Mechanisms underlying Alcohol Approach Bias and its Modification

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Commentary on Alcohol Approach Bias is Associated with both Behavioral and Neural Pavlovian-to-Instrumental Transfer Effects in Alcohol-Dependent Patients. Chen et al., 2023, Biological Psychiaty: Global Open Science.

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The interesting paper of Chen and colleagues in this issue (1) argues that the mechanisms underlying alcohol approach bias may overlap with those underlying Pavlovian-to-Instrumental transfer (PIT). It was found that patients who showed a stronger PIT effect in a task without alcohol cues, showed a stronger tendency to approach alcohol cues in an indirect alcohol approach avoidance task (aAAT), and this correlation was stronger in individuals with more severe alcohol dependence and individuals who scored high on trait-impulsivity. The strength of the behavioral approach bias was also related to neural activation of the NAcc in the PIT task, an area involved in reinforcement learning, processing of alcohol cues and craving. What do these findings tell us about mechanisms underlying an approach bias for alcohol in alcohol dependence and what is the clinical relevance of these findings?

Alcohol-dependent patients, as well as heavy drinkers, have often been demonstrated to show an automatically activated tendency to approach alcohol cues, the so-called alcohol approach bias. This is clinically relevant, as a number of well-powered clinical Randomized Controlled Trials (RCTs) have demonstrated that this approach bias can be modified by approach bias modification (ApBM), which has yielded a consistent reduction in relapse rates of approximately 10% one year after treatment discharge, when added to abstinence-oriented clinical treatment (review: 2, see Refs 30-33 in 1). While clinically relevant, we should acknowledge that this is a small effect, similar to the effect size of the most effective medication in this domain. The small effect size also makes clear that ApBM is not a silver bullet solution and its effects are not yet well understood. For instance, it is unclear why this training is not effective in changing drinking behavior in healthy volunteers or in problem drinkers who wish to reduce their drinking in an online training (3), that is to say: ApBM helps them to reduce, but not better than sham training (in contrast to

the clinical findings). A better understanding of the cognitive (and neurological) mechanisms underlying the alcohol approach-bias might aid the development of more effective varieties of training.

The authors interpret their findings from dual process models that inspired the original development of ApBM and other varieties of cognitive bias modification (CBM), that differentiate between impulsive/associative processes and reflective processes (e.g., 4). Specifically, it is argued that approach bias and PIT effects may both depend on the activation of impulsive processes that also underpin alcohol dependence. From this perspective, the results can be interpreted as indicating that the (neuro)cognitive processes of (a subgroup of) addicted people are qualitatively different from other people. This is related to discussions surrounding the chronic brain disease model of addiction (5) as it may seem that (a subgroup of) addicted people have lost their ability to voluntarily make choices when faced with conditioned stimuli related to their addiction.

Notably, basic cognitive research on ApBM in healthy volunteers has yielded results that better fit with a single-process inferential perspective than with a dual-process perspective (6). For example, training effects require conscious awareness and can sometimes be generated by instruction only, rather than requiring repeated training. From an inferential account, behavior is the results of inferences (e.g., causal inferences or predictions) that are goal-directed, also if the behavior is self-defeating in the long run, as is the case with addictive behaviors. The predictive brain evokes behavior (e.g., drinking alcohol) because it predicts that this behavior can be a means to achieve a goal (e.g., relaxation after stress). Importantly, these inferential processes can often be highly automatic and context-dependent such that a given situational cue (e.g., stress) may readily evoke goal-directed inferences to engage in (addictive) behavior. Hence, this alternative

account suggests that it is important to include contextual antecedents as well as goals in training, as proposed in a new variety of cognitive bias modification: ABC-training (7). In this new variety of training, patients train in personally-relevant antecedent contexts (A, e.g., coming home stressed) to achieve their goals (Consequences, e.g., relaxation) in another way than by drinking alcohol (Behavioral alternatives, e.g., going for a walk). This new variety has yielded promising results in healthy volunteers (8), but still awaits testing in patients.

It is important to note that, from the inferential perspective, addiction is not the result of qualitative differences in processing for (subgroups of) addictive people. Instead, differences in (addictive) behavior result from people having learned to apply different automatic inferences throughout their (ontogenetic and epigenetic) learning history (their learned inferential network: Figure 1). It is therefore important to study which inferences underlie addictive behavior and to what extent practicing alternative inferences allows to better bring behavior under voluntary control by helping patients automatize behaviors that are more in line with their long-term objectives.

From this perspective, the results of Chen et al. (6) might be informative because they indicate that, for alcohol-dependent patients, alcohol approach bias and PIT rely on similar inferences. For instance, both PIT and alcohol approach bias may depend on cuebased inferences that a certain outcome is wanted (goal activation inferences that also play a role in nudging effects, see 9) or inferences that one is likely to readily engage in behaviour that fosters these outcomes (goal-directed active inferences, see 10). These inferences may relate to both alcohol dependence and trait impulsivity and partly rely on neurological activation in networks including the Nucleus Accumbens, that play a role in reward prediction. Furthermore, (changes in ) these inferences might relate to treatment

success which might explain the observed stronger association between approach bias and PIT in patients who relapsed (although the evidence for this effect was weak and the effect warrants replication). It can therefore be useful to assess whether targeting such inferences (as is done in ABC-training) provides opportunities for intervention.

In sum, we agree that testing the (neuro-) cognitive mechanisms underlying the approach-bias for alcohol, as well as other biases in information processing that play a role in addiction, is important for a better scientific understanding of the puzzles surrounding addiction. As such, the results of Chen et al. provide information that could also be used for improving treatment, especially when this information is integrated with other empirical findings in reference to recent theorizing. Ultimately, it remains to be tested whether inference-based cognitive training indeed has stronger effects in patients as would be predicted from theory and promising findings, and how this relates to PIT and it's neural underpinnings.

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## **FIGURES**

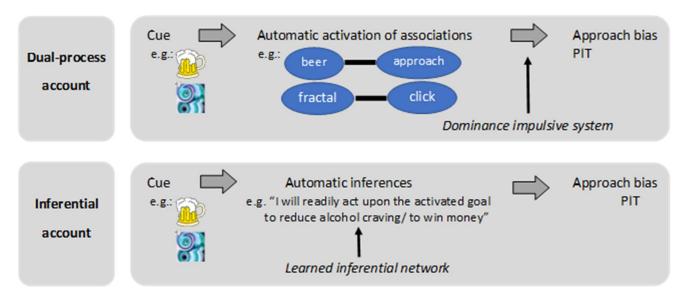


Figure 1. Illustration of the mental processes underlying PIT and approach alcohol bias according to dual-process and inferential accounts. In the dual-process account, a cue (e.g., an image of a beer or a fractal image previously paired with a wanted outcome) may lead to the automatic activation of mental associations (e.g., the association between beer and approach or between the fractal image and a response that previously led to the wanted outcome). Depending on the dominance of their impulsive system (trait impulsivity), this activation may determine approach bias (e.g., faster responses to beer cues) and PIT responding (e.g., more responses that previously led to the wanted outcome). In contrast, in the inferential account, the same cues are thought to evoke automatic inferences such as the inference that a certain outcome is wanted and that one is likely to readily engage in actions that previously served this outcome. These inferences depend on a person's network of learned inferences and may determine approach bias and PIT responding.