Original Article

Drunk decisions: Alcohol shifts choice from habitual towards goal-directed control in adolescent intermediate-risk drinkers

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Elisabeth Obst[1*], Daniel J Schad[2,3*], Quentin JM Huys[4,5,6], Miriam Sebold[2,3], Stephan Nebe[1], Christian Sommer[1], Michael N Smolka[1] and Ulrich S Zimmermann[1]

Abstract

Background: Studies in humans and animals suggest a shift from goal-directed to habitual decision-making in addiction. We therefore tested whether acute alcohol administration reduces goal-directed and promotes habitual decision-making, and whether these effects are moderated by self-reported drinking problems.

Methods: Fifty-three socially drinking males completed the two-step task in a randomised crossover design while receiving an intravenous infusion of ethanol (blood alcohol level=80 mg%), or placebo. To minimise potential bias by long-standing heavy drinking and subsequent neuropsychological impairment, we tested 18- to 19-year-old adolescents.

Results: Alcohol administration consistently reduced habitual, model-free decisions, while its effects on goal-directed, model-based behaviour varied as a function of drinking problems measured with the Alcohol Use Disorders Identification Test. While adolescents with low risk for drinking problems (scoring <8) exhibited an alcohol-induced numerical reduction in goal-directed choices, intermediate-risk drinkers showed a shift away from habitual towards goal-directed decision-making, such that alcohol possibly even improved their performance.

Conclusions: We assume that alcohol disrupted basic cognitive functions underlying habitual and goal-directed decisions in low-risk drinkers, thereby enhancing hasty choices. Further, we speculate that intermediate-risk drinkers benefited from alcohol as a negative reinforcer that reduced unpleasant emotional states, possibly displaying a novel risk factor for drinking in adolescence.

Keywords

Computer-assisted Alcohol Infusion System, habitual learning, model-free and model-based decision-making, two-stage Markov decision task, subjective response to ethanol, drinking problems, real-life drinking behaviour

Decision-making has been shown to rely on at least two neurobiologically and behaviourally distinct systems: A flexible goal-directed system, which helps choosing actions prospectively based on anticipated action-outcome contingencies, and a rather inflexible, but fast, habitual system that is based on previously learned stimulus-response contingencies (Daw et al., 2005, 2011; Daw and O'Doherty, 2014; Dickinson and Balleine, 2010; Dolan and Dayan, 2013; Huys et al., 2012). Both systems share commonalities with dual-process models of substance use proposing that explicit and implicit processes guide drinking behaviour (Ostafin et al., 2008; Stacy and Wiers, 2010). However, 'explicit' here often refers to linguistic reasoning, which is why it is difficult to use dual-process models of substance use to explain animal behaviour (Daw and O'Doherty, 2014). On a computational level, the goal-directed and habitual systems have been suggested to rely on model-based and model-free reinforcement learning, respectively (Dolan and Dayan, 2013; Huys et al., 2014; Rangel et al., 2008; Redish et al., 2008). Goal-directed, model-based decisions are cognitively demanding, because they depend on the anticipation of possible future states and consequences of the own behaviour (Daw et al., 2005; Dolan and Dayan, 2013; Huys et al., 2012). Faced with the choice of having a drink before driving home by car, for example, the goal-directed system would be sensitive to local driving laws, while the habitual, model-free system would be driven by past enjoyments of drinking. In the present study, both systems were operationalised using the two-step task, in which a choice at a first task-stage (step 1) induced a common (or rare) transition to one of two second-stage states, where a second choice resulted in a win of money or no win. In this task, control by the habitual, model-free system predicts that step 1 choices are repeated in the next trial if they were followed by a win, irrespective of transition type, whereas the goal-directed, model-based system predicts that step 1 choices are

[1]Department of Psychiatry and Psychotherapy, Technische Universität Dresden, Germany
[2]Department of Psychiatry and Psychotherapy, Charité Universitätsmedizin Berlin, Germany
[3]Social and Preventive Medicine, University of Potsdam, Germany
[4]Institute of Biomedical Engineering, University of Zürich, Switzerland
[5]Swiss Federal Institute of Technology, Zürich, Switzerland
[6]Department of Psychiatry, Psychosomatics, and Psychotherapy, University of Zürich, Switzerland

*The authors contributed equally to this work.

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

repeated only if a common transition was followed by a win or if a rare transition was followed by no win.

The extent to which individuals rely on goal-directed and habitual decision-making varies substantially, and the factors determining the tradeoff have attracted great interest. Goal-directed, model-based decisions, for example, are promoted by high working memory capacity (Otto et al., 2013) and fast processing speed (Schad et al., 2014), but they are impaired in disorders involving compulsive behaviour, such as obsessive-compulsive disorder, binge eating and addiction (Gillan et al., 2016; Voon et al., 2015a). Chronic alcohol abuse is known to have toxic effects on the frontal cortex (Guillot et al., 2010), which is thought to be important for goal-directed decision-making. In addition, alcohol-dependent patients were found to act more habitually than non-dependent controls by showing a greater bias to approach alcohol cues (Wiers et al., 2014) and being less able to adapt responses after errors in stop signal tasks (Lawrence et al., 2009). A pilot study of our research consortium also suggested that there is poor engagement of goal-directed decisions after losses in alcohol-dependent patients compared to controls (Sebold et al., 2014). Further studies (Gillan et al., 2016; McKim et al., 2016; Vanes et al., 2014) provided evidence for a similar shift in addiction, while others failed to find differences between controls and alcohol-dependent or obsessive-compulsive patients (Sebold et al., 2017; Voon et al., 2015a, 2015b).

None of the above mentioned studies examined acute alcohol effects. Since chronic effects are thought to result from the accumulation of acute effects, we tested whether acute alcohol administration would result in a shift from goal-directed to habitual decision-making. Indeed, rats showed aversion-resistant lever pressing for alcohol after three to four months of voluntary, intermittent alcohol consumption (Hopf et al., 2010). With respect to healthy, socially drinking humans, low alcohol doses were found to increase habitual responses for chocolate in the extinction phase (Hogarth et al., 2012) and to impair planning and adaptive thinking in a virtual reality task (Montgomery et al., 2011). Low and high alcohol doses impaired the detection of performance errors in the anterior cingulate cortex (Ridderinkhof et al., 2002). Further, moderate alcohol doses reduced the ability to adapt responses to changing prospective rewards (George et al., 2005), impaired instrumental learning from punishment (Loeber and Duka, 2009), decreased training effects on set-shifting tasks (Korucuoglu et al., 2017), impaired stop signal and go/no-go performance (Gan et al., 2014; Ramaekers and Kuypers, 2006), disrupted working memory functions (Saults et al., 2007) and promoted self-reported trait impulsivity (McCarthy et al., 2012). Finally, moderate and high alcohol doses increased perseverative errors in set switching tasks (Guillot et al., 2010). However, whether acute alcohol administration actually promotes habits or merely impairs goal-directed decisions in humans is unknown.

