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Decision Making in Alcoholic Patients and Its Contribution to Relapse

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It is not surprising that people who anticipate alcohol's positive effects (positive alcohol expectancies) are more likely to drink. More formally, alcohol expectancies are generated by the interoceptive experiences that alcohol consumption generates, giving rise to mental representations of its reinforcing effects. Thus, positive expectancies that represent the reinforcing properties of alcohol can result from strong interoceptive cues and lead to drug seeking and consumption according to pavlovian conditioning theories of addiction.

Several studies have examined the associative power between positive alcohol expectancies and alcohol drinking, as well as their contribution to relapse in alcoholic patients during abstinence (1).

Perhaps it is surprising that Sebold *et al.* (2) in this issue of *Biological Psychiatry* found that alcohol expectancies were not higher in alcoholic-dependent individuals who relapse compared with successful abstainers. However, alcohol expectancies did moderate behavior in relapsers. In this group, more positive alcohol expectancies were associated with less goal-directed behavior, while in the abstainers and healthy subjects the opposite relationship held. The authors suggest that healthy subjects and abstainers with high positive alcohol expectancies make more informed decisions about their drinking using control mechanisms. Relapsers with high alcohol expectancies, on the other hand, are less likely to make informed decisions and instead are influenced by habitual responses that are generated by interoceptive cues acting as positive expectancy representations.

The task used by Sebold *et al.* (2) is a two-step task that challenges the learning of strategies in order to choose actions that lead to positive outcomes. In two steps the subject either follows an action by using the information given in the two-step process of choices (model-based learning) or performs an action based on the value of the outcome but without taking into account the information provided (model-free learning). Model-based learning uses the mental representation of the outcome and the ways to obtain it (goal-directed behavior), whereas model-free learning is only concerned with the response for the outcome (habitual response). Thus, the task challenges control mechanism processes and is based on dual process models supporting addictive behaviors (3). Dual process models of addiction suggest that the behavior to get the reward associated with the drug is driven both by goal-directed (model-based) behavior and habitual (or model-free) behavior; as addiction progresses, a shift of behavior from goal-directed to habitual occurs.

Earlier work examining goal-directed and habitual behavior and their association with alcohol has not taken into account alcohol expectancies. Donamayor *et al.* (4) found that binge drinking is associated with reduced goal-directed behavior in a two-step task, indicating a tendency of this population to make decisions on the basis of habitual rather than reflective processes. However, the Donamayor *et al.* study (4) did not look at alcohol expectancies, so it is not clear whether binge drinkers in their study also had high alcohol expectancies. There have been controversies with regard to findings on this task in alcoholic patients. In the current study, Sebold *et al.* (2) show reduced goal-directed behavior only in severe relapsing alcoholic patients who had high positive alcohol expectancies. However, a previous study by Sebold *et al.* (5) in which positive alcohol expectancies were not taken into account found that alcoholic patients who are early in abstinence behave more habitually in this task. On the other hand, in a study with alcoholic patients, Voon *et al.* (6) did not find any differences between alcoholic patients and healthy subjects and suggested that lack of an effect was due to timing of testing (late in abstinence). Thus, findings with alcoholic patients in this task may vary depending on time of testing. It would therefore be important to know if alcohol expectancies in alcoholic patients differ in their intensity depending on time after initiation of abstinence (i.e., if the different findings are caused by differing intensity of positive alcohol expectancies at the time of testing).

