American College of Neuropsychopharmacology

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CORRESPONDENCE

Increasing ecological validity in neuropsychopharmacology research on the relationship between alcohol use and uncertain stressors

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TO THE EDITOR:

We enthusiastically read Gorka et al. [1]. Earlier laboratory work from both their group and authors of this letter (e.g., refs. [2, 3]) highlight stressor uncertainty as a key moderator of alcohol's long reported but inconsistently observed stress response dampening effects. Importantly, this research identifies exaggerated stress reactivity to uncertain stressors as either a consequent "disease marker" of repeated alcohol use (i.e., drug induced neuroadaptation; [3]) or, as suggested by Gorka et al. [1], a pre-morbid risk factor for alcohol use disorder. Gorka et al. [1] provided critical adjudication between these competing hypotheses using a rigorous longitudinal approach and a well-validated psychophysiological task. Though the sample's preexisting alcohol exposure limits evidence for premorbidity, Gorka et al.'s [1] study provides intriguing data for the premorbid risk factor hypothesis which may inform intervention efforts for excessive alcohol use.

Gorka et al. [1] speculated that those "hyper-reactive to [uncertain threat] express vulnerability to coping oriented motives, or 'self-medication,'" and, "The subjective… relief gained from intoxication can contribute to [alcohol] expectancies … and promote coping-motives for alcohol use." Although speculation about potential clinical implications of basic research is common, empirical confirmation of even a tenuous connection between implicit measures (e.g., fMRI & startle) with drinkers' subjective perceptions, cognitions, and subsequent drinking is sparse. Therefore, we agree with Gorka et al. [1] that reactions to uncertainty "can be captured at multiple units of analysis and similarly relate to real-world drinking behaviors." and we propose this relationship will only be established if the units of analysis include subjective expectations and experience ([2, 4]). This will not only better connect neurobiology to real-world behavior, but also inform research in related sub-fields (e.g., expectancy).

Demonstrating this in an undergraduate sample similar to Gorka et al.'s [1], we used a novel experimental affective forecasting task (https://osf.io/pskg7/) wherein 158 drinkers (Mean (SD) age = 19.7 (1.8); 63% female, 1% nonconforming; past-month binge-drinking = 67.1%;) reported expectations about their anxiety and alcohol's effects during imaginal stressor exposures based on social anxiety measures (e.g., ref. [5]). Exposure presentation was counterbalanced, once with a relatively uncertain negative outcome and once with a relatively certain one (see https://osf.io/pskg7/ for details). Participants forecasted (1–100) significantly less anxiety when they imagined being intoxicated relative to sober for uncertain scenarios ($\eta_p^2 = 0.81, b = -21.58$, $t(156) = -26.31$, $p < 0.001$) than for certain scenarios ($\eta_p^2 = 0.82$, $b = -19.76$, $t(156) = -25.24$, $p < 0.001$); interaction ($\eta_p^2 = 0.07$, $b = -1.82$, $t(156) = -3.41$, $p < 0.001$; Fig. 1). Neither gender nor binge-drinking moderated results (p's > 0.645). This complements Gorka et al. 2023 and related work (e.g., refs. [2, 3]) by suggesting that youth indeed *expect* alcohol to lower their anxiety more in relatively uncertain compared to certain social situations. Such nuance has not been a focus in alcohol expectancy research and its discovery was motivated by neuropsychopharmacology research like Gorka et al.'s [1].

These results are an initial step towards connecting Gorka et al.'s and our own lab's findings to drinking motivations. Only through simultaneously measuring varied response domains (e.g., neural; self-reported expectations; overt choice), phenomena that predicts drinking (e.g., salience and craving [6]), manipulating additional stressor characteristics (e.g. uncontrollability [2]), in and outside the laboratory (e.g., mobile psychophysiology and ecological momentary assessment) we will strengthen these connections and build a robust foundation for transformative understanding of problematic alcohol use. This may support therapeutic development targeting neurotransmitter systems involved in uncertain stressor reactivity