Another important question is whether or not drinking problems moderate the impact of alcohol on decision-making. So far, there has only been one field study that investigated low-risk, hazardous and harmful drinkers with blood alcohol levels ranging between 0 and 150 mg% (Lyvers and Tobias-Webb, 2010). While perseverative errors increased with alcohol dose, the authors observed no effect of self-reported drinking problems on these errors. However, they did not test for an interaction, although drinking problems might mark pre-existing decision-making impairments, which would show up only in sober subjects. In line with that concept, Malone et al. (2014) found that drinking problems of adolescent twins were associated with poorer performance in the Iowa Gambling Task and a reduced volume of the left lateral orbital-frontal cortex. Besides that, drinking problems might reflect an increased vulnerability towards ethanol, as some people are less able to inhibit prepotent, habitual responses after alcohol intake (Quinn and Fromme, 2016). Such an alcohol-induced disinhibition has been identified as potential risk factor for drinking in 18–19-year-olds (Gan et al., 2014) and was linked to greater experiences of stimulating alcohol effects (Quinn and Fromme, 2016), another risk factor for drinking (King et al., 2016). Finally, drinking problems might as well reflect a lower vulnerability towards ethanol, as higher real-life alcohol intake has been associated with lower sensitivity towards the functional, metabolic and reinforcing effects of alcohol (Gilpin and Koob, 2008), and a low level of response towards the effects of alcohol is a known risk factor for drinking (Quinn and Fromme, 2011; Schuckit et al., 2008).

The present study was designed to bridge the gap between research in patients and animals suggesting that chronic alcohol intake promotes habits. We examined the impact of acute alcohol administration on decision-making in the two-step task (Daw et al., 2011), which examines the relative contribution of habitual and goal-directed choices using subtle valuation shifts. In order to eliminate biological differences in alcohol pharmacokinetics and control for environmental factors, alcohol was administered intravenously (O'Connor et al., 1998; Zimmermann et al., 2013). We tested adolescents, who, owing to less life-time alcohol exposure, are less affected by neuropsychological deficits in basic decision-making than older samples. Our first hypothesis was that alcohol administration would promote habitual, model-free decisions and reduce goal-directed, model-based behaviour. Secondly, higher scores in the Alcohol Use Disorders Identification Test (AUDIT) (Babor et al., 2001) were expected to weaken the effects of ethanol on decision-making, due to lower sensitivity towards the effects of alcohol.

Methods

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

Our study was part of a bi-centric research consortium investigating Learning and Alcohol Dependence (LeAD; funded by Deutsche Forschungsgemeinschaft, Forschergruppe 1617). Adolescents were recruited by mailing invitation letters to 1100 18-year-old citizens of Dresden, whose addresses were provided by the local registration office.

All subjects had undergone another two assessment days as part of the LeAD research consortium some weeks earlier. During this part of the study, subjects had already given written informed consent, had been interviewed using the computerised Composite International Diagnostic Interview (CIDI; Jacobi et al., 2013; Wittchen and Pfister, 1997), and had completed several learning

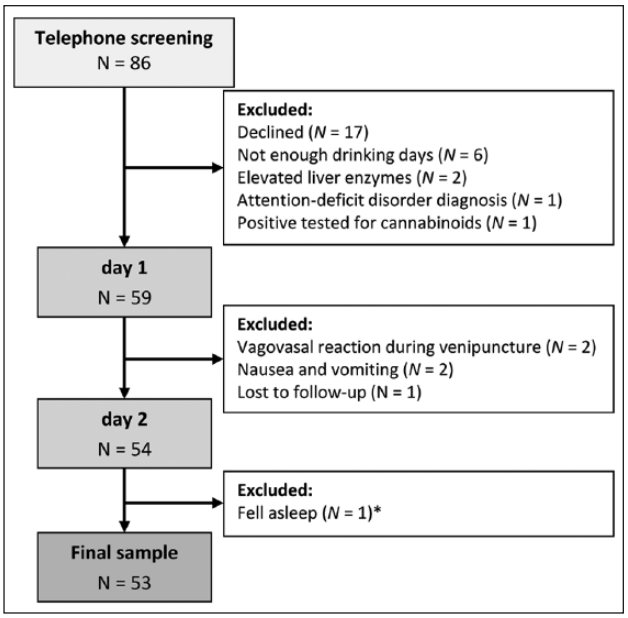

Figure 1. Recruitment flowchart. *N*=Number; *One participant fell asleep during the two-step task and missed 42 trials.

paradigms including the two-step task (Nebe et al., 2017), partly during functional magnetic resonance imaging (fMRI). Only participants of the Dresden study centre were involved in the here described procedures after completing an additional telephone screening for drinking behaviour and health problems since the fMRI session. The first infusion session was carried out 44–381 days after the fMRI session (median=94 days).

We tested 18–19-year-old native German-speaking males who reported two or more drinking days per month during the last three months. Adolescents were excluded if they had a current or past substance dependence except nicotine dependence; current or past severe major psychiatric or neurologic disorders; elevated liver enzymes indicating excessive alcohol use; a positive drug screening; current medication that could interact with alcohol; reported alcohol consumption at the test day or the day before; were left-handed.

Figure 1 displays the sample size in each recruitment step.

The final sample consisted of 53 adolescents, aged 18 (n=43) to 19 (n=10) years, who drank their first alcoholic beverages at ages 10–16 (median=14), 40% scored eight or higher in the AUDIT (mean (M)=7.7, standard deviation (SD)=4.3), suggesting risky alcohol use (Babor et al., 2001), and 21% were regular smokers. In the past year, they drank 27–207 g per occasion (M=76, SD=41) on either '1–3 days a month' (38%), '1–2 days a week' (51%) or '3–4 days a week' (11%). Table 1 displays the sample characteristics of low-risk drinkers (AUDIT<8) and intermediate-risk drinkers (AUDIT≥8). Five low-risk and seven intermediate-risk drinkers fulfilled one Diagnostic- and Statistical Manual (DSM-IV) alcohol abuse criterion (American Psychiatric Association, 2000). None fulfilled any dependence criterion.