Across the many studies using the two-step task, including the study by Sebold *et al.* (2), the brain signature of both model-based and model-free systems includes the medial prefrontal cortex (mPFC) (in particular lateral and ventromedial PFC [vmPFC]) and striatum (7). In an early study (8) we demonstrated the involvement of striatum and vmPFC using the incentive conflict task, which challenges relapse-related behavior. The incentive conflict task puts demands on decision making under conditions requiring conflict resolution. Alcoholic patients attempting abstinence experience intense conflict between the desire to take the drug and the requirement to abstain. Resolving such a conflict requires controlled decision making, a process similar to the process required in the two-step task for the model-based response. In the incentive conflict task, the subject first learns that two independent discrete cues (e.g., A and B) signal reward availability, so that they acquire incentive properties. However, in a second phase, while the individual cues continue to signal reward availability, when presented together as a compound (AB) they signal unavailability of reward, or the potential for punishment. Thus, when the cues are presented in combination, there is a mixed message: on one hand, the individual cues elicit positive expectations and prompt reward-seeking; on the other hand,

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at the same time the combination signals that reward is unavailable, requiring a re-evaluation of the reward contingencies and abstinence from reward-seeking behaviors. Alcoholic patients are impaired in this task.

Importantly, the incentive conflict task showed a larger impairment of performance in alcoholic patients with multiple detoxifications, and I was interested to see that relapsers in the Sebold *et al.* (2) study had experienced more previous detoxifications and that the number of detoxifications was associated with more habitual behavior. The contribution of alcohol expectancies in these effects is not surprising, because it indicates that high expectancies and their association to habitual behavior can lead to relapse repeatedly (i.e., after every effort to abstain and therefore to multiple detoxifications). Sebold *et al.* (2) argue that the effect of the number of detoxifications is confounded by age, because correcting for age takes away the effect of the number of detoxifications. However, the groups (healthy subjects, abstainers, and relapsers) did not differ with regard to their age. Age can be associated with the number of detoxifications (i.e., older patients are more likely to have undergone more detoxifications). However, age has also been shown to modulate alcohol expectancies across the life span (9), so it is possible that age contributes to some of the alcohol expectancy effects in the study by Sebold *et al.* (2).

Sebold *et al.*'s (2) voxel-based morphometry findings indicated reduced gray matter density in mPFC in relapsers compared with healthy subjects. Similarly, we have previously shown that the number of detoxifications in alcoholic patients is associated with decreased gray matter volume in vmPFC (8). With regard to functional imaging, they found in relapsers, when compared with abstainers and healthy subjects, a reduced activation in a region of mPFC associated with model-based (reflective) behavior. It was surprising that the Sebold *et al.* study (2) did not show an association between the number of detoxifications and model-based neural correlates in the mPFC.

In studying the neural signature associated with the incentive conflict task, we found it captures a specific function associated with resolving a conflict generated by the need to withhold reward seeking in a context that encouraged reward seeking activating the vmPFC. When subsequently the subject has to withhold the behavioral response (a type of habitual overlearned response) required during reward seeking, the superior frontal gyrus is activated. In our study, both structures (the vmPFC and superior frontal gyrus) were damaged in alcoholic patients, and, in particular, those who had experienced a higher number of detoxifications. Drawing parallels between the two studies by Sebold *et al.* (2) and Duka *et al.* (8) suggests that future studies should examine the role of alcohol expectancies on behaviors leading to relapse and, in particular, decision making.

Data from a study that investigated alcohol acute effects on reflection impulsivity, a form of decision making under conditions of uncertainty, suggest that negative alcohol expectancies also play an important role on how alcohol affects decision making (10). Participants anticipating that greater levels of cognitive and behavioral impairment will result from alcohol (i.e., high negative alcohol expectancies) showed reduced reflection impulsivity as measured with the Information Sampling Task. Alcohol expectancies were stronger at modulating behavior in this task than alcohol itself, suggesting that cognitive alcohol outcome expectancies affect this form of impulsive decision making. These data suggest that the impact of negative alcohol expectancies may also be of importance in contributing to relapse.

Taken together, the findings reported by Sebold *et al.* (2) highlight the development of habit-like and maladaptive decision-making processes as addiction progresses, in keeping with previous evidence, while at the same time introducing the importance of positive alcohol expectancies as contributors to these processes.

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Article Information

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