instrumental factors in the AAT with a Pc task, and (e) we controlled for general reactivity to emotional stimuli with monetary stimuli. Finally, (f), we examined the links between our measures of motivation to drink alcohol and real-life problem drinking in the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001). Our primary research question was whether explicit measures are linked with implicit measures of motivation to drink alcohol. As suggested by Roberts and Fillmore (2015), we expected no direct links between alcohol desire and implicit measures of motivation to drink alcohol. (1) Instead, we hypothesized that thirst, general well-being and stimulating alcohol effects would be positively

correlated with implicit motivation, whereas negative alcohol effects and sedation should be negatively correlated with implicit motivation to drink alcohol. Besides that, we had the following secondary hypotheses: (2) Alcohol administration was expected to increase explicit alcohol desire as well as positive alcohol effects, in line with the above-cited studies. (3) Accordingly, we expected alcohol-induced increases in Pc choices of alcoholic drink-CS as well as AAT alcohol-approach bias scores. On a related note, we wanted to explore whether the null finding of Korucuoglu et al. (2014) could be attributed to their smaller sample ($N = 23$) or their lower alcohol dose (50 mg%).

Methods

All study procedures were approved by the ethics committee of the Technische Universität Dresden (EK 227062011) and fully complied with the World Medical Association Declaration of Helsinki as revised in 2013.

Participants and recruitment

The study was part of a research consortium investigating the relations between Learning and Alcohol Dependence (LeAD, DFG FOR1617). Participants were recruited by mailing invitation letters to 1100 18-year-old males from the greater Dresden area, whose addresses were provided by the local registration office. After giving written informed consent, respondents participated in another project of our research consortium (Garbusow et al., 2013) where they were interviewed using the computerized Composite International Diagnostic Interview (CIDI; Jacobi et al., 2013; Wittchen and Pfister, 1997) and completed learning tasks in a separate fMRI session. All participants who consented to participate in our study then completed a telephone screening; see Figure 1 for the sample size in each recruitment step. Inclusion criteria were: 18- to 19-year-old male native German speakers, who reported at least two drinking days per month during the last three months. Subjects were excluded if they had a lifetime DSM-IV substance dependence diagnosis except for nicotine dependence; reported current substance abuse except for nicotine; had a medical disorder which would place them at risk if receiving alcohol; had elevated liver enzymes indicating excessive alcohol use; produced a drug screen positive for amphetamines, benzodiazepines, barbiturates, cannabinoids, cocaine, ecstasy, antidepressants and opiates; were on any medication possibly interacting with alcohol; reported alcohol consumption on the test day or the day before; or were left-handed.

Our final sample consisted of 51 males, aged 18 ($N = 42$) or 19 years ($N = 9$), who had their first alcoholic drink at ages 10–16 (*Median* = 15), 46% were above the 8-point cut-off suggesting risky alcohol use in the AUDIT ($M = 7.5$, $SD = 4.1$) and 22% were regular smokers.

General experimental procedure

Participants underwent two identical experimental sessions, separated by 6–22 days (*Median* = 7), involving intravenous infusion of alcohol or normal saline in a randomized crossover design. Subjects were misinformed that they would receive 'different alcohol dosages' on either day in order to uphold alcohol expectancy

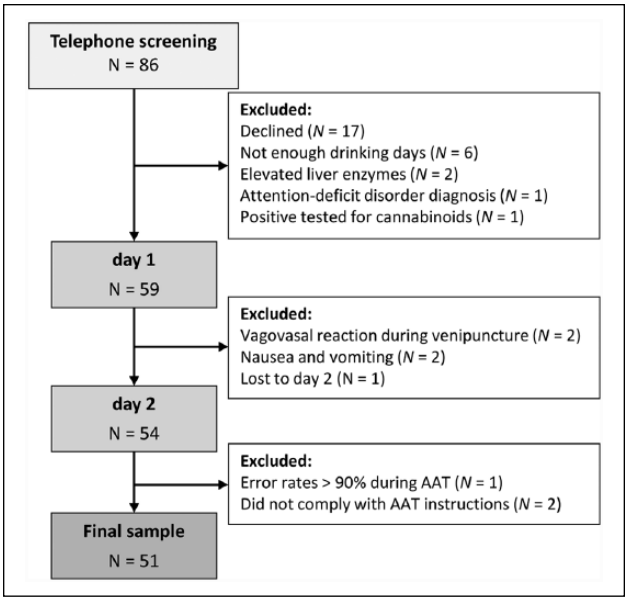

Figure 1. Sample size in each step of the recruitment process. AAT = Approach Avoidance Task; N = Number. See Data analysis section for exclusion reasons.

even on the placebo day. Participants reported to the lab at 12:45 p.m. and provided a urine sample to screen for drugs using a Nal von Minden Multi 12TF test (Moers, Germany). In a brief structured interview, we assessed drinking behavior and health problems during the time since the last experimental session.

Figure 2 illustrates the experimental procedure. At 1:40 p.m., an 18G i.v. line was established using a cubital fossa vein of the non-dominant arm, while participants sat on a reclining arm chair facing a 32-inch (approx. 81 cm) video screen. Here, they rated subjective measures (described below). At 1:50 p.m. the alcohol infusion was started, linearly increasing arterial Blood Alcohol Concentration (aBAC) to 80 mg% within 25 min, then holding it stable at this level for 2 h.

Participants reached the target aBAC at 2:15 p.m. and again rated subjective measures. Then they were transferred to a swivel chair facing a computer monitor and completed four tasks in the following order: 1) the Pc task including the 2) lexical decision task; 3) a two-stage Markov decision-task, which will be reported elsewhere; and 4) the AAT.

Back in the arm chair, participants again rated subjective measures, followed by a paper-pencil questionnaire assessing explicit knowledge of the Pc stimuli and the AUDIT (Babor et al., 2001). At 4 p.m., the i.v. line was removed. To keep participants blind for the treatment condition, they all waited for 2 h, resulting in an aBAC below 45 mg%, before they were picked up by car (e.g. paid taxicab). At the end of each day, participants received their task winnings. At the end of the second day, participants were debriefed and received 100€ study compensation.

Alcohol administration methods

We used the Computer-assisted Alcohol Infusion System (CAIS; O'Connor et al., 1998) for both alcohol and placebo administration. Alcohol infusions were prepared by mixing 0.9% saline

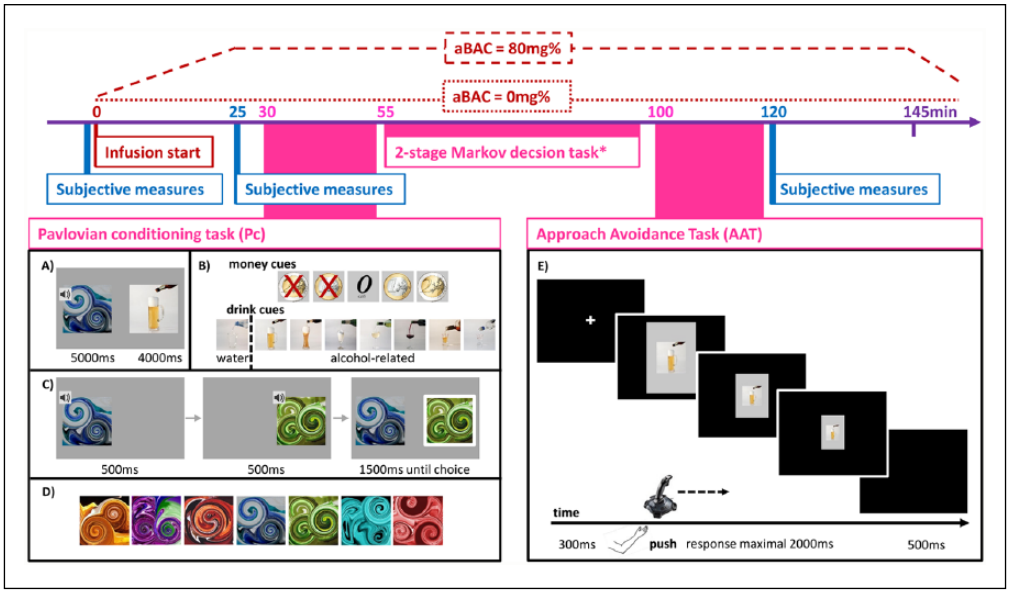

Figure 2. Schematic overview of the infusion experiment. On alcohol days, arterial Blood Alcohol Concentration (aBAC) was clamped at 80 mg% from 25 min to 145 min. The Pc task contained an A) conditioning phase B) using seven cues. After a short lexical decision task (not shown) participants chose their preferred Conditioned Stimulus (CS) out of two options. Explicit knowledge was assessed with a D) paper-pencil questionnaire at 140 min asking for the corresponding cue given each CS. The E) AAT task required participants to pull or push landscape or portrait pictures containing the same B) money cues (–2€, 0€, +2€) and drink cues that were used in the Pc task. *The 2-stage Markov decision task is reported elsewhere.