General experimental procedure

Participants underwent two infusion sessions (day 1 and day 2), separated by 6-22 days (median=7), that involved infusion of placebo (0.9% saline) or alcohol (6.0% (v/v) ethanol in saline) in random order. Adolescents were misinformed that they would receive 'different alcohol dosages' in order to uphold alcohol-expectancy during both sessions. At 12:45, participants reported to the laboratory and provided a urine sample to screen for amphetamines, benzodiazepines, barbiturates, cannabinoids, cocaine, ecstasy, tricyclic antidepressants and opiates using a Nal von Minden Multi 12TF (Moers, Germany). A brief history of drinking behaviour and health problems covering the time since the fMRI session was obtained, and we ensured that baseline arterial blood alcohol concentration (aBAC) was zero using an Alcotest 6810 med breathalyser (Draeger Sicherheitstechnik, Lübeck, Germany). Participants sat in a comfortable arm chair facing a 32-inch video monitor at a viewing distance of 1.5 m. Here, they rated subjective alcohol effects at baseline (0 min), 25 min, and 120 min.

At 13:40, an 18G intravenous (i.v.) line was established using a cubital fossa vein of the non-dominant arm, and at 13:50, the Computer-assisted Alcohol Infusion System (CAIS) was started (O'Connor et al., 1998). aBAC was linearly increased up to the predefined target of 80 mg% within 25 min and then held stable at this level for two hours.

Once the target aBAC was reached at 14:15, participants moved to a swivel chair facing a computer monitor and completed a Pavlovian conditioning and a lexical decision task, both of which were reported in Jünger et al. (2017), followed by the two-step task. Thereafter, they completed an approach-avoidance task, which was also reported in Jünger et al. (2017). At 16:00, the i.v. line was removed, and participants were paid their task winnings. To avoid unblinding of the infusion condition, participants had to wait for two hours, while their aBAC fell below 45 mg%, before being picked up by car (e.g. paid taxicab). At the end of the second experimental day, participants were debriefed and received full compensation (100 €).

Alcohol administration methods

We used two volumetric infusion pumps (Infusomat fms, BBraun, Melsungen, Germany) for i.v. administration. Participant's age, gender, height and weight were used as parameters for the Physiologically-Based PharmacoKinetic (PBPK) model (Plawecki et al., 2012; Ramchandani et al., 1999). By that, CAIS controlled for all inter-individual differences in pharmacokinetics and allowed us to keep aBAC stable throughout the experiment (Zimmermann et al., 2013; O'Connor et al., 1998). Breath alcohol readings were obtained at 11 time-points (6, 12, 18, 24, 27, 35, 45, 85, 90, 105, 125 min) during alcohol and placebo infusion. The breathalyser converted these readings into units of aBAC by applying a 1:2100 air/blood partition coefficient. These data were entered in real time to improve the individual pharmacokinetic model and adapt prescribed infusion rates accordingly. The mean of all breath alcohol readings shortly before the two-step task at 35 min was 83 mg% (SD=4).

Two-step task

The two-step task (Daw et al., 2011) was programmed in MATLAB 2010b (MathWorks) with the Psychophysics Toolbox 3beta extension. In the separate fMRI session, which was carried out before both infusion sessions, we used the task version

Table 1. Sample characteristics of low-risk and intermediate-risk drinking adolescents.

n=53	Low-risk drinkers AUDIT<8 (*n*=32)	Intermediate-risk drinkers AUDIT≥8 (*n*=21)	*p* (Wilcoxon test)
AUDIT	5.1 (1.4)	11.6 (4.4)	
Age of drinking onset	14.7 (0.8)	13.5 (1.6)	0.003
% Smokers	13	33	0.27[a]
Drinking frequency			0.02[a]
1–3 days a month	50	19	
1–2 days a week	47	57	
3–4 days a week	3	24	
Drinking quantity (g per occasion)	69 (37)	86 (45)	0.19
A: Placebo infusion			
aBAC (mg%)	0 (0)	0 (0)	1[b]
Estimated aBAC (mg%)	33 (25)	35 (16)	0.39
Stimulation	11 (18)	20 (25)	0.41
Sedation	15 (24)	25 (23)	0.04
Negative effects	1 (5)	0 (0)	0.16
Feeling drunk	8 (12)	11 (18)	0.84
B: Alcohol infusion			
aBAC (mg%)	84 (4)	83 (5)	0.43[b]
Estimated aBAC (mg%)	88 (50)	98 (52)	0.42
Stimulation	53 (27)	56 (26)	0.78
Sedation	40 (26)	42 (23)	0.66
Negative effects	9 (15)	3 (6)	0.25
Feeling drunk	51 (27)	51 (24)	0.94
C: Difference alcohol - placebo			
Stimulation	42 (30)	36 (28)	0.56
Sedation	25 (33)	18 (22)	0.26
Negative effects	8 (14)	3 (6)	0.32
Feeling drunk	43 (27)	40 (22)	0.75

aBAC: arterial blood alcohol concentration; AUDIT: Alcohol Use Disorders Identification Test.
aBAC was measured via breathalyser before the two-step task at 35 min; subjective alcohol effects were measured before the two-step task at 25 min. The table displays means and standard deviations in parentheses.
[a]Pearson's Chi-squared test for count data; [b]Welch two sample *t*-test.

described by Sebold et al. (2014). In both infusion sessions, participants again completed the 35 min experimental block with 201 trials, but we used two different sets of random walks and two different sets of stimuli, which were presented in random order across both days (see Figure 2). Participants were instructed to choose one of two stimuli at step 1, followed by another stimulus pair at step 2. Step 2 choices were either rewarded (20 cents) or unrewarded (0 cents) with changing reward probabilities over time according to independent random walks (see Figure 2(b)). Step 1 choices led to a given pair with a fixed probability of 70% (common transition) or to another pair with 30% (rare transition). Subjects were also informed that one-third of the total amount they earned (minimum of three and maximum of 10 €) was paid out at the end.

There are two theoretical response patterns for entirely habitual, model-free and entirely goal-directed, model-based choice behaviour (Figure 2(c)). Subjects showing perfect habitual behaviour will repeat step 1 choices that led to a reward at step 2 on the preceding trial, irrespective of transition, causing a main effect of *reward*. Perfect goal-directed behaviour requires knowledge of the task structure and produces an interaction between *reward* and *transition*. Goal-directed subjects will repeat step 1 choices only if they experienced a reward within a common transition or a loss within a rare transition at the preceding trial. In both other cases, they will switch to the other step 1 stimulus because this strategy maximises gained rewards.

Self-reported drinking measures

Drinking problems were assessed with the AUDIT questionnaire (Babor et al., 2001). Age of drinking onset, drinking frequency and quantity were assessed within the CIDI interview. Age of drinking onset was determined by asking participants how old they were when they had their first alcoholic drink. To measure drinking frequency, we asked participants to indicate how often they drank at least one alcoholic drink during the past 12 months by choosing one of four options: '(almost) daily'=5, '3–4 days a week'=4, '1–2 days a week'=3, '1–3 days a month'=2, 'less than once a month'=1.

