Model-based and model-free decisions in alcohol dependence

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Abstract

**Background:** Human and animal work suggests a shift from goal-directed to habitual decision-making in addiction. However, the evidence for this in human alcohol dependence is as yet inconclusive.

**Methods:** Twenty-six healthy controls and twenty-six recently detoxified alcohol-dependent patients underwent behavioral testing with a two-step task designed to disentangle goal-directed and habitual response patterns.

**Results:** Alcohol-dependent patients showed less evidence of goal-directed choices than healthy controls, particularly after losses. There was no difference in the strength of the habitual component. The group differences did not survive controlling for performance on the digit symbol substitution task.

**Conclusion:** Chronic alcohol use appears to selectively impair goal-directed function, rather than promoting habitual responding. It appears to do so particularly after non-rewards, and this may be mediated by the effects of alcohol on more general cognitive functions subserved by the prefrontal cortex.

**Keywords:** Alcohol dependence, Decision making, Reinforcement learning, Dopamine, Computational Psychiatry
Introduction

Substance dependence is characterized by maladaptive choices that contrast with subjects’ explicitly stated desires, such as the failure to abstain despite the desire to quit drinking. This inflexible and compulsive behavior in addiction suggests a failure or disruption of several components of the underlying decision-making systems.

Two well-defined components of decision-making have been computationally characterized. On the one hand, a flexible, goal-directed, model-based planning system, explicitly considers the consequences of actions [1]. It is ‘model-based’ in that it relies on a model of the world (in simple experiments often just the action-outcome contingencies), and then deduces from this model the best sequence of actions. Although it is computationally costly, requiring the explicit consideration of future outcomes, it can be immediately sensitive to environmental changes and lead to rapid behavioral adaptation. In parallel, a more rigid habitual system repeats actions that were in the past associated with reward [2,3]. The learning process that leads to habits relies on iterative updates of expectations through putatively dopaminergic [4-6] prediction errors, but unlike the goal-directed system does not rely on an explicit model. Hence, it is termed model-free. Because it relies on iterative updating, it is also slow, requiring substantial and repeated experience before behavioral adjustments. Tasks that require rapid shifting between behavioral strategies have been used to distinguish model-based and model-free components behaviorally and neurobiologically in humans and animals. Examples of such tasks are devaluation or motivational shift experiments, whereby the signature of habitual responding is a continued responding for an outcome that is no longer desired. This is reminiscent of drug taking persisting in the face of negative consequences.

Numerous studies in animals have shown that drugs of abuse shift the balance towards habits. Studies using for instance devaluation paradigms [4-7] have shown persistence of responding increasing with alcohol. The processes that speed up habitization have been suggested to also facilitate transformation into compulsions [8-13]. Work in humans with addictions has also shown evidence of inflexible choices, even in terms of non-drug related rewards such as monetary gains. For instance, alcohol [14] and stimulant [15-17] dependent patients show impairments in shifting their responses in probabilistic reversal learning and fail to adapt their responses after errors in stop signal tasks [18,19]. Moreover shifts towards automatic action tendencies temporally precede relapses [20] and can be trained to improve treatment outcome.
There have also been attempts to directly examine how substance dependence affects the relationship between goal-directed and habitual control in humans. A satiety devaluation paradigm did not reveal evidence of habitual responding for either cigarettes or chocolate in smokers, suggesting that not all responses for drug-related stimuli are necessarily habitual in drug users [22]. Interestingly, however, alcohol expectancy [23] and acute alcohol administration [24] did reduce the effect of satiety devaluation, suggesting that alcohol can specifically impair goal-directed decisions. Indeed, the goal-directed system is likely to depend on the kind of cognitive processes that are known to be impaired by alcohol [25,26].

Sjoerds et al., 2013 used an instructed devaluation in a slips of action task which involves complex relationships between stimuli, outcomes and responses. They find evidence for a shift towards habits in alcohol dependent patients, which was accompanied by increased fMRI signal in habit-related areas like the posterior putamen [27] and decreased signal in goal-directed ventromedial prefrontal and anterior putamen areas [28-30], which parallels findings in animals [31].