with 95% ethanol (Alkohol Konzentrat 95% Braun, Melsungen, Germany) giving a final concentration of 6.0% (v/v). We used two volumetric infusion pumps (Infusomat fms, BBraun, Melsungen, Germany). Participant's age, gender, height and weight were fed into a Physiologically-Based PharmacoKinetic (PBPK) model (Plawecki et al., 2012; Ramchandani et al., 1999). ABAC (in mg% = German unit ‰*100) was validated with 11 aBAC readings (at 6, 12, 18, 24, 27, 35, 45, 85, 90,105,125 min) using an Alcotest 6810med breathalyzer (Draeger Sicherheitstechnik, Lübeck, Germany). These data were entered into the CAIS software in real time to improve individual pharmacokinetic models and adapt the prescribed infusion rates accordingly. The breathalyzer measured alcohol concentration in end-expiratory breath, which is closely related to arterial BAC during intravenous ethanol infusion (Lindberg et al., 2007). Since alcohol exposure is conventionally communicated as BAC, the breathalyzer applied the usual 1:2100 air/blood partition coefficient to approximate aBAC (mg%) from breath readings (mg ethanol/ liter of air). Owing to the high cerebral perfusion index, aBAC provides a reliable estimate of brain alcohol exposure, which is the key factor driving both behavior and subjective alcohol effects.

Subjective measures and behavioral tasks

Subjective measures. We used eight statements to measure: (1) *stimulation*: 'Right now, I am experiencing stimulating alcohol effects, e.g., cheerful, excited, full of energy, full of zest for action…'; (2) *sedation*: 'Right now, I am experiencing sedating alcohol effects, e.g., relaxed, tired, sluggish…'; (3) *negative effects*: 'Right now, I am experiencing negative alcohol effects, e.g., nausea, dizziness, ringing in the ear…'; (4) *alcohol desire*: 'I would like to consume more alcohol right now'; (5) *general well-being*: 'Overall, I am feeling well right now'; (6) *drinks number*: 'Right now, I feel like I had … drinks'; (7) *feeling drunk*: 'I am feeling drunk right now'; (8) *thirst*: 'I am thirsty (e.g., for soda, cola,…)'. Statements were programmed in Presentation (Neurobehavioral Systems), presented sequentially on the video screen and answered using a computer mouse on vertical visual analog scales anchored at 0 (not at all) and 100 (extremely), or by choosing a number between 0–30 for estimated drinks number.

For analyses of explicit motivation to drink, we used individual visual analogue scale ratings and estimated *drink numbers*. Higher ratings of *alcohol desire, thirst, well-being* and *stimulation* indicated higher motivation to approach alcoholic drinks, whereas higher ratings of *sedation* and *negative effects* indicated higher motivation to avoid alcoholic drinks.

Pavlovian conditioning task. The Pc task (Figure 2A–D) was a modified version of the Pavlovian-to-Instrumental Transfer (PIT) task used by Garbusow et al. (2014). The task was programmed in MATLAB 2010b (MathWorks) and presented on a 19-inch (approx. 48 cm) monitor. Participants were provided with headphones (Beyerdynamic DT 770, Heilbronn, Germany) and a two-button (blue, yellow) response pad (Current Designs, Philadelphia, USA).

During the first 6 min of the task, participants observed 56 (= 7 cues × 8 repetitions) Pavlovian conditioning trials (Figure 2A), in which five money (−2€, −1€, 0€, 1€, 2€) and two drink cues (water, alcohol; Figure 2B) were sequentially presented with one of seven abstract audio-visual stimuli (Figure 2D). Through

simultaneous presentation with one of the cues, unconditioned stimuli were transformed into money- and drink-CS. All CS consisted of 350 ms mono sounds and abstract pictures with equal mean luminance and equal root-mean-square contrasts of the luminance (Peli, 1990). Two different sets of sounds and pictures were used for the two days; their order and assignment to cues were randomized for each participant. Participants were instructed that money cues indicated real gains and losses which were added or subtracted from their payment. Since all money cues were presented equally often, the total winning was 0€, but subjects received the information that they earned 2€ on day1 and 3€ on day2.

During the last 5 min of the task, participants were asked to choose the CS they liked best when being exposed to all possible pairs of CS, which were presented four times in random order (21 pairs × 4 = 84 trials; Figure 2C). Each audio-visual CS appeared for 500 ms on the left or right side of the screen, immediately followed by simultaneous presentation of both visual CS until participants made their choice via response pad. For responses slower than 1500 ms, the phrase 'Too slow!' appeared, and the respective pair was repeated at the end of the task.

For analyses of implicit motivation to drink alcohol, we collected CS choices (0 = not chosen, 1 = chosen) for each valid trial. Higher numbers of alcoholic drink-CS choices indicated higher implicit motivation to drink alcohol.

Explicit knowledge of the CS-cue combinations was assessed at the end of the experiment. Participants were handed out a color copy with all visual CS (Figure 2D), and asked to write down the corresponding drink or money cue. For analyses of explicit knowledge, we coded for each CS whether the US was correctly recalled (0 = false, 1 = correct). Higher numbers of correctly recalled stimuli indicated better explicit knowledge of the Pc stimuli.

Lexical decision task. This task took 2 min and was presented during the Pc task, right after the Pavlovian conditioning phase, in order to minimize potentially confounding primacy and recency effects on memory during forced choice trials. Moreover, it served as a measure of general decision-making impairments. Participants were instructed to work fast and accurately. Verbal stimuli were presented sequentially and remained on the screen center until participants indicated a word (left arrow key) or a non-word (right arrow key). Ten practice trials were followed by 40 experimental trials. Two sets of 25 words and 25 non-words were used for the two days, presented in random order across participants. Non-words were derived from neutral words by changing one vowel (e.g. 'lamp' to 'lomp'). All words were rated neutral by three independent raters. In addition, words had equal length and frequency values according to Potsdamer dlexDB database (www.dlexdb.de).

For lexical decision task analyses, we used accuracies (0 = false, 1 = correct) of each trial and Reaction Times (RT) of correct responses in milliseconds (ms). Higher numbers of false responses and longer RTs indicated higher decision-making impairments.