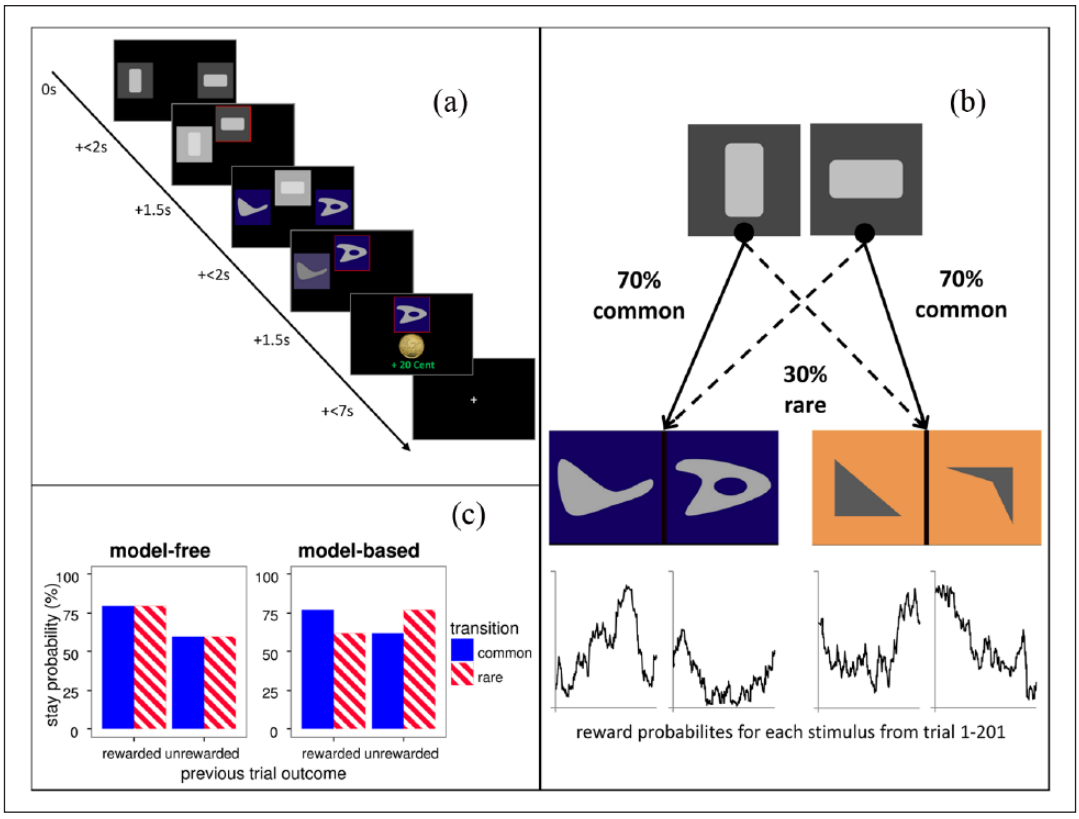

Figure 2. Two-step task: (a) procedure and timing; (b) step 1 stimuli led to step 2 stimuli in either 70% (common transition) or 30% (rare transition) of all trials. Step 2 stimuli were either rewarded or not with a given probability that changed over time (from trial 1–201); (c) theoretical example of stay probability patterns for purely model-free (left) and model-based (right) behaviour.

To assess drinking quantity, participants used pictures of beverages to indicate what exactly they drank on an average drinking day. Their answers were then converted into grams (g) of pure alcohol.

Subjective alcohol effects

We used visual analogue scale ratings of four statements to measure: (a) stimulation: 'Right now, I am experiencing stimulating alcohol effects, e.g. cheerful, excited, full of energy, full of zest for action…'; (b) sedation: 'Right now, I am experiencing sedating alcohol effects, e.g. relaxed, tired, sluggish…'; (c) negative effects: 'Right now, I am experiencing negative alcohol effects, e.g. nausea, dizziness, ringing in the ear…'; (d) feeling drunk: 'I am feeling drunk right now'. Statements were programmed in Presentation (Neurobehavioural Systems), presented sequentially on the video screen, and answered using a computer mouse on vertical visual analogue scales anchored at zero (not at all) and 100 (extremely).

As manipulation check, we asked participants to estimate their actual BAC (estimated aBAC) shortly after the i.v. line was removed.

Data analysis

Behavioural data were analysed using individual stay probabilities, which coded whether each step 1 choice was a repetition of the preceding step 1 choice. Further, we coded the previous trial's step 2 *reward* (rewarded vs unrewarded) and *transition* (common vs rare). A significant main effect of *reward* would indicate habitual, model-free decision-making, whereas a *reward* x *transition* interaction would indicate goal-directed, model-based decision-making (Figure 2(c)). For analyses, we used *R 3.4.3* (https://www.r-project.org/). A binomial (logit) mixed-effects model (*glmer*, package: *lme4*) was used to predict trial-by-trial stay probabilities (0=change vs 1=stay) out of *reward* (0.5=reward vs −0.5=no reward) and *transition* (0.5=common vs −0.5=rare), as well as *treatment* (0.5=alcohol infusion vs −0.5=placebo infusion). To reach convergence, we removed the *treatment* factor from the maximum random effects structure (Barr et al., 2013).

We explored whether self-reported drinking problems moderated alcohol effects on decision-making by adding the fixed factor *AUDITbinomial* (score <8=low-risk drinker vs ≥8= intermediate-risk drinker; coded as −0.5 vs 0.5) to the above described model. We repeated that procedure for raw *AUDIT* scores. To display the strength of reward main effects and *reward* x *transition* interactions, we computed the following differences in stay probabilities: individual model-free scores (% rewarded common+% rewarded rare–% unrewarded common–% unrewarded rare) and model-based scores (% rewarded common–% rewarded rare–% unrewarded rare+% unrewarded common) as described by Sebold et al. (2014). We then subtracted individual model-free from model-based scores to estimate each adolescent's weight of goal-directed relative to habitual decision-making (Smittenaar et al., 2013). Differences in theses relative weights were then analysed using a type-III analysis of variance (*ezANOVA*, package: *car*) with *treatment* and *AUDITbinomial* as factors.

Spearman's rank correlations between AUDIT scores and age of drinking onset, drinking quantity as well as drinking frequency were obtained (*cor.test*, package: *stats*). Further, we used Welch two sample *t*-tests (*t.test*, package: *stats*) for differences in breath alcohol readings of (aBAC), Wilcoxon rank sum tests (*wilcox.test*, package: *stats*) for differences between low-risk and intermediate-risk drinkers with respect to estimated aBACs, age of drinking onset, drinking quantity, and subjectively experienced alcohol effects. Pearson's Chi-squared tests (*chisq.test*, package: *stats*) for count data were used for differences in drinking frequency and smoking status.

