

Editorial: Heavy Adolescent Alcohol Use: An Accelerant of Impulsivity?

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It has been difficult to disentangle factors conferring vulnerability to substance use disorders (SUDs) from the consequences of substance use. Reward sensitivity and impulsivity have been identified as adolescent risk factors that confer vulnerability for later problematic substance use.^{1,2} Studies also suggest, however, that substance use itself affects brain development and behavior and that some of the same risk factors that predispose youth to SUD (eg, reward sensitivity and impulsivity) may be brought on or worsened by the neurotoxicity of drugs of abuse.^{3,4} Studies examining neural and behavioral correlates of SUDs commonly include youth with varying degrees of substance exposure; thus development of vulnerabilities to substance abuse are difficult to separate from the effects of substance use. In this issue of *JAACAP*, Ivanov *et al.*⁵ advance our field's knowledge in this area by leveraging longitudinal data from the European IMAGEN dataset ($n = 2,200$)⁶ in order to characterize predictors of alcohol use at age 16 as well as trajectories of impulsivity. This design allows investigation into whether alcohol drinking in adolescence may actually be related to worsening impulsivity. The authors followed a subset of the IMAGEN sample, 304 substance-naïve 14-year-olds over 2 years. Reward system function in the brain was assessed at baseline by collecting functional magnetic resonance imaging scans during a Monetary Incentive Delay (MID)⁷ task which assessed neural response to reward anticipation and outcome. Impulsivity and delay discounting, the propensity to select smaller immediate rewards versus larger, delayed rewards, were also assessed at baseline and follow-up. Linear regression was used to evaluate longitudinal associations among the frequency of alcohol use at age 16 and impulsivity, delay discounting, and reward system function at age 14. Reward system function was measured by activation in medial orbitofrontal cortex (mOFC) and ventral striatum regions of interest during the highest versus the lowest reward levels on the MID task. These regions are involved in key aspects of reward processing, including valuation of rewarding stimuli and outcomes.^{8,9}

The authors reported an interesting nonlinear relationship between impulsivity and frequency of alcohol use across time. Specifically, youth who did not initiate alcohol use or who used alcohol on only a few occasions from ages 14 to 16 showed a developmentally expected decline in impulsivity. In contrast, youth who used alcohol very frequently (eg, on 40 or more occasions) actually showed an increase in impulsivity across time. Subjects started without significantly different levels of impulsivity at age 14, suggesting that impulsivity is a factor that, while contributing to problematic substance use maintenance, may also be worsened by increasing use of alcohol. Regarding the neuroimaging findings, blunted reward responsiveness in the mOFC at baseline was associated with greater alcohol use at age 16, even after accounting for impulsivity and delay discounting rates at age 14. Given the role of the mOFC in reward processing, the authors speculated that this blunted responsiveness reflects difficulty representing the value of rewards, perhaps interfering with differentiation between small versus large amounts of drugs of abuse, and contributing to problematic substance use. Thus, blunted mOFC responsiveness to reward in substance-naïve adolescents may represent a neural “marker” of vulnerability for later problematic substance use.

Findings in the study by Ivanov *et al.*⁵ advance the field in several ways. First, these results suggest a nuanced role of impulsivity and delay discounting in SUD risk. These constructs have been implicated in SUD trajectories across adolescence, including risk for substance initiation among substance-naïve youth and escalation to problematic substance use among substance-exposed youth.¹⁰ In the current sample, baseline impulsivity and delay discounting did not differ between groups of adolescents who went on to use alcohol at different frequencies. This likely reflects the nature of the sample, which was selected to limit risk factors for substance abuse related to exposure at any point in development and across generations (ie, in-utero substance exposure and family history of SUDs) and excluded youth who had already begun using. Thus, the population studied here likely represents only a subtype of youth who develop

SUDs. Youth at higher risk may have different trajectories of impulsivity, sensation seeking, brain activation findings, and influences from alcohol than the currently studied sample.

Furthermore Ivanov *et al.*'s⁵ findings highlight the possibility of identifying neural markers of vulnerability to SUDs and the complexity of associations between substance abuse risk and components of the reward processing system across development. Adolescents on varying substance abuse trajectories were distinguished by mOFC activation during reward outcome, rather than reward anticipation, suggesting that a key area in need of intervention is atypical encoding of the valuation of rewards for future experience. Indeed, the authors speculate this pattern of dysfunction reflects compromised stimulus value assessment, which could lead to difficulty distinguishing between rewarding properties of, for example, small versus large amounts of alcohol and ultimately facilitate SUDs through a need to consume more alcohol to experience its rewarding properties.

The authors note that the utility of brain-level measurements has been questioned^{11,12}; however, the current data highlight the utility of neural markers above and beyond report-based measurements in models evaluating risk for youth substance abuse, particularly in clarifying underlying mechanisms. These findings are a first step toward understanding how neural and report-based measurements can be used to identify adolescents at risk for problematic substance use and thereby inform indicated prevention strategies. Effective therapies for substance abuse (eg, contingency management) already focus on altering maladaptive substance-related contingencies facilitated by reward processing.¹³ Preventing initiation to substance use

and transition to SUDs in adolescents with blunted mOFC activation to reward outcomes may involve therapies focused on bolstering rewarding properties of adaptive activities (eg, healthy social relationships, physical activity) and supporting strong formation of these contingencies. Establishing the clinical utility of neural markers for intervention will involve careful replication as well as longitudinal examination of risk trajectories as predictors of treatment response. As this research unfolds, it is likely that the strongest predictive/selective models will integrate information gathered from multiple levels of measurement, including neural, behavioral, and report-based measurements.¹⁴ The authors' present study represents an exciting advance toward using brain-level data to inform assessment and treatment.⁵

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