Approach-Avoidance Task. The AAT was programmed in MATLAB 2010b (MathWorks) and performed according to Wiers et al. (2013) and Wiers et al. (2009; Figure 2E). The task took 8 min, was presented on the computer monitor, and participants used a joystick (Logitech Attack 3, Newark, USA). In each trial, a cue was placed centrally in a landscape or portrait frame. Participants were randomly instructed to either pull landscape and push portrait formats on both experimental days, or vice versa. We instructed participants to work fast and accurately, and to always look at the screen center. We presented money cues (−2€, 0€, +2€) and drink cues (water, alcohol; see Figure 2B). The AAT included a zooming feature. Whenever the joystick was pulled, the picture grew bigger, and when it was pushed, it grew smaller. Ten practice trials with neutral gray rectangles were followed by 200 experimental trials (= 5 cues × 2 formats × 20 repetitions), presented sequentially in a quasi-random order fulfilling two conditions: the same cue and the same format were maximally presented four times in a row. After 100 trials, there was a break, which could be ended by pushing a joystick button. Cues remained on the screen until participants fully pushed or pulled them. Whenever this action took longer than 2000 ms, the trial was aborted and a sand clock appeared on the screen. For incorrect responses, a sad emoticon was presented, whereas no feedback was given for correct responses. To make sure the joystick was in the center position before each trial, a yellow filled circle appeared. It turned into a fixation cross whenever the joystick was successfully moved back to the starting position, which was then followed by the next cue.

The AAT approach bias was computed as described by Wiers et al. (2014). Wrong responses and missed RTs were discarded, and then all RTs exceeding the individual mean plus three standard deviations (7% of all RTs) were removed. Finally, the approach bias for each cue was computed by subtracting individual median push RTs from median pull RTs. Higher approach bias scores towards alcoholic drink cues (alcohol-approach bias) indicated higher implicit motivation to drink alcohol.

Sample characteristics. Age of first drinking and smoking status (0 = no, 1 = yes), were already assessed in the other project of our research consortium. However, if participants reported current smoking in our brief structured interview, we set their smoking status to 1. We used AUDIT scores of the second infusion session, because there was only one missing (compared to two in the first session).

Data analysis

Three subjects were excluded resulting in 51 data sets. One participant answered too slowly in the AAT resulting in an error rate above 90%. Two subjects reported in the day1 posttest interview that they did not follow the AAT instructions: one always pulled money gain cues, another focused on the upper screen margin in order to not get distracted by the cues.

All analyses were conducted using R 3.2.3 (R Core Team, 2015). We mainly used mixed-effects models (lmer & glmer, package: lme4), since they are known to have a greater power to detect true effects than (M)ANOVAs (Jaeger, 2008) and allowed us to test all contrasts of interest with a minimum number of models.

Explicit motivation to drink alcohol was analyzed using linear mixed-effects models predicting each subjective rating out of the following fixed effects: *time* (reference = 25 min), *treatment* (0.5 = alcohol vs −0.5 = placebo) and their interaction. We expected subjective ratings at 25 min and 120 min to be higher during alcohol compared to placebo infusion (positive main effect of

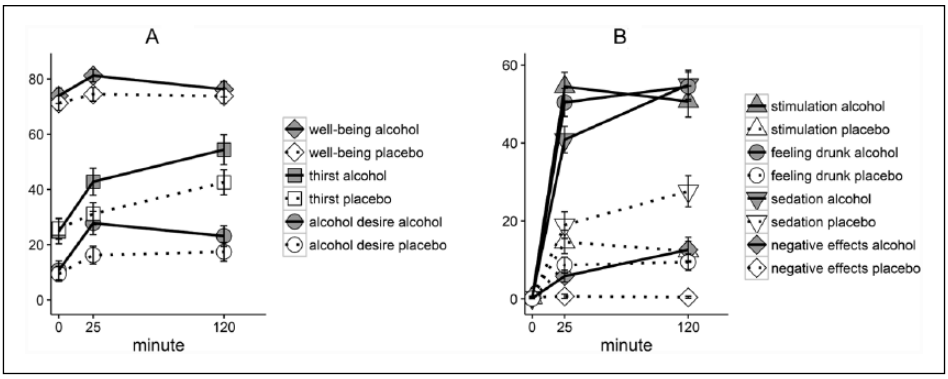

Figure 3. Means and standard errors of the mean (error bars) of subjective ratings (0–100) for A) motivational states and B) alcohol effects, measured during alcohol and placebo infusion. Treatment main effects: all ratings were higher during alcohol compared to placebo infusion at 25 min (t-values > 2.2); the same was true for 120 min for all ratings, besides well-being (t-values > 2.0). See Results section for significant main effects of time and interactions between treatment and time.

treatment and/or positive *time* × *treatment* interactions). In all models, we had to remove the random *time* × *treatment* interaction from the maximum random effects structure (Barr et al., 2013), because there was only one observation for each factor level combination. We interpreted |*t-values*|> 2 as significant (Kliegl et al., 2010). Regarding subjective alcohol effects, we removed baseline measurements (0 min) from analyses, because they consisted of zero values only, which caused a non-normal distribution of the residuals and therefore violated an assumption of mixed-effects models (Magezi, 2015). Regarding motivational states, we used all measurements, but nine data sets for *thirst* were missing owing to the later integration of *thirst* in the study protocol.

Implicit motivation to drink alcohol in the Pc task was analyzed using binomial mixed-effects models. First, we analyzed how often each CS was chosen when presented together with any other CS, testing the fixed effects of *CS* (reference = alcoholic drink-CS), *treatment* (0.5 = alcohol vs −0.5 = placebo) and their interaction. We expected alcoholic drink-CS choices to be higher during alcohol compared to placebo infusion (positive *treatment* main effect). To achieve convergence, we had to remove the random *CS* × *treatment* interaction from the maximum random effects structure. Then, we analyzed trials in which the alcoholic drink-CS was chosen when presented together with any other CS, with *alternative* (reference = −2€ CS), *treatment* (0.5 = alcohol vs −0.5 = placebo) and their interaction as fixed effects, using the maximum random-effects structure. Compared to placebo infusion and −2€, we expected more alcoholic drink-CS choices during alcohol infusion when the alternatives were −1€, 0€, 1€, 2€ or water CS (positive *alternative* × *treatment* interactions).

Implicit motivation to drink alcohol in the AAT was analyzed using a linear mixed-effects model predicting approach bias scores out of *cue* (reference = alcoholic drink cue), *treatment* (0.5 = alcohol vs −0.5 = placebo) and their interaction. We expected higher alcohol-approach bias scores during alcohol compared to placebo infusion (positive *treatment* main effect). Again, we had to remove the random interaction term, because there was only one observation for each factor level combination.

Interrelations between our measures of motivation to drink alcohol and sample characteristics were analyzed with Pearson correlations or Spearman correlations (cor.test, package: stats) whenever Shapiro-Wilk tests (shapiro.test, package: stats) indicated non-normal distributions. We expected significant correlations between Pc alcoholic drink-CS choices, or AAT alcohol-approach bias scores, and thirst, general well-being, as well as subjective alcohol effects.

To explore memory impairments, we tested differences in explicit knowledge of the Pc stimuli with Mc Nemar tests (mcnemar.test, package: stats).

General decision-making impairments in the lexical decision task were examined using two mixed-effects models with the maximum random-effects structure. A binomial model predicted accuracies, and a linear model predicted RTs out of *stimulus* (0.5 = word vs −0.5 = non-word), *treatment* (0.5 = alcohol vs −0.5 = placebo infusion) and their interaction.

Results

Alcohol effects on explicit motivation to drink alcohol

We expected higher subjective ratings of *alcohol desire, thirst* and *well-being* during alcohol compared to placebo infusion. In fact, all three motivational states were rated higher during alcohol compared to placebo infusion at 25 min (*t-values* > 2.3; Figure 3A). The same was true at 120 min for *alcohol desire* and *thirst* (*t*-values > 2.0), but not for *well-being*, according to additional models with 120 min as reference. Moreover, significant interactions indicated that *alcohol desire* and *thirst* ratings increased more strongly from 0 min to 25 min (*t-values* > 2.5) during alcohol compared to placebo infusion. Besides that, we found that irrespective of treatment, *alcohol desire, thirst* and general *well-being* increased from baseline (0 min) to 25 min (*t*-values > 3.1). Later on, only *thirst* increased towards 120 min (*Estimate* = 11.5, *SD* = 2.6, *t* = 4.3).