To control for real-life alcohol intake, we added the factors *age of drinking onset, drinking frequency*, and *drinking quantity* to the above described models after standardising all three of them by creating z-scores (*scale*, package: *base*). To control for order effects of treatment we created an extra fixed factor *order* (–0.5=alcohol at day 1 vs 0.5=alcohol at day 2) and added it to the above described models.

For each choice at step 1, we measured the time between stimulus onset and response in seconds. Alcohol effects on these response latencies were analysed using a linear mixed-effects model testing the same effects as described above. We interpreted |*t*-values|>2 as significant (Kliegl et al., 2010).

A priori power and observed effect size calculations were carried out using G*Power (http://www.gpower.hhu.de/), based on previous work reporting learning parameters that were measured after drinking moderate alcohol doses in humans (George et al., 2005; Guillot et al., 2010; Loeber and Duka, 2009; Ramaekers and Kuypers, 2006). Observed effect sizes ranged between 0.2 and 2 (M=0.9). Then, we computed the required sample size for repeated-measures analysis of variance with an effect size of 0.4 for *treatment* (alcohol vs placebo), an alpha level of 0.05, and a power of 0.8, which was 52 people. Further, we performed a power analysis to find a between-within interaction (*treatment* x *AUDITbinomial*) with the same parameters, resulting in a sample size of 54 people. During analyses, we switched to mixed-effects models, because they allowed us to use trial-by-trial data and can properly account for within-subject correlations and unbalanced data (Gueorguieva and Krystal, 2004).

Graphics were created using *ggplot* (package: *ggplot2*) and the GNU Image Manipulation Program (GIMP; https://www.gimp.org/). Standard errors (*SE*s) of the mean were corrected for repeated measures according to Morey (2008) using *summarySEwithin* (package: *Rmisc*).

Results

Manipulation check

Self-assessment of current aBAC (in mg%) by the adolescents was significantly lower after placebo than alcohol administration ($M_{placebo}$=34 (SD=22)<$M_{alcohol}$=92 (SD=51); p<0.001), without any difference between low-risk and intermediate-risk drinkers (see Table 1). Four low-risk drinkers and one intermediate-risk drinker correctly guessed that their aBAC was 0 mg% after being infused with placebo, but this difference was not significant.

Alcohol effects on stay probabilities

Figure 3 displays stay probabilities observed during both treatment conditions.

Collapsing both treatment conditions, we observed habitual, model-free components of decision-making: Choices were more likely to be repeated after rewarded than unrewarded trials ($Estimate_{reward}$=0.45, SE=0.07, z=6.5, p<0.001). There were also goal-directed, model-based components across treatment conditions, as indicated by a significant *reward* x *transition* interaction ($Estimate_{reward\ x\ transition}$=1.51, SE=0.24, z=6.3, p<0.001).

Alcohol significantly reduced the size of both the *reward* effect ($Estimate_{reward\ x\ treatment}$=−0.14, SE=0.07, z=−2.0, p=0.047; Figure 3(c)) and the *reward* x *transition* interaction ($Estimate_{reward\ x\ transition\ x\ treatment}$=−0.30, SE=0.14, z=−2.1, p=0.036; Figure 3(d)), suggesting that alcohol administration impaired both model-based and model-free components of decision-making. Combining all four task conditions, overall stay probabilities were also reduced during alcohol compared to placebo administration ($Estimate_{treatment}$=−0.11, SE=0.04, z=-2.9, p=0.004).

Alcohol effects on decision-making remained significant after controlling for *order* of treatment when adding this factor as fixed main effect to the above described model and when allowing *order* to interact with all other factors.

AUDIT as moderator for the alcohol effects on decision-making

We tested whether self-reported drinking problems moderated the effects of ethanol on decision-making by adding the binary AUDIT factor to the above described models. Just like in the previous model, we observed significant effects of *reward, treatment*, their interaction and the *reward* x *transition* interaction (all p-values<0.041). Besides that, *AUDITbinomial* moderated the alcohol effect on model-based decision-making. Compared to intermediate-risk drinkers, low-risk drinkers showed significantly stronger alcohol-induced impairments in model-based decisions ($Estimate_{AUDITbinomial\ x\ reward\ x\ transition\ x\ treatment}$=1.2, SE=0.29, z=4.0, p<0.001). *AUDITbinomial* did not significantly moderate alcohol effects on model-free decisions (p=0.34). Figure 4 depicts that alcohol administration numerically reduced model-based behaviour in low-risk drinkers (Figure 4(c)), while increasing it in intermediate-risk drinkers (Figure 4(d)).

For raw AUDIT scores, we found a similar four-way interaction ($Estimate_{AUDIT\ x\ reward\ x\ transition\ x\ treatment}$=0.6, SE=0.14, z=4.2, p<0.001), again indicating that a lower number of self-reported drinking problems was associated with stronger impairment of model-based decision-making during alcohol administration.

To examine the relative contribution of goal-directed and habitual decision-making, we analysed differences between model-based and model-free scores. In an analysis of variance, we tested whether these differences were affected by *treatment* and *AUDITbinomial*. A significant interaction between both factors indicated that low-risk drinkers showed an alcohol-induced relative shift towards model-free choices, whereas intermediate-risk drinkers made a shift in the opposite direction, towards model-based choices (F(1,51)=4.3, p=0.044, see Figure 4(e) and (f)), with an observed effect size f=0.29.

Comparing each individual bar with any other bar using paired and unpaired Wilcoxon tests (Figure 4(a)–(d)) or *t*-tests (Figure 4(e) and (f)), we found no significant differences (all p-values>0.12).