Devaluation experiments involve single, sudden and large changes. On the one hand, these changes are obvious to human subjects and such salient changes might therefore lead to potent re-engagement of flexible goal-directed behavior. On the other hand, the slips of actions task is very complex, and the performance of goal-directed decisions might be hampered by impairments affecting upstream cognitive functions including working memory [32]. We here use a third type of task [30] that has been developed based on computational arguments about the statistical efficiency of habitual and goal-directed systems [3]. It examines the relative contributions of habitual and goal-directed choices using continuous, subtle valuation shifts rather than few large or instructed ones. This task is also particular in that it allows us to compare the consequences of gains and non-gains. Furthermore, given the sensitivity of goal-directed choices to cognitive load [25] and the recently reported importance of other cognitive measures [32,33] we also examine whether any effects of alcohol dependence on the structure of decision-making might be accounted for by differences in more general cognitive measures.
Methods

26 recently detoxified alcohol dependent patients (5 females) and 26 healthy comparison subjects (5 females) participated in this study. Demographic and clinical group characteristics of the final sample are outlined in Table 1. Groups were matched for age, gender and years of education. All participants were examined for past and present psychiatric disorders using the Screening Version of the Structured Clinical Interview for DSM-IV [34]. All patients fulfilled DSM-IV criteria for alcohol dependence without axis I co-morbidity. The days of alcohol abstinence before study participation in the patient group ranged from 2 to 39 with a mean of $15.1 \pm 10.4$ days. All healthy controls had no current or past major psychiatric disorder. All participants had normal or corrected-to-normal vision, and were also screened for neurological diseases. After detailed verbal and written instruction on the procedures of the study, participants gave their written informed consent. The study was approved by the local ethics committee of Charité Universitätmedizin, Berlin and Universitätsklinikum Dresden.

Task and Procedure

All participants underwent neuropsychological testing including standard tests assessing crystallized intelligence, cognitive speed, memory and executive functioning (see Table 1). Participants additionally performed the two-stage Markov decision task as described by Daw et al. 2011 [30] (see Figure 1 for detailed task description).

The task was re-programmed in MATLAB, using the Psychophysics Toolbox extensions [35,36] and used different stimuli. Prior to the experiment, participants were explicitly informed about the task structure. Critically, the very detailed subject instructions were carefully translated from the English version. Participants were told that the transition matrix from first step choices to second stages would stay constant and that the selection of one stimulus on the first stage would lead to a particular stimulus pair on the second stage more often than it would lead to the other second stage stimulus pair. Participants were instructed that second stage reward probabilities were independent of each other and would slowly change over the course of the experiment. Participants were familiarized with the paradigm before the task by performing a shortened version of the paradigm (50 trials) with different reinforcement probabilities and a different stimulus set. They were instructed to maximize their monetary outcome throughout the experiment. Participants’ overall payout was 13 Euros plus the accumulated reward of one third of all trials. The maximal payout was limited to 20
Euros. The task consisted of 201 trials. Trials were separated by an exponentially distributed inter-trial interval (ITI), ranging between 1 and 7 seconds. The maximum response time was 2000 ms for first and for second stage choices. If participants failed to make a response in this time window the german phrase for “too slow!” appeared on the screen for 2000 ms, and the trial was aborted. The two stimuli at the first and second stage were assigned randomly between left and right from trial to trial.

**Figure 1.** A: Trial configuration for the experiment. Each trial consisted of two different stages, and each stage involved a choice between two stimuli. In the first stage, subjects chose between two abstract stimuli on a grey background. The chosen stimulus was highlighted by a red frame and moved to the top of the screen, where it remained visible for 1.5s; at the same time, the other stimulus faded away. Subjects then reached a subsequent second stage. Here subjects saw one of two further pairs of coloured stimuli and again chose between these. The monetary outcome following this second stage choice (gain or no gain of 20cent) was then presented centrally on the screen.

B: One pair of coloured second stage stimuli occurred commonly (on 70% of trials; “common trials”) after choice of one first stage grey stimulus, while the other second stage pair was associated equally strongly with the other first stage stimulus (common). On the remaining 30% of trials, the chosen first stage option resulted in a transition to the other second stage stimulus pair (rare).