All alcohol effects (Figure 3B) were rated higher during alcohol compared to placebo infusion at 25 min (*t-values* > 2.2) and 120 min (*t-values* > 5.2). Further, there was a stronger increase in *negative effects* (*Estimate* = 7.0, *SD* = 1.9, *t* = 3.7) over time

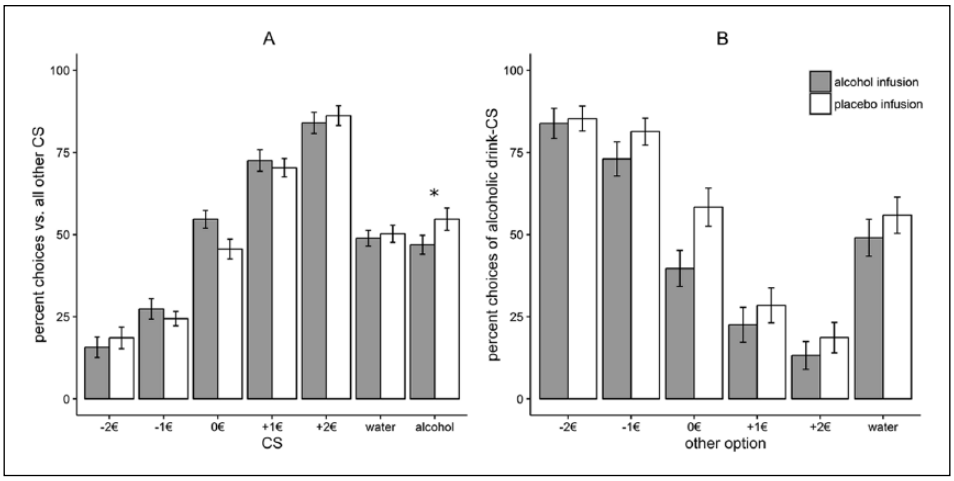

Figure 4. Pavlovian conditioning task means and standard errors of the mean (error bars) of A) percent of trials in which the respective Conditioned Stimulus (CS) was presented together with any other CS; and B) trials forcing a choice between the alcoholic drink-CS and any other CS. *Significant main effect of treatment. See Results section for significant main effects of CS and interactions between treatment and CS.

during alcohol compared to placebo infusion. Besides that, we found that participants reported stronger *sedation* and *negative effects* at the end of the experiment (120 min), compared to the beginning (25 min; all *t-values* > 2.5), irrespective of treatment.

To summarize, alcohol compared to placebo infusion increased explicit motivation to drink alcohol measured by self-ratings of *alcohol desire*, *thirst*, *well-being* and *stimulation*.

Alcohol effects on implicit motivation to drink alcohol – Pc task

First, we analyzed how often a given CS was chosen when presented together with any other CS and expected alcoholic drink-CS choices to be higher during alcohol compared to placebo infusion. However, we found a negative *treatment* main effect indicating that alcoholic drink-CS were chosen less often during alcohol compared to placebo infusion (*Estimate* = −0.3, $z = -4.0$, $p < 0.001$; Figure 4A). There were several interactions between *CS* and *treatment*: when comparing alcoholic drink-CS and 0€ CS during alcohol infusion, the alcoholic drink-CS was less likely to be chosen than during placebo ($p < 0.001$). The same was true for the comparison of alcoholic drink-CS with +1€, −1€ ($p < 0.001$, respectively) as well as water CS ($p = 0.02$). Apart from that, we found significant main effects of *CS*, indicating that participants chose more often money gain-CS (+1€, +2€), and less often money loss-CS (−1€, −2€) compared to alcoholic drink-CS (all *p-values* <0.001, see Figure 4A).

Next, we focused on those trials forcing a choice between alcoholic drink-CS and any other CS to investigate the relative preference for alcohol-related over non-alcohol-related CS (Figure 4B). The alcoholic drink-CS was chosen most often when the other option was the -2€ CS, compared to all other alternatives ($p = 0.02$ for −1€; $p < 0.001$ for 0€, 1€, 2€, water). We expected more alcoholic drink-CS choices than choices of other alternatives during alcohol infusion, but interactions went in the opposite direction: compared to -2€, there was a stronger drop in alcoholic drink-CS choices when the alternative was 0€ ($p = 0.02$), 1€ ($p = 0.01$), or 2€ ($p = 0.03$) during alcohol compared to placebo infusion.

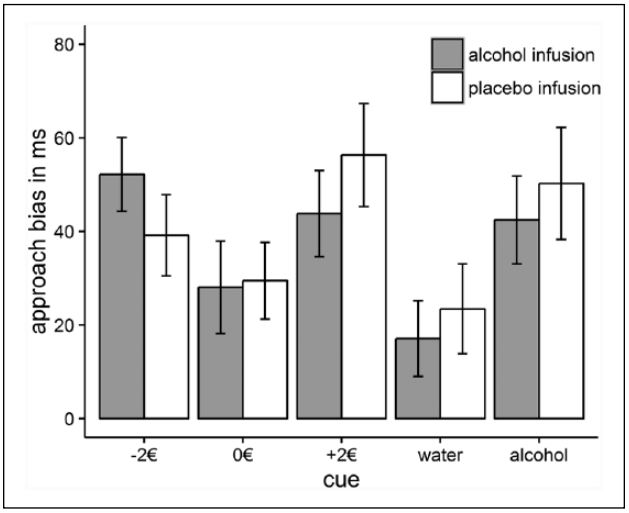

Figure 5. Approach bias (median push – median pull reaction time) means and standard errors of the mean (error bars) during alcohol and placebo infusion. Cue main effect: The approach bias to alcoholic drink cues was significantly higher than to 0€ and water cues (t-values > 2.0). There were no significant main effects of treatment or interactions between treatment and cue.

In short, alcohol compared to placebo infusion reduced implicit motivation to drink alcohol measured by alcoholic drink-CS choices.

Alcohol effects on implicit motivation to drink alcohol – AAT

Although we expected higher alcohol-approach bias scores during alcohol compared to placebo infusion, there were no significant main effects of *treatment* or interactions between *treatment* and *cue* (Figure 5). There were only main effects of *cue*, suggesting that the approach bias towards alcoholic drink cues was higher than that towards 0€ and water cues (*t-values* > 2.0).

Briefly, alcohol administration had no effect on implicit motivation to drink alcohol measured by alcohol-approach bias scores.

Interrelation between explicit and implicit motivation to drink

Within each treatment condition, we analyzed correlations between those explicit and implicit measures of motivation to drink alcohol which were assessed close in time. In line with our hypotheses, we expected significant correlations between Pc alcoholic drink-CS choices or AAT alcohol-approach bias scores and thirst, general well-being, as well as alcohol effects.

However, for the Pc task, none of the subjective measures rated at 25 min were significantly related to the percentage of choices of alcoholic drink-CS during either alcohol or placebo infusion. For the AAT, we only found a significant positive association between the alcohol-approach bias and feeling drunk at 120 min during alcohol infusion ($\rho(49) = 0.32$, $p = 0.02$), representing a medium effect size according to Cohen (1988). All other subjective measures were not significantly related to the alcohol-approach bias (Table 1).

Next, we tested whether alcohol-induced changes in subjective measures were linked to changes in approach behavior to alcoholic drink stimuli. Correlating the difference scores (placebo measurement–alcohol measurement) with each other, we only found that alcohol-induced increases in *well-being* were related to alcohol-induced decreases in alcohol-approach bias ($r(49) = -0.29$, $p = 0.04$; Table 1).

Taken together, explicit and implicit measures of motivation to drink alcohol were not directly linked with each other.