AUDIT, real-life drinking, and subjective alcohol effects

Raw AUDIT scores correlated negatively with age of drinking onset (Spearman's ρ=−0.40, p=0.003) and positively with

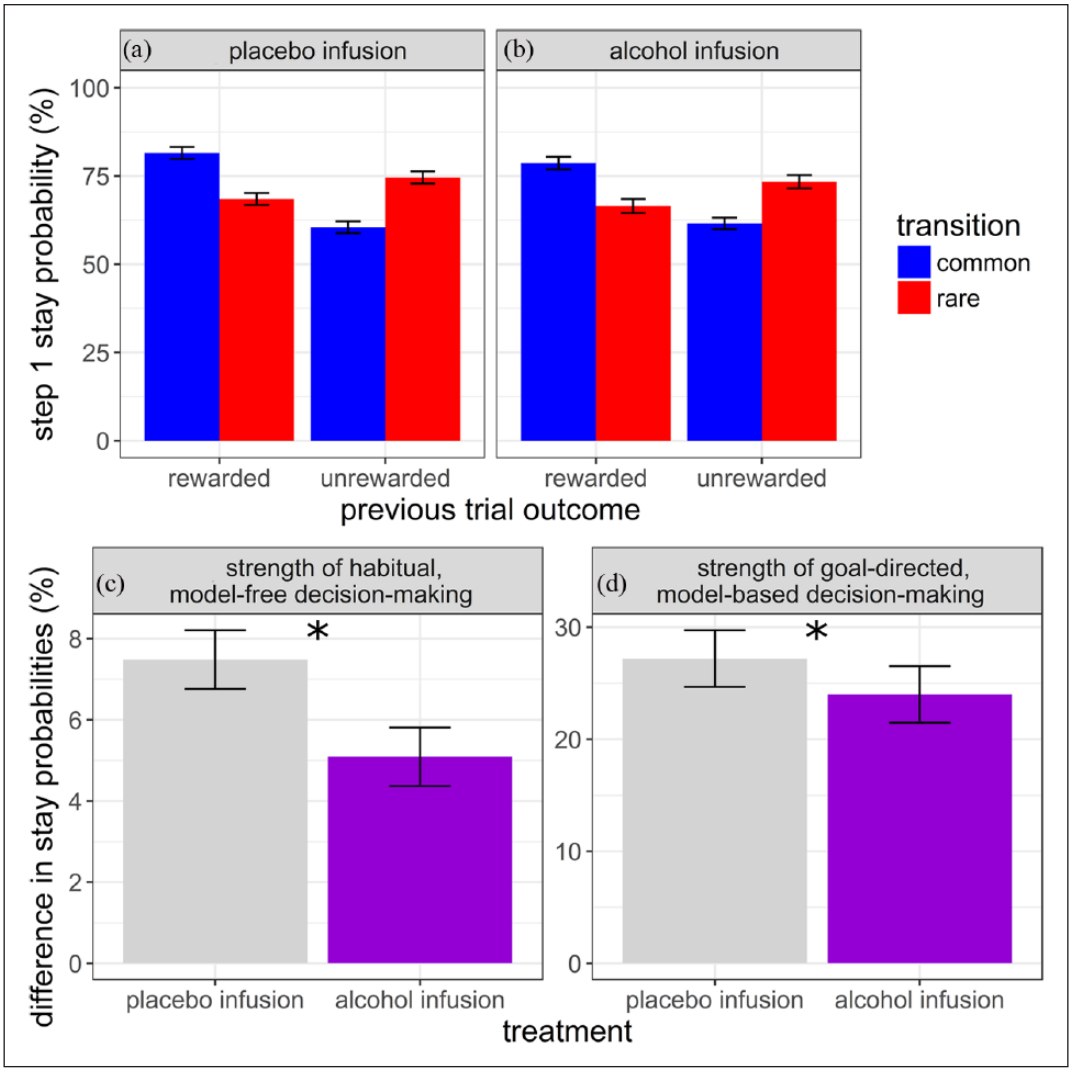

Figure 3. Mean stay probabilities and standard errors of the mean (error bars) as a function of reward and transition at the preceding trial during (a) placebo infusion and (b) alcohol infusion. Overall stay probabilities were significantly reduced during alcohol compared to placebo infusion ($p<0.01$). Lower panels display the strength of model-free (c) and model-based (d) components of decision-making as measured by differences in stay probabilities as described in the Data analysis section. *$p<0.05$.

drinking quantity (Spearman's $\rho=0.28$, $p=0.039$), drinking frequency (Spearman's $\rho=0.35$, $p=0.011$), and sedation during placebo administration (Spearman's $\rho=0.29$, $p=0.038$).

With respect to *AUDITbinomial*, we found that intermediate-risk drinkers reported an earlier age of drinking onset, higher drinking frequency and stronger sedation during placebo infusion (p-values<0.05) than low-risk drinkers (see Table 1). Both groups did not significantly differ in any other experience of subjective alcohol effects.

The moderating effects of raw and binary AUDIT scores on stay probabilities at step 1 remained significant after controlling for age of drinking onset, drinking frequency, drinking quantity and order of treatment in four separate models. There were no additional interactions between real-life drinking and model-free or model-based decision-making. With respect to order, the moderating effect of raw *AUDIT* scores on the alcohol effect on model-based learning was significantly weaker when alcohol was administered at day 2 compared to day 1 ($Estimate_{order\ x\ AUDIT\ x\ reward\ x\ transition\ x\ treatment}=-0.55$, $SE=0.28$, $z=-2.0$, $p=0.0496$).

Alcohol effects on response latency

We predicted individual response latencies recorded at step 1 by *reward, transition, treatment, AUDITbinomial*, and their interactions. Combining all four task conditions, alcohol generally slowed down choices at step 1 ($Estimate_{treatment}=0.01$, $SE=0.004$, $t=3.1$). This alcohol-induced slowing was stronger in intermediate-risk drinkers than low-risk drinkers at step 1 ($Estimate_{AUDITbinomial\ x\ treatment}=0.02$, $SE=0.008$, $t=2.9$). Alcohol also slowed down model-based decisions ($Estimate_{reward\ x\ transition\ x\ treatment}=0.04$, $SE=0.02$, $t=2.3$) at step 1. Model-free response times were not significantly affected by treatment.

Discussion

We examined the effects of acute alcohol administration on decision-making in the two-step task. Alcohol relative to placebo administration reduced both habitual, model-free and goal-directed, model-based decisions in the entire sample of healthy male