C: Reinforcement probabilities for each second stage stimulus changed slowly and independently according to Gaussian random walks with reflecting boundaries at .25 and .75. Win probabilities are displayed as a function of trial number, according to Daw et al, 2011 [30].
Behavioral Analysis

We performed a simplified analysis focusing only on first-stage choices. Model-based and model-free strategies predict different patterns of first-stage choices. A model-free strategy predicts purely reinforcement-guided action selection: first stage choices should be repeated after a previous trial’s second stage choice resulted in reward whereas a first-stage switch should occur after a previous trial ended up being not rewarded. Thus, model-free action selection should occur irrespective of whether the transition to the second stage in the previous trial was a common or a rare one (Figure 2A). In contrast, model-based action selection includes the consideration of the task structure its transition. This results in an inverted response behavior following rare trials. Consider a trial in which a first stage response uncharacteristically results in a second stage stimulus pair to which it usually does not lead (rare) and in which the second stage selection is then rewarded. Model-based action selection would then predict a decreased probability of choosing this first stage stimulus again, as the selection of the first stage stimulus that has initially not been chosen has a higher likelihood of leading to the rewarded second-stage stimulus pair (common; Figure 2B).

Figure 2: First stage behavior as a function of reward and frequency of the previous trial for pure model-free vs. pure model-based strategies. A pure model-free decision-making strategy would lead to a main effect of reward (Figure A), but no effect of or interaction with frequency, while a pure model-based decision strategy would lead to an interaction between reward and frequency without a main effect of reward (Figure B).
The major aim of this investigation was to specifically assess whether alcohol dependent patients displayed a shift from model-based to model-free control. For this purpose we calculated two individual scores, one for model-based and one for model-free control. Individual model-free scores reflected the individual main effect of reward (\( \% \text{ Reward Common} + \% \text{ Rewarded Rare} - \% \text{ Unrewarded Common} - \% \text{ Unrewarded Rare} \)), whereas individual scores for model-based control reflected the interaction between transition frequency and reward (\( \% \text{ Reward Common} + \% \text{ Unrewarded Rare} - \% \text{ Rewarded Rare} - \% \text{ Unrewarded Common} \)). We computed one-tailed t-test in each group (which compares both scores in each group against zero), in order to test whether both decision-making systems were evident within each group.

We then conducted independent-samples t-tests to assess our a-priori hypotheses that model-free contributions would be larger in alcohol-dependent patients than in healthy controls and conversely that model-based contributions would be larger in healthy controls than in alcohol-dependent patients. As we had explicit hypotheses on the direction of within-group and between-group effects of both model-free and model-based control we tested all comparisons regarding these hypotheses against a one tailed criterion.

In order to assess whether the neuropsychological variable that differed between groups (Digit Symbol Substitution Test (DSST)) had an influence on model-free or model-based control we first regressed the outcome variables (total earnings and individual model-based scores) onto the neuropsychological variable, and performed independent-samples t-tests on the residuals. All statistical analyses were performed using MATLAB version R2007a [37].
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Results

Participants

Participant characteristics are shown in Table 1. Patients and controls were matched for age, sex and education. Nevertheless, there was a significant difference in one measure of cognitive functioning (DSST, \( p < .05 \)) and groups showed a tendency towards differing on verbal IQ (WST: \( p = .061 \)).

Table 1. Demographic and clinical characteristics of 26 patients and 26 matched controls. Each group included 5 females. Comparisons are based on independent sample t-Tests. P-values indicating statistical significance at a level less than .05 are displayed in bold digits.

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ALC, Alcohol dependent patients; HC, Healthy controls; Verbal IQ assessed by German Vocabulary Test (Wortschatztest [38]); Cognitive Speed assessed by Digit Symbol Substitution Test (DSST) from Wechsler WAIS-R [39]; Verbal Working Memory assessed by Digit Span (DS) Backwards Test [39]; Executive Functioning assessed by Trail Making Test TMT(A), TMT(B) [40]; Verbal memory assessed by Wordlist from the Consortium to Establish a Registry for Alzheimer's Disease (CERAD, [41]).
Participants rarely missed any responses (Mean = 1.8%, SD = 2.43%). Missed trials were omitted from analysis. Patients and controls did not differ in their average Stay/Switch behavior at the first stage (no group difference in overall probability of stay/switch $t(50) = .65$, $p = .52$).

**Model-free choices**

Both groups showed significant model-free influences in their choice behavior (model-free scores greater than zero, ALC (one-tailed t-test $t(25) = 5.03$, $p < .001$), HC (one-tailed t-test, $t(25) = 4.1$ $p < .001$). Thus, subjects tended to choose the same first stage stimulus when rewarded in the previous trial, but switched to the opposing first stage stimulus when not rewarded. Against our prediction, patients did not show a stronger model-free component (individual model-free scores ALC vs. HC one-tailed t-test, $t(50) = 1.08$, $p = 0.14$).