Interrelation between AUDIT and motivation to drink alcohol

Testing the links between real-life drinking problems and our measures of explicit motivation to drink alcohol, we found significantly positive correlations between the AUDIT and alcohol desire measured during placebo administration at 120 min ($\rho(48) = 0.29$, $p = 0.04$; not surviving Bonferroni correction) as well as during alcohol administration at 25 min ($\rho(48) = 0.46$, $p = 0.001$) and at 120 min ($\rho(48) = 0.42$, $p = 0.003$; not surviving Bonferroni correction). None of the other explicit ratings were significantly associated with the AUDIT. With respect to implicit measures of motivation to drink alcohol, the AUDIT correlated positively with Pc choices of alcoholic drink CS during alcohol administration ($\rho(48) = 0.29$, $p = 0.05$; not surviving Bonferroni correction; see Table1).

Alcohol effects on explicit memory of the Pc stimuli

Alcohol administration did not significantly affect recall of alcoholic drink-CS or money gain-CS (+1€, +2€). All other CS-US combinations, namely −2€ ($p = 0.02$), −1€ ($p = 0.008$), 0€ ($p = 0.03$) and water ($p = 0.002$), were recalled significantly worse during alcohol compared to placebo infusion (only the difference in water CS survived Bonferroni correction for multiple testing).

Table 1. Correlations between sample characteristics, explicit measures (rows) and implicit measures (columns) of motivation to drink alcohol, measured during A: placebo or B: alcohol administration; as well as C: their difference.

N = 51	Pc alcoholic drink CS choices	*p*	AAT alcohol-approach bias	*p*
	A: placebo infusion			
smoking	0.20°	0.16	0.11°	0.46
age first drink	−0.24°	0.09	−0.00°	0.99
AUDIT (*N* = 50)	0.01°	0.93	0.13°	0.36
	25 min		120 min	
alcohol desire	0.11°	0.42	−0.09°	0.52
well-being	−0.01°	0.96	−0.03°	0.83
thirst (*N* = 44)	0.09°	0.55	−0.09°	0.59
stimulation	0.18°	0.20	−0.04°	0.80
sedation	−0.10°	0.48	−0.09°	0.53
negative effects	−0.18°	0.22	−0.03°	0.83
drinks number	0.00°	0.98	0.00°	0.97
feeling drunk	−0.15°	0.28	−0.05°	0.75
	B: alcohol infusion			
smoking	−0.10°	0.48	−0.22°	0.12
age first drink	−0.07°	0.63	0.07°	0.64
AUDIT (*N* = 50)	0.28°	0.05	0.05°	0.71
	25 min		120 min	
alcohol desire	0.10°	0.50	−0.05°	0.74
well-being	0.03°	0.85	−0.07°	0.62
thirst (*N* = 44)	−0.05°	0.77	0.20°	0.19
stimulation	0.04	0.80	0.04	0.79
sedation	0.08	0.59	0.11	0.43
negative effects	−0.12°	0.40	0.15°	0.30
drinks number	0.02	0.92	0.26°	0.07
feeling drunk	−0.12	0.42	0.32°	0.02
	C: difference alcohol – placebo			
difference in:	25 min		120 min	
alcohol desire	−0.06°	0.68	−0.02°	0.89
well-being	0.02°	0.90	−0.29	0.04
thirst (*N* = 44)	0.09°	0.56	0.25°	0.10
stimulation	0.12	0.39	−0.03	0.81
sedation	−0.02	0.87	0.13	0.37
negative effects	−0.13°	0.37	0.11°	0.46
drinks number	0.15°	0.31	0.15°	0.28
feeling drunk	−0.05	0.73	0.11	0.44

Note. *N* = Number; AUDIT = Alcohol Use Disorders Identification Test; Pc = Pavlovian conditioning task, AAT = Approach-Avoidance Task; °Spearman's rank correlation due to non-normal distribution.

Alcohol effects on general decision-making

In the lexical decision task, there were no significant effects of treatment on accuracies, only words were better recognized than non-words (Estimate = 0.8, $z = -3.2$, $p = 0.0013$). Regarding RTs, participants responded significantly slower during alcohol than placebo infusion (Estimate = 42.1, $SD = 18.5$, $t = 2.3$) and words were accepted faster than non-words were rejected (Estimate = 106.5, $SD = 12.5$, $t = 8.5$).

Taken together, during alcohol compared to placebo infusion participants responded equally accurately, but more slowly.

Discussion

We aimed to examine the links between explicit and implicit motivation to drink alcohol. In line with our hypothesis, we found that alcohol administration increased explicit motivation to drink alcohol, measured by ratings of alcohol desire, thirst, well-being and stimulation. With respect to implicit motivation to drink alcohol, we found opposite effects, i.e., choices of alcoholic drink-CS were decreased during alcohol compared to placebo administration, whereas there was no alcohol effect on the alcohol-approach bias. Moreover, explicit and implicit measures of motivation were not associated with each other, but correlated with real-life drinking problems.

Explicit motivation to drink alcohol

In line with previous studies (Amlung et al., 2015; Christiansen et al., 2013; de Wit, 1996), our results support that both alcohol administration and the expectancy to receive alcohol increase participants' explicit motivation to drink alcohol, because desire for alcohol significantly increased in both treatment conditions, but more strongly so during alcohol infusion. The same effects were found for subjective ratings of thirst, further suggesting that alcohol administration promoted explicit approach motivation to alcoholic drinks. Phillips et al. (1985) attributed increased thirst during saline infusion to increases in plasma sodium, as well as 'dry' and 'sticky' mouth sensations. The isotonic saline itself may therefore have increased thirst in our placebo session, whereas adding ethanol led to an extra boost in thirst owing to diuretic effects of alcohol (Shirreffs and Maughan, 1997). To control for thirst, future alcohol administration studies should therefore provide non-alcoholic beverages in all experimental conditions.

We also measured subjective alcohol effects, such as feelings of stimulation and sedation. Numerous studies confirmed alcohol-induced increases in both stimulation and sedation (Hendler et al., 2013), which is also what we found. Typically, stimulation increases at the ascending limb of the BAC curve, whereas sedation increases at the descending limb (Hendler et al., 2013). In our study, sedation and negative alcohol effects were rising until the end of the experiment, whereas aBAC was kept constant and neither rising nor falling. Moreover, negative effects increased more strongly during alcohol compared to placebo infusion, suggesting that shifts in subjective alcohol effects do not only occur at the descending limb, but also after a certain time of alcohol exposure. In line with that concept, Morzorati et al. (2002) observed that subjects' perceptions of sedation showed acute sensitization over time during an alcohol clamp at 60 mg%, whereas perceptions of stimulation showed acute tolerance.

Our findings of alcohol-induced increases in positive and negative alcohol effects raises the question which of these aspects prevailed, because an increase in explicit motivation requires that positive effects outweighed negative effects. Since general well-being was rated higher during alcohol compared to placebo infusion, we think that alcohol infusion mainly promoted positive mood and therefore explicit motivation to drink alcohol, which is in line with previous findings of Duka and Townshend (2004).

Implicit motivation to drink alcohol

Contrary to what we expected, moderate alcohol intoxication reduced preferences for alcoholic drink-CS for the benefit of neutral, −1€, and 1€ CS in the Pc task. This result cannot be explained by worse learning of alcoholic drink-CS, because we found no differences in explicit knowledge of alcoholic drink-CS and previous studies reported no effects of alcohol on implicit learning (Ray et al., 2004; Tracy and Bates, 1999). Since alcoholic drink-CS were chosen less often during alcohol infusion, it seems as if alcohol reduced the incentive valence of our alcoholic drink cues. This alcohol-induced devaluation of alcoholic drink cues might be attributed to satiation, as suggested by Duka and Townshend (2004) and Roberts and Fillmore (2015). Thus, alcohol-induced satiation might have led to a devaluation of alcoholic drink cues during second-order Pavlovian conditioning, which later on decreased adolescents' preference for alcoholic drink-CS. To determine if the lower preference for alcoholic drink-CS reflected satiation or an inability of our Pc paradigm to detect increased incentive motivation to drink alcohol, future studies using a dose-response curve are needed.