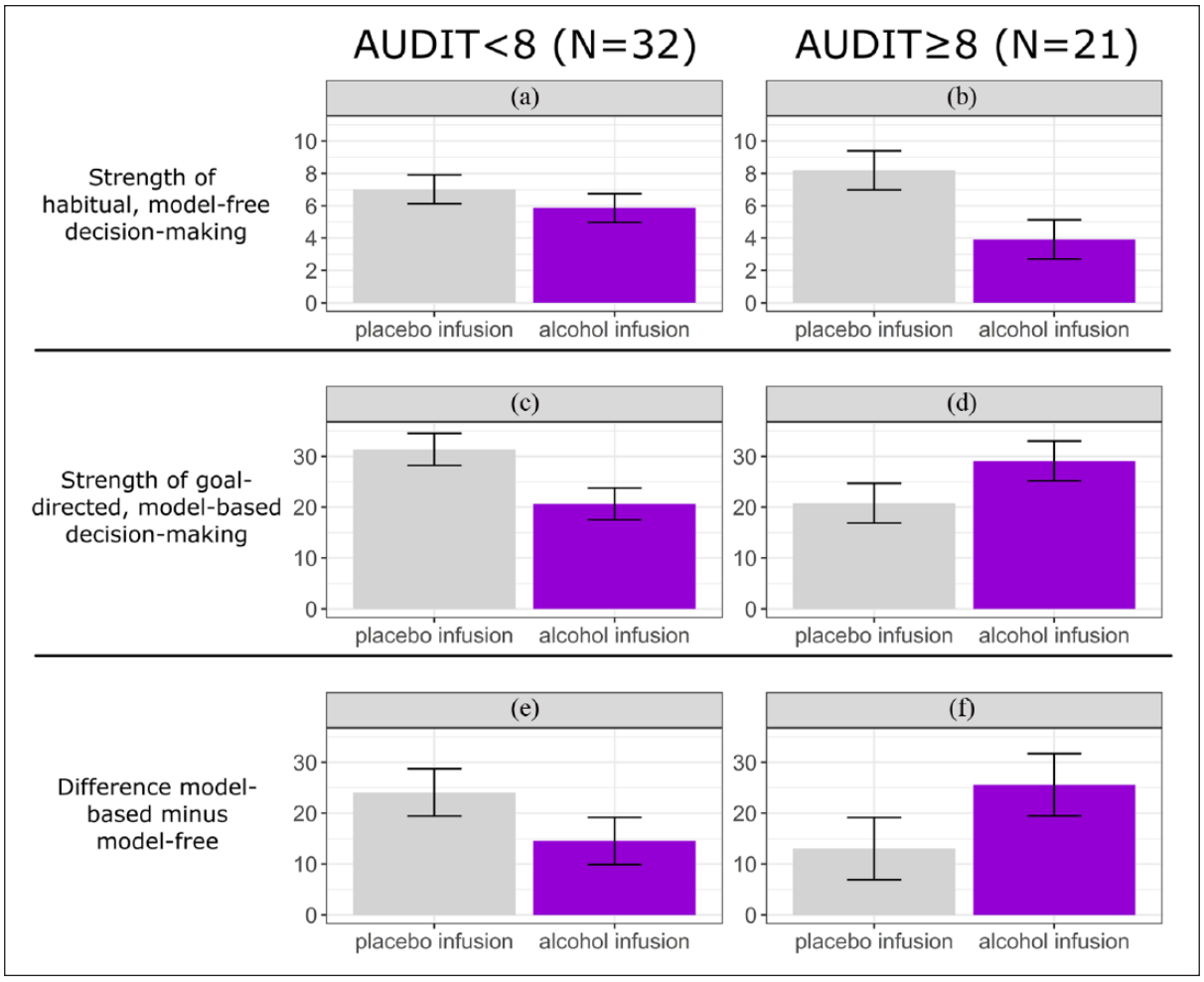

Figure 4. Differences in stay probabilities determining the absolute strength of model-free ((a), (b)) and model-based ((c), (d)) decision-making, and relative strength of model-based over model-free behaviour ((e), (f)) with standard errors of the mean (error bars). Alcohol generally reduced model-free decisions (p<0.05, (a) and (b)). Low-risk drinkers showed significantly stronger alcohol-induced impairments of model-based decisions than intermediate risk-drinkers (p<0.001, (c) and (d)). Low-risk drinkers showed an alcohol-induced relative shift towards model-free choices, whereas intermediate-risk drinkers made a shift in the opposite direction, towards model-based choices (p<0.05, (e) and (f)).

adolescents. Subdividing the sample based on individual AUDIT scores, we found that alcohol effects on goal-directed, model-based decisions varied as a function of drinking problems. Hence, adolescents with intermediate compared to low risk for drinking problems showed an unexpected alcohol-induced shift from habitual towards goal-directed behaviour.

Concerning the entire sample, our first hypothesis was partly confirmed. Instead of reducing goal-directedness while promoting habitual choices, alcohol reduced both components of decision-making. An increase in perseverative errors (Guillot et al., 2010; Lyvers and Tobias-Webb, 2010) cannot explain these impairments, because alcohol significantly reduced stay probabilities and therefore perseveration. The alcohol-induced decline in habitual decision-making was unexpected given the work of Hogarth et al. (2012), but might be explained by our higher alcohol dose and the more complex two-step task. Hoffman et al. (2015) suggested that the effects of alcohol on cognitive performance vary by dose, with beneficial effects for low doses and no effect for moderate doses. Consequently, our alcohol dose might have been sufficiently large to disrupt key aspects of habitual decision-making in the two-step task, such as memory for sequences of visual information (Saults et al., 2007), executive functioning and prospective planning (Montgomery et al., 2011), the detection of performance errors in the anterior cingulate cortex (Ridderinkhof et al., 2002) or the ability to process motivationally salient outcomes (Euser et al., 2011). In our sample, low-risk drinkers appeared to suffer most from such cognitive impairments. These adolescents might have simply switched more randomly between options in response to alcohol, which caused their decline in overall stay probabilities and goal-directed choices.

Our primary finding that intermediate-risk drinkers' goal-directed choices were not impaired by alcohol was partly in line with our second hypothesis. We expected that intermediate-risk drinkers would be less sensitive towards the effects of alcohol due to more drinking experience. In line with that view, drinking problems were significantly associated with earlier age of drinking onset, higher drinking frequency and quantity. However,

compared to low-risk drinkers, intermediate-risk drinkers neither showed lower sensitivity towards the effects of alcohol (Gilpin and Koob, 2008) nor an increased level of stimulation (King et al., 2016), as subjectively experienced alcohol effects did not differ between groups during alcohol infusion. There were also no group differences in the changes of these experiences from placebo to alcohol infusion. The lack of group differences in subjective responses might be explained by the fact that we administered alcohol intravenously, which eliminates typical alcohol-related cues (e.g. taste, smell) that may evoke conditioned responses. Besides that, alcohol administration seemed to improve decisions of intermediate-risk relative to low-risk drinkers, which would not be explained by lower sensitivity towards the effects of alcohol.

The shift towards goal-directed behaviour in intermediate-risk relative to low-risk drinkers came along with longer response latencies during alcohol administration, which suggests that we measured deliberation time instead of reaction time. In fact, participants were not instructed to respond as fast and accurate as possible and there were no obvious error trials (Salthouse and Hedden, 2002). Consequently, intermediate-risk relative to low-risk drinkers might have invested more mental effort at step 1 during alcohol administration, because goal-directed choices are cognitively demanding. This view is supported by computational accounts for the balance between goal-directed and habitual behaviour, which suggest that goal-directed behaviour relies on a speed-accuracy tradeoff, where goal-directed computations improve choice accuracy at the cost of deliberation time (Keramati et al., 2011).