**Model-based choices**

Goal-directed components were present in both groups (individual model-based score greater than zero, (one-tailed tests: HC $t(25) = 3.32$, $p < .001$, ALC $t(25) = 1.95$, $p < .05$). Hence, switches tended to occur when the outcome of the previous trial was a reward, but the transition rare, or when the outcome was a non-reward and the transition a common one. Healthy controls used significantly more model-based strategies than alcohol dependent patients, as indicated by between group differences in individual model-based scores ($t(50) = 1.90$, $p < .05$, one-tailed).

Figure 3 displays the stay probabilities for healthy controls (3A), alcohol dependent patients (3B) and between group differences in stay probabilities for all four trial types (Figure 3C). Visual inspection suggests that the groups mainly differed in stay probabilities after unrewarded trials. In order to test for differential between-group differences in model-based choice behavior for unrewarded and rewarded trials, we calculated individual model-based scores for unrewarded and rewarded trials separately and used independent sample t-tests to compare these between groups. These post hoc t-tests confirmed that controls modulated their responses after losses according to a model-based strategy (i.e. were sensitive to transition frequency) more than patients (one-tailed test: $t(50) = 2.27$, $p < .05$). However model-based control after rewarded trials was not greater in controls than patients (one-tailed test: $t(50) = .57$, $p = .28$). Thus, the difference in terms of model-free/model-based choices between
controls and patients was driven by a failure of goal-directed control after non-rewards in patients.

**Figure 3:** Observed first stage behavior as a function of reward and frequency of the previous trial for healthy controls (Figure A) and alcohol dependent patients (Figure B). Error bars represent standard errors of means. Figure C displays standardized differences in stay probabilities between healthy controls and alcohol dependent patients.
On average, subjects earned 16.4 € (Total range 13.60 – 18.00). Patients earned less money than controls (two-tailed t-test, $t(50) = 2.53, p < .05$, Figure 4A). As the optimal response strategy exploits the structure of the task, model-based responding was expected to improve the overall outcome. Individual model-based scores were indeed positively correlated with the total monetary outcome (Pearson's $r = .33, p < .05$; Figure 4B). As expected, total outcome was not related to the score for model-free behavior (Pearson’s $r = -.13, p = .36$). However, the group differences in earnings remained marginally significant after correcting for model-based scores ($t(47) = 1.96, p = .06$), indicating that goal-directedness only partially accounted for between group differences in total monetary outcome (Figure 4C).

**Figure 4:** Group differences in total monetary outcome (Figure A). Correlation between total monetary outcome and individual model-based scores (Figure B). Total monetary outcome corrected for differences in model-based scores (Figure C).
Effect of cognitive measures on model-based behavior

Despite carefully matching for education, groups differed on the digit symbol substitution test (DSST) – a measure of cognitive speed (Table 1.). We therefore asked whether the apparent group differences in model-based reasoning might instead be explained by group differences in DSST. To correct for DSST, we again calculated one-tailed independent-sample t-tests after regressing out individual DSST scores. Although patients continued to be less model-based, this correction removed the significant group difference ($t(47) = 1.13, p = .13$) Figure 5: Group differences in model-based scores (Figure A) and model-based scores corrected for DSST (Figure B).

Figure 5: Group differences in model-based scores (Figure A) and model-based scores corrected for DSST (Figure B).
Discussion

The current study suggests a disruption of model-based choice behavior in alcohol dependent patients. Importantly, we found no difference in the strength of model-free choice tendencies, and the disruption appears to be present after non-reward outcomes only. Despite carefully matching patients for educational level, patients and controls differed on one measure of cognitive speed. Patients were less model-based than controls even after controlling for this, but the difference was no longer significant ($p = 0.13$).

The results are in line with theories suggesting a shift from controlled, goal-directed (outcome-guided) to automatic, habitual (stimulus-guided) decision making in substance dependence [8-11]. They also speak to the critical question of whether chronic drug intake affects the goal-directed or the habitual system, or both [13,42]. Crucially, inflexible, habitual action tendencies in substance dependence could derive from either an overactive habit system or an under-active goal-directed system or a change in the balance between these two systems [43]. Non-sequential tasks, such as devaluation paradigms, cannot address this question as they do not allow specifications on whether habitual action tendencies rather rely on amplified stimulus-response associations (habit system) or on an impairment to update or modify action-outcome contingencies (goal-directed system), or a combination of both. Thus, we here used a Markov decision task which allows precise specifications on the individual contribution of each system on decision-making. The results presented here suggest mainly an effect on goal-directed choices; and particularly after non-rewards. This is in line with data showing orbitofrontal [44,45] and action-outcome impairments in substance dependence [13] and with accounts emphasizing the importance of re-asserting goal-directed control after losses or punishment [7,46-48]. Interestingly, administration of L-Dopa in this task selectively enhances goal-directed action selection on unrewarded trials [49]. This may speak to the profound alterations in the dopaminergic system in addiction [50-52]. Learning from non-rewards is known to rely on D2 receptors in the indirect, inhibitory loop of the basal ganglia [53,54]. While this has mainly been examined in the context of habitual, prediction-error based learning, Frank’s model also provides routes for influences on the prefrontal cortex via internal actions that update working memory [55].