Although alcohol infusion reduced implicit motivation to drink alcohol in the Pc task, we found no such differences in the AAT. We therefore replicated the finding of Korucuoglu et al. (2014), who attributed their null effect to a relatively small sample size and the fact that they examined healthy subjects. Our sample was twice as big, but also healthy and even younger. Thus, lack of drinking experience and drinking problems might explain why the alcohol-approach bias was low in general and therefore barely susceptible to acute alcohol administration.

Besides that, we can think of three possibilities to explain the AAT null finding. First, the AAT measures Pavlovian or habitual stimulus–response behavior, whereas the Pc task measures goal-directed behavior. Since habitual actions rely on the subjective valence of well-known cues, which invariably trigger the same responses, they are thought to be largely independent of current states such as acute alcohol intoxication (Daw and O'Doherty, 2014). Assuming this to be true, Pavlovian cues in the AAT might have consistently promoted the same approach bias in both treatment conditions. If, on the other hand, the Pc task measures goal-directed behavior, choices would be based on current reward-expectancies (Daw and O'Doherty, 2014). Consequently, alcohol infusion might have reduced expectancies of rewarding alcohol effects which in turn reduced choices of alcoholic drink-CS. Indeed, the AAT alcohol-approach bias and the Pc percentage of alcoholic drink-CS choices had less than 10% shared variance during alcohol infusion ($r(49) = 0.27$, $p < 0.05$), suggesting that both tasks rely on different learning systems. In line with Schoenmakers et al. (2008), we found a significant correlation between both motivational measures only in the alcohol session. To explain this finding, Schoenmakers et al. (2008) reasoned that alcohol administration increases the 'attention-grabbing' properties of substance-related cues, which then evoke more automatic responses.

Money cues strongly affected choice behavior in the Pc task and participants preferred the two neutral CS over the alcoholic drink-CS during alcohol infusion, whereas the opposite was found during placebo infusion. Hence, Pavlovian cues were not perceived as neutral. A second potential explanation for the lack of an alcohol effect on the AAT is therefore that participants

learned the instrumental behavior across trials, so that they could neither be influenced by cues nor by alcohol administration. To exclude such an unspecific training effect, we reanalyzed our data using only the first 100 of 200 trials. Results remained unchanged. Moreover, neutral cues had a lower approach bias than alcoholic drink cues, suggesting that the cues actually did have an impact on behavior.

A study by Roberts and Fillmore (2015) offers a third explanation. Using a visual-probe task, they found that the attentional bias towards alcohol-related cues was reduced at the ascending limb of the BAC curve, but returned back to baseline later, at the descending limb. The authors presumed an alcohol-induced temporary reduction in motivation to drink which diminishes over time. Therefore, the order of our paradigms might have influenced our findings, and by reordering paradigms, we may have found an alcohol effect on the AAT rather than on the Pc task. Consequently, clamping aBAC at a constant level might have led to a temporary reduction in expected rewarding alcohol effects, which in turn reduced approach behavior in the Pc task as previously discussed by Watson et al. (2012). Later on, subjects' implicit motivation to drink alcohol may have gone back to baseline, which caused the null effect on the AAT. In other words, a person who is feeling well after a few drinks does not necessarily have rewarding outcome expectancies when it comes to more alcohol intake. Based on their prior drinking experience, the person might even expect to feel worse after more alcohol intake. Although our participants might have expected to feel less well after more alcohol intake at the beginning of our experiment, we did not measure alcohol expectancy and can therefore only speculate whether reward expectancies for consuming alcoholic drinks changed over time.

Interrelation between explicit and implicit motivation to drink

We found no interrelation between explicit and implicit motivation to drink alcohol, which is in line with previous results (Roberts and Fillmore, 2015; Schoenmakers et al., 2008) and suggests that both aspects of motivation are independent from each other, not only in male adolescents, but also in adults and women. Schoenmakers et al. (2008) concluded that the incentive-motivational properties of alcohol-related stimuli may motivate goal-directed behavior in the absence of conscious awareness of 'wanting'. Based on our results, we suggest that the incentive-motivational properties of alcohol-related stimuli may motivate goal-directed behavior independent of actual 'wanting'. One possible explanation for the missing link between explicit and implicit measures of motivation to drink alcohol is that both aspects of motivation are weakly correlated in real life, which is why our sample size was too small to detect significant effects. In fact, there were several correlations between 0.1 and 0.3 in Table 1, indicating small effect sizes according to Cohen (1988).

Alternatively, our data suggest that actual 'wanting' increased independently of the implicit reactivity towards alcoholic drink stimuli. Hence, adolescents' ratings of alcohol desire might have been based on masculine gender roles or previous pleasant drinking experiences, especially during alcohol infusion. Alcoholic drink cues, on the other side, might have activated the current incentive value of these beverages. As highlighted above, our finding that alcoholic drink-CS were chosen less often during alcohol infusion indicates that alcohol reduced their incentive value, possibly owing to satiation or lower rewarding outcome expectancies at an early state of alcohol intoxication. An interesting research question would therefore be, whether subjects are explicitly aware of those reductions in subjective valence by asking them how much alcohol desire the alcohol-related cues evoke.

Schoenmakers and Wiers (2010) pointed out that the satiation explanation contradicts their finding of dose-dependent increases in craving, and our participants also reported higher alcohol desire during alcohol compared to placebo infusion. Nevertheless, we did not directly ask for satiation, defined as 'satisfaction one feels with respect to the drug' (Cousijn et al., 2013), and can therefore only speculate whether satiation increased somehow independent from alcohol desire.

Alternatively, Schoenmakers and Wiers (2010) proposed that the alcohol-induced reduction in alcohol-approach bias might be more closely related to sedation rather than craving. Our results, however, do not support this assumption, because we did not observe a correlation between explicit sedation and approach behavior to alcoholic drink stimuli, neither in the Pc task nor the AAT.

Whereas the drift diffusion model (Trimmer et al., 2013) postulates that current mood states directly bias approach and avoidance actions (or implicit motivation), Hofmann et al. (2008) proposed that mood states moderate the relationship between impulsive approach and avoidance reactions (or implicit motivation) and health-related behavior, such as alcohol consumption. Therefore, subjective alcohol effects might not directly affect implicit motivational measures but moderate their relationship with real-life drinking behavior. So far, the moderating effect of mood was found on eating behavior (Holland et al., 2012) and future research needs to show whether this theoretical framework also applies to drinking behavior.

Interrelation between AUDIT and motivation to drink alcohol

Examining the links between real-life drinking problems and our measures of motivation to drink alcohol, we found that AUDIT scores were significantly and positively related to both explicit alcohol desire and implicit choices of alcoholic drink-CS. With respect to explicit motivation to drink alcohol, our findings imply that adolescents reporting high alcohol desire are at risk to develop alcohol use disorders. In line with this concept, Fazzino et al. (2013) found a bidirectional relationship between craving and alcohol intake in heavy drinkers, and King et al. (2011) reported that alcohol-induced increases in alcohol wanting predict more real-life drinking in heavy drinkers. Regarding implicit motivation to drink, our study revealed that adolescents displaying pronounced approach behavior to alcoholic drink stimuli when being intoxicated may also be at increased risk for alcohol use disorders. The latter is a novel finding which, to the best of our knowledge, has never been reported before.

The AUDIT correlations with explicit alcohol desire during alcohol and placebo infusion and their selective association (albeit weaker) with alcoholic drink-CS selection during alcohol infusion seem to provide genuinely new information about 'priming' drinking motivation in young drinkers. That is, alcohol administration might augment the incentive value of alcohol and

alcohol-related cues as a function of alcohol problems in young drinkers, i.e., rather than satiating, hazardous drinkers want alcohol more, and responses to alcohol-related Pavlovian cues may mark the departure from healthy social drinking to problematic drinking. Alternatively, the association between AUDIT and alcoholic drink-CS selection in the Pc task may indicate a pre-existing trait factor (e.g., susceptibility to Pavlovian reward conditioning) that puts problem drinkers at risk. Either way, the AUDIT data seem to be important for explaining explicit and implicit motivation to drink alcohol in young drinkers and suggest that interventions targeting high risk individuals may be more effective than global prevention strategies.

Besides that, our results imply that interventions might as well target adolescents after alcohol intake. While cognitive interventions could address adolescents' explicit alcohol desire, a web-based combination of attention control training and approach-bias re-training might be used to change adolescents' implicit action tendencies, as suggested by Wiers et al. (2015).

With respect to clinical interventions, our observation that an association between alcohol problems and approach behavior to alcoholic drink stimuli specifically occurs when subjects are intoxicated implies that the re-training method of Wiers et al. (2011) might be even more effective in patients who are still drinking, i.e., before detoxification. This is an intriguing thought because up to now, there are only a few concepts how to help actively drinking alcoholics who did not yet develop sufficient motivation to change their behavior.

Limitations

Since we tested male adolescents using intravenous alcohol administration, a modified version of the AAT, and a new Pc task, the comparability of our results with previous results might be limited. However, we found no interrelation between explicit and implicit motivation to drink alcohol, which is in line with previous results (Roberts and Fillmore, 2015; Schoenmakers et al., 2008) and suggests that both aspects of motivation are independent from each other, across different ages, sexes, modes of administration and task features. Limitations of our study arise from the facts that intravenous alcohol clamping is an extraordinary experience to the subjects, creating novel interoceptive cues, and that we infused alcohol much faster than most subjects drink it. Both issues raise the possibility that we elicited more pronounced dopamine release which in turn would question the generalizability of our results to real-life drinking. Human PET studies, however, do not appear to support this concern, since alcohol-induced dopamine release during intravenous infusion following the same dynamics as reported here (Pfeifer et al., 2016) was rather lower than higher compared to oral alcohol administration (Boileau et al., 2003). Nevertheless, one might argue that our alcohol infusion method does not necessarily represent real-life drinking, where aBACs are usually not kept constant, but permanently rising or falling. An oral alcohol administration study producing the same alcohol clamp would therefore be an important follow-up study to validate our results. Finally, it is unlikely that our results reflect impaired decision making abilities, because alcohol had no effects on lexical decision task accuracy. Other placebo-controlled studies using different variants of the lexical decision task also reported no differences in accuracies, but a general slowing during alcohol, with lower impairments for men than women (Haut et al., 1989; Marinkovic et al., 2014; Maylor and Rabbitt, 1993).

Conclusions

Our results suggest that moderate alcohol intoxication increases explicit motivation, but decreases implicit motivation to drink alcohol. Future studies are needed to determine, whether this combination of results is caused by satiation with respect to alcoholic drink cues, the fact that the Pc task measured goal-directed behavior and the AAT habitual behavior, a temporary reduction in rewarding outcome expectancies at an early state of alcohol intoxication, or the rapid ascending limb phase. Another valuable follow-up study would be to replicate the exact same procedure with a conventional drinking paradigm. Moreover, non-alcoholic beverages should be offered in future alcohol infusion experiments to appease thirst as a potentially confounding factor. In our study, explicit and implicit motivation to drink alcohol were not connected with each other, but correlated positively with AUDIT scores, especially during alcohol administration. These findings suggest that both self-reported motivation to drink and implicit approach tendencies might independently contribute to adolescents' actual alcohol intake. Preventive interventions should therefore target adolescents after alcohol intake and aim to reduce their explicit alcohol desire and implicit cue-driven behavior.

Acknowledgements

We thank Lucia Hämmerl and Luise Olbricht for their outstanding assistance in recruitment, data acquisition, digitization and quality checking. Further, we thank Luci Scholl for recruitment, Daniel J. Schad for his extraordinary helpful comments on the statistical analyses and Michael Schmidt for his essential technical support.

Declaration of conflicting interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: USZ declares that, over the past three years, he has received money from the Sächsische Landesärztekammer, Gewerkschaft für Erziehung und Wissenschaft, Parkkrankenhaus Leipzig, ABW Wissenschaftsverlag, Servier, Janssen and Lundbeck. The authors EJ, AHJ, CEW, CS, MG, NB, SKP and MNS declare that there is no conflict of interest.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the German Research Foundation (Deutsche Forschungsgemeinschaft), DFG, FOR 1617 [grant numbers ZI 1119/4-1, ZI 1119/3-1, ZI 1119/3-2, SM 80/7-1, SM 80/7-2, WI709/10-1, WI709/10-2] and Bundesministerium für Bildung und Forschung, BMBF [grant number 01ZX1311H].

References

Amlung M, McCarty KN, Morris DH, et al. (2015) Increased behavioral economic demand and craving for alcohol following a laboratory alcohol challenge. *Addiction* 110: 1421–1428.

Babor TF, Higgins-Biddle JC, Saunders JB, et al. (2001) *AUDIT The Alcohol Use Disorders Identification Test Guidelines for Use in Primary Care*, 2nd ed. Geneva: World Health Organization, Department of Mental Health and Substance Dependence.

Bargh JA (1994) The four horsemen of automaticity: Awareness, intention, efficiency, and control in social cognition. In: Wyer RS and Srull TK (eds) *Handbook of Social Cognition*, 2nd ed. Hillsdale: Erlbaum, pp.1–40.

Barr DJ, Levy R, Scheepers C, et al. (2013) Random effects structure for confirmatory hypothesis testing: Keep it maximal. *J Mem Lang* 68: 255–278.

Boileau I, Assaad J-M, Pihl RO, et al. (2003) Alcohol promotes dopamine release in the human nucleus accumbens. *Synapse* 49: 226–231.

Bradizza CM, Stasiewicz PR and Maisto SA (1994) A conditioning reinterpretation of cognitive events in alcohol and drug cue exposure. *J Behav Ther Exp Psychiatry* 25: 15–22.

Christiansen P, Rose AK, Cole JC, et al. (2013) A comparison of the anticipated and pharmacological effects of alcohol on cognitive bias, executive function, craving and ad-lib drinking. *J Psychopharmacol* 27: 84–92.

Cohen J (1988) *Statistical Power Analysis for the Behavioral Sciences*, 2nd ed. Hillsdale: Erlbaum.

Cousijn J, Snoek RWM and Wiers RW (2013) Cannabis intoxication inhibits avoidance action tendencies: A field study in the Amsterdam coffee shops. *Psychopharmacology* 229: 167–176.

Daw ND and O'Doherty JP (2014) *Multiple Systems for Value Learning*, 2nd ed. In: Glimcher PW and Fehr E (eds), *Neuroeconomics: Decision Making and the Brain*. San Diego: Academic Press, pp.393–410.

de Wit H (1996) Priming effects with drugs and other reinforcers. *Exper Clin Psychopharmacol* 4: 5–10.

Delgado MR, Jou RL and Phelps EA (2011) Neural systems underlying aversive conditioning in humans with primary and secondary reinforcers. *Front Neurosci* 5: Article 71.

Duka T and Townshend JM (2004) The priming effect of alcohol preload on attentional bias to alcohol-related stimuli. *Psychopharmacology* 176: 353–361.

Ernst LH, Plichta MM, Dresler T, et al. (2014) Prefrontal correlates of approach preferences for alcohol stimuli in alcohol dependence. *Addict Biol* 19: 497–508.

Fazzino TL, Harder VS, Rose GL, et al. (2013) A daily process examination of the bidirectional relationship between craving and alcohol consumption as measured via interactive voice response. *Alcohol Clin Exp Res* 37: 2161–2167.

Field M, Munafò MR and Franken IHA (2009) A meta-analytic investigation of the relationship between attentional bias and subjective craving in substance abuse. *Psychol Bull* 135: 589–607.

Garbusow M, Friedel E, Sebold M, et al. (2013) Wege in die Abhängigkeit. *Sucht* 59: 187–199.

Garbusow M, Schad DJ, Sommer C, et al. (2014) Pavlovian-to-instrumental transfer in alcohol dependence: A pilot study. *Neuropsychobiology* 70: 111–121.

