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Abstract

Alcohol Use Disorder (AUD) is a common mental disorder characterized by the gradual escalation of alcohol consumption and cycles of remission and relapse. Although much research focuses on the etiology of AUD, a comprehensive understanding of the cognitive factors that may predispose individuals to develop this disorder is still lacking. In recent decades, increasing attention has been given to the role of cognitive bias as a significant factor influencing vulnerability to various mental disorders, such as depression and anxiety, which are often among the reasons for turning to alcohol. In the case of AUD, cognitive bias has been shown to affect how individuals with alcohol dependence perceive and interpret alcohol-related cues. However, studying the cause-and-effect relationship between cognitive bias and AUD is challenging, particularly before the onset of addiction.

To better understand this relationship, I utilized an animal model, which allows for the assessment of cognitive bias in rats before long-term alcohol exposure. The study aimed to determine the role of various aspects of biased cognition, such as sensitivity to positive and negative feedback, as well as judgement bias, defined as optimism and pessimism, in individual susceptibility to transitioning from controlled alcohol use to uncontrolled alcohol abuse.

In the initial studies, I investigated whether sensitivity to positive and negative feedback, measured as stable cognitive traits, affects the acquisition and maintenance of alcohol-seeking and consumption behaviors in rats. Sensitivity to positive and negative feedback was assessed using a series of probabilistic reversal learning tests. I induced alcohol consumption escalation in rats through intermittent free access to alcohol. I then examined the interaction of feedback sensitivity and propensity to the development of compulsive alcohol seeking when it was punished. Additionally, I measured motivation to seek alcohol, the rate of extinction of instrumental responses, and the reinstatement of alcohol-seeking behaviors after a period

of abstinence. Furthermore, together with colleagues from the Laboratory of Biochemical Pharmacology at the Institute of Pharmacology PAS, we measured mRNA levels in selected brain regions and levels of corticosterone and adrenocorticotropic hormone in the blood to correlate behavioral results with biological mechanisms.

I showed that lower sensitivity to positive feedback in rats was associated with an increased motivation to seek alcohol after negative experiences related to it. Rats insensitive to positive feedback were more likely to reinstate alcohol-seeking after a period of abstinence and had higher levels of stress hormones in their blood compared to rats sensitive to positive feedback. Conversely, higher sensitivity to negative feedback reduced susceptibility to compulsive alcohol-seeking and accelerated the extinction of such behaviors when alcohol was no longer available. These behavioral effects were associated with changes in gene expression related to various neurotransmitter systems in the brain and ethanol metabolism.

I then analyzed how optimism and pessimism, measured as stable and enduring behavioral traits, interact with alcohol-related behaviors in rats. The animals underwent ambiguous-cue interpretation tests to assess their tendencies towards optimism or pessimism. Using free access and instrumental paradigms, I examined their alcohol-seeking and consumption behaviors. We also conducted gene expression analysis in selected brain structures and determined the density of 5-HT_{1A}, 5-HT_{2A}, and D_2 receptors using autoradiographic analysis. We found that under free access conditions, "pessimistic" rats consumed more alcohol than "optimistic" rats, which was associated with changes in gene expression and 5-HT_{2A} receptor density in the nucleus accumbens.

The results suggest that various aspects of biased cognition, such as sensitivity to positive and negative feedback and tendencies towards optimism or pessimism, significantly interact with individual susceptibility to transitioning from controlled to uncontrolled alcohol abuse. These findings may enhance our understanding of the mechanisms underlying AUD and contribute to the development of new therapeutic strategies.