The study identified a difference in DSST between patients matched for educational level. This finding is in line with other studies demonstrating deficits in the DSST in alcohol dependent patients [56,57] and addiction disorders are well known not only to relate to
striatal changes, but also decreased activation in the prefrontal cortex [52]. This may hint at an effect of alcohol on more general measures of cognitive functioning [57]. Goal-directed control has also been associated with prefrontal areas [58-60]. This raises the question of whether drugs directly affect goal-directed choices, or do so only secondary to their effects on other, more general cognitive functions. It will be important to also correct carefully for other measures of global function, such as working memory [25]. Indeed, confounding factors from even further afield may play a role, too. Stress, for instance, is known to affect the deployment of the goal-directed system [61] by decreasing activity of prefrontal regions [62], and it is not entirely implausible that patients may have felt more stressed during the experiment than controls. Moreover, it has been demonstrated that trait impulsivity is linked to decreased goal-directed control [63]. Given the finding, that self-reported impulsivity tends to be increased in substance dependent subjects [64,65], this might be another potential mediator for the effects reported here.

We did not find a difference on model-free learning. Very detailed computational theories map phasic dopamine signals decisively onto model-free learning [66-69]. Given the impact of drugs of abuse on dopamine [70], the absence of this finding is rather striking. However, the failure to observe an effect on model-free learning is a negative effect. Similarly, the study was powered to detect a group difference in either of the two components, but not a difference between them, and we therefore did not ask whether the difference in the model-based component was larger than the difference in the model-free component. Hence these findings need to be treated with caution and require replication. Furthermore, while animal studies have convincingly shown a shift towards model-free choices in addiction, and indeed with alcohol [4,5,7], there have been only limited investigations to substantiate this in humans so far [23,59]. One reason may be that it has been difficult to measure these two systems in humans, and often has required rather laborious tasks involving extended training [71,72]. While the current task is more subtle, and measures devaluation in a more continuous way, one caveat is that it is not clear whether it fully differentiates between goal-directed and habitual components at a neurobiological level [30]. Moreover, it is yet unclear, how different paradigms that have been designed to investigate dual-control mechanisms in humans indeed do examine a common psychological and neurobiological construct. Thus, further research should investigate within-subject correlations between performance in different dual-control tasks, such as paradigms that devalued outcomes by satiation
or by omission [72] and sequential learning tasks such as the 2 Step Task [30] or even more complex Markov-decision tasks [73].

We found that patients earned slightly less than controls. As a goal-directed strategy earns more, we initially thought this would be explained by the measure of goal-directedness. This was not so, suggesting that there might be further factors, possibly beyond the current model-free/model-based account affecting subjects’ performance on the task. However, this need not necessarily be the case, and in the future could be addressed by fitting the computational models of Daw and colleagues and examining specifically the softmax terms.

Finally, it is yet unclear whether disruption in model-based control in alcohol-dependent subjects is caused by excessive chronic alcohol intake or rather reflects a predisposition to alcohol abuse. Evidence for alcohol induced disruption of goal-directed behavior comes from demonstrations of devaluation insensitivity after chronic alcohol intake in rodents [4] and humans revealing disruption of goal directed behavior [24] and inhibitory top-down control [74] after acute alcohol administration. As it has been shown that impairments in cognitive control serve as a vulnerability marker for an increased risk for substance dependence [65,75-77] further research should use longitudinal designs in order to answer this chicken-and-egg-question.

In conclusion, we have shown rather selective and specific effects of chronic alcohol intake on model-based reasoning, and highlighted that this might arise from the impact of chronic alcohol intake on more general cognitive functions. Further research should pay detailed attention to how impairments in the goal-directed system are related to prefrontal and cognitive functioning.

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