Haut JS, Beckwith BE, Petros TV, et al. (1989) Gender differences in retrieval from long-term memory following acute intoxication with ethanol. *Physiol Behav* 45: 1161–1165.

Hendler RA, Ramchandani VA, Gilman J, et al. (2013) Stimulant and sedative effects of alcohol. *Curr Top Behav Neurosci* 13: 489–509.

Hofmann W, Friese M and Wiers RW (2008) Impulsive versus reflective influences on health behavior: A theoretical framework and empirical review. *Health Psychol Rev* 2: 111–137.

Holland RW, De Vries M, Hermsen B, et al. (2012) Mood and the attitude–behavior link the happy act on impulse, the sad think twice. *Soc Psychol Person Sci* 3: 356–364.

Jacobi F, Mack S, Gerschler A, et al. (2013) The design and methods of the mental health module in the German Health interview and Examination Survey for Adults (DEGS1-MH). *Int J Methods Psychiatr Res* 22: 83–99.

Jaeger TF (2008) Categorical data analysis: Away from ANOVAs (transformation or not) and towards logit mixed models. *J Mem Lang* 59: 434–446.

King AC, de Wit H, McNamara PJ, et al. (2011) Rewarding, stimulant, and sedative alcohol responses and relationship to future binge drinking. *Arch Gen Psychiatry* 68: 389–399.

Kliegl R, Masson MEJ and Richter EM (2010) A linear mixed model analysis of masked repetition priming. *Vis Cogn* 18: 655–681.

Korucuoglu O, Gladwin TE and Wiers RW (2014) Preparing to approach or avoid alcohol: EEG correlates, and acute alcohol effects. *Neurosci Lett* 559: 199–204.

Lindberg L, Brauer S, Wollmer P, et al. (2007) Breath alcohol concentration determined with a new analyzer using free exhalation predicts almost precisely the arterial blood alcohol concentration. *Forensic Sci Int* 168: 200–207.

Magezi DA (2015) Linear mixed-effects models for within-participant psychology experiments: an introductory tutorial and free, graphical user interface (LMMgui). *Front Psychol* (6): Article 2.

Marinkovic K, Rosen BQ, Cox B, et al. (2014) Spatio-temporal processing of words and nonwords: Hemispheric laterality and acute alcohol intoxication. *Brain Res* 1558: 18–32.

Martin Braunstein L, Kuerbis A, Ochsner K, et al. (2016) Implicit alcohol approach and avoidance tendencies predict future drinking in problem drinkers. *Alcohol Clin Exp Res* 40: 1945–1952.

Maylor EA and Rabbitt PMA (1993) Alcohol, reaction time and memory: A meta-analysis. *Br J Psychol* 84: 301–317.

Morzorati SL, Ramchandani VA, Flury L, et al. (2002) Self-reported subjective perception of intoxication reflects family history of alcoholism when breath alcohol levels are constant. *Alcohol Clin Exp Res* 26: 1299–1306.

O'Connor S, Morzorati S, Christian J, et al. (1998) Clamping breath alcohol concentration reduces experimental variance: application to the study of acute tolerance to alcohol and alcohol elimination rate. *Alcohol Clin Exp Res* 22: 202–210.

Ostafin BD, Marlatt GA and Greenwald AG (2008) Drinking without thinking: An implicit measure of alcohol motivation predicts failure to control alcohol use. *Behav Res Ther* 46: 1210–1219.

Peli E (1990) Contrast in complex images. *J Opt Soc Am A* 7: 2032–2040.

Pfeifer P, Tüscher O, Buchholz HG, et al. (2016) Acute effect of intravenously applied alcohol in the human striatal and extrastriatal D2 /D3 dopamine system. *Addict Biol*. DOI: 10.1111/adb.12424.

Phillips PA, Rolls BJ, Ledingham JG, et al. (1985) Osmotic thirst and vasopressin release in humans: A double-blind crossover study. *Am J Physiol* 248: R645–R650.

Plawecki MH, Zimmermann US, Vitvitskyi V, et al. (2012) Alcohol exposure rate control through physiologically based pharmacokinetic modeling. *Alcohol Clin Exp Res* 36: 1042–1049.

R Core Team (2015) *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing. Available at: https://www.R-project.org/.

Ramchandani VA, Bolane J, Li T-K, et al. (1999) A Physiologically-based pharmacokinetic (PBPK) model for alcohol facilitates rapid BrAC clamping. *Alcohol Clin Exp Res* 23: 617–623.

Ratcliff R, Thapar A, Gomez P and McKoon G (2004) A Diffusion model analysis of the effects of aging in the lexical-decision Task. *Psychol Aging* 19: 278–289.

Ray S, Bates ME and Ely BM (2004) Alcohol's dissociation of implicit and explicit memory processes: Implications of a parallel distributed processing model of semantic priming. *Exp Clin Psychopharmacol* 12: 118–125.

Roberts W and Fillmore MT (2015) Attentional bias to alcohol-related stimuli as an indicator of changes in motivation to drink. *Psychol Addict Behav* 29: 63–70.

Schoenmakers T and Wiers R (2010) Craving and attentional bias respond differently to alcohol priming: A field study in the pub. *Eur Addict Res* 16: 9–16.

Schoenmakers TM, Wiers RW and Field M (2008) Effects of a low dose of alcohol on cognitive biases and craving in heavy drinkers. *Psychopharmacology* 197: 169–178.

Shirreffs SM and Maughan RJ (1997) Restoration of fluid balance after exercise-induced dehydration: Effects of alcohol consumption. *J Appl Physiol* 83: 1152–1158.

Stacy AW and Wiers RW (2010) Implicit cognition and addiction: A tool for explaining paradoxical behavior. *Annu Rev Clin Psychol* 6: 551–575.

Tracy JI and Bates ME (1999) The selective effects of alcohol on automatic and effortful memory processes. *Neuropsychology* 13: 282–290.

Trimmer PC, Paul ES, Mendl MT, et al. (2013) On the evolution and optimality of mood states. *Behav Sci* 3: 501–521.

Watson P, De Wit S, Hommel B, et al. (2012) Motivational mechanisms and outcome expectancies underlying the approach bias toward addictive substances. *Front Psychol* 3: 440.

Wiers CE, Gladwin TE, Ludwig VU, et al. (2016) Comparing three cognitive biases for alcohol cues in alcohol dependence. *Alcohol*.

Wiers CE, Kühn S, Javadi AH, et al. (2013) Automatic approach bias towards smoking cues is present in smokers but not in ex-smokers. *Psychopharmacology* 229: 187–197.

Wiers CE, Stelzel C, Park SQ, et al. (2014) Neural correlates of alcohol-approach bias in alcohol addiction: The spirit is willing but the flesh is weak for spirits. *Neuropsychopharmacology* 39: 688–697.

Wiers RW, Eberl C, Rinck M, et al. (2011) Retraining automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. *Psychol Sci* 22: 490–497.

Wiers RW, Houben K, Fadardi JS, et al. (2015) Alcohol cognitive bias modification training for problem drinkers over the web. *Addict Behav* 40: 21–26.

Wiers RW, Rinck M, Dictus M, et al. (2009) Relatively strong automatic appetitive action-tendencies in male carriers of the OPRM1 G-allele. *Genes, Brain Behav* 8: 101–106.

Wittchen H-U and Pfister H (1997) *DIA-X-Interviews: Manual für Screening-Verfahren und Interview; Interviewheft Längsschnittuntersuchung (DIA-X-Lifetime); Ergänzungsheft (DIA-X-Lifetime); Interviewheft Querschnittuntersuchung (DIA-X-12 Monate); Ergänzungsheft (DIA-X-12 Monate); PC-Programm zur Durchführung des Interviews (Längs-Und Querschnittuntersuchung); Auswertungsprogramm*. Frankfurt: Swets & Zeitlinger.