The observation that alcohol improved intermediate-risk drinkers` performance more strongly at day 1 than day 2 suggests that alcohol might have served as negative reinforcer by neutralising unpleasant states. Quite a few participants spontaneously mentioned that they perceived the two-step task as 'boring' or 'exhausting', and complained that it lasted up to 50 min. We assume that the task got more bothersome from session to session. As a result, intermediate-risk drinkers might have struggled most with it at day 2 during placebo administration, which boosted their goal-directed, model-based behaviour at day 1 during alcohol administration. In accordance with that idea, moderate alcohol intake has been found to facilitate non-drug-related behaviours by reducing stress, enhancing mood and improving cognitive performance (Baum-Baicker, 1985; Müller and Schumann, 2011). Our own data further supports the role of alcohol as negative reinforcer, as drinking problems correlated positively with sedation during placebo administration and intermediate-risk drinkers felt more sedated than low-risk drinkers in that condition. These findings might imply that intermediate-risk drinkers experienced the two-step task as more boring than low-risk drinkers. Indeed, boredom susceptibility and the expectancy to escape from boredom are important risk factors for alcohol consumption in adolescence (Biolcati et al., 2016; Peltzer et al., 2012). Alternatively, alcohol may have reduced mental fatigue instead of boredom, since the former was shown to arise from sustained performance and to impair goal-directed behaviour by reducing executive control (van der Linden et al., 2003). However, we did not measure boredom or subjectively perceived mental effort and can therefore only speculate whether the more sedated intermediate-risk drinkers felt less bored or mentally exhausted than low-risk drinkers during alcohol compared to placebo administration. An important question for future research is therefore, whether boredom and/or mental fatigue during the two-step task differentiate between low-risk and intermediate-risk drinkers.

The alternative explanation that alcohol reduced withdrawal symptoms in intermediate-risk drinking adolescents is unlikely, since none of them fulfilled any DSM-IV alcohol dependence criterion. Compensatory strategies also fail to explain our results, because, just like low sensitivity, perfect compensation would predict no alcohol effect instead of a performance increase in intermediate relative to low-risk drinkers (Testa et al., 2006). One might argue that intermediate-risk drinkers overcompensated for the expected cognitive deficits in the alcohol condition, because they unmasked this condition more easily than low-risk drinkers, based on their longer drinking experience. However, analyses of participants'estimated aBACs indicated that the numbers of low-risk and intermediate-risk drinkers, who successfully unmasked this condition, did not differ significantly.

On a neuronal level, higher AUDIT scores might have been associated with stronger striatal reward prediction error signals during alcohol compared to placebo administration. In line with that concept, Nebe et al. (2017) reported an association between earlier age of drinking onset and stronger blood oxygenation dependent responses to reward prediction errors, which were found to reflect both model-free and model-based predictions in the two-step task (Daw et al., 2011). Further, intermediate-risk compared to low-risk drinkers might have benefited more strongly from the gamma-aminobutyric acid (GABA)-like effects of alcohol, since excitation of GABA(B) receptors in rats was shown to enhance set-switching performance (Beas et al., 2016). Given the close link between cogntive abilities and goal-directed choices (Schad et al., 2014), this may have facilitated a shift towards goal-directed control. Finally, intermediate-risk relative to low-risk drinkers might have released more dopamine in response to alcohol, as dopamine was found to promote goal-directed over habitual choices (Wunderlich et al., 2012). However, based on our behavioural data we can only speculate about neuronal mechanisms, emphasising the need for future alcohol administration studies on decision-making using neurobehavioural methods.

Limitations of our findings include the lack of significant post-hoc comparisons. The significant four-way interaction might therefore solely reflect alcohol-induced reductions in goal-directedness in low-risk drinkers, while the numerical increase in intermediate-risk drinkers occurred by chance. As mentioned above, our sample size was sufficiently large to detect main effects and interactions with a size of 0.4, given an α-level of 0.05 and a power of 0.8. Thus, our study was underpowered for detecting small or medium effects of alcohol in one of the two subsamples. To check the power of our four-way interaction, we used the web-based tool Power ANalysis for GEneralised Anova designs (PANGEA; https://jakewestfall.shinyapps.io/pangea/), using the default experimental parameters and our number of intermediate-risk drinkers (21) as number of subjects in each AUDIT group. We found a power of 0.83 for our four-way interaction, indicating that our sample size was sufficiently large to test four-way interactions. Futher, all information provided by the four-way interaction was also covered by the significant two-way interaction between AUDIT and treatment on differences between model-based and model-free scores. We therefore think that the shift towards goal-directed behaviour in adolescents with intermediate relative to low risk for drinking problems was a reliable result. In line with this possibility, the relative shift was no artifact of task training.

Although model-based performance should improve across sessions and, by chance, the majority of intermediate-risk drinkers (13 out of 21) received alcohol at day 2 (compared to 13 out of 32 low-risk drinkers), we found that the alcohol-induced improvement in intermediate-risk drinkers was consistent when controling for treatment order, and that it was actually stronger when receiving alcohol at day 1 compared to day 2. Other limitations include the young male sample and the fact that we clamped aBAC at 80 mg%. Thus, we can only speculate whether our results pertain to women, older participants and other alcohol doses. Finally, i.v. alcohol clamping is an extraordinary experience questioning the generalisability of our results to real-life drinking, where aBACs are 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. Nevertheless, intravenous alcohol clamping yields several advantages compared to oral alcohol administration, as it eliminates biological differences in alcohol pharmacokinetics and reduces inter-individual variation in aBAC. It also minimises the impact of environmental factors, including alcohol-related contextual cues and social pressure (O'Connor et al., 1998; Zimmermann et al., 2013). Our findings therefore reflect pharmacological effects of alcohol on decision-making that are largely unbiased by the before-mentioned environmental or biological factors.

To fill the gap between research in patients and animals suggesting that chronic alcohol intake promotes habits, we examined the effect of acute alcohol exposure on decision-making in the two-step task in a sample of healthy male adolescents. Instead of promoting habits, alcohol reduced habitual decision-making in the entire sample. At the same time, alcohol reduced goal-directed choices in low-risk relative to intermediate-risk drinkers, possibly due to alcohol-induced disruptions of cognitive operations leading to rash choices at step 1. Intermediate-risk relative to low-risk drinkers, on the other hand, showed a shift away from habitual towards goal-directed decision-making, such that alcohol possibly even improved their performance. Based on the current results we speculate that intermediate-risk drinkers benefited from alcohol as negative reinforcer possibly displaying a novel risk factor for drinking in adolescence.

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ORCID iDs

Elisabeth Obst https://orcid.org/0000-0001-8841-3886
Stephan Nebe https://orcid.org/0000-0003-3968-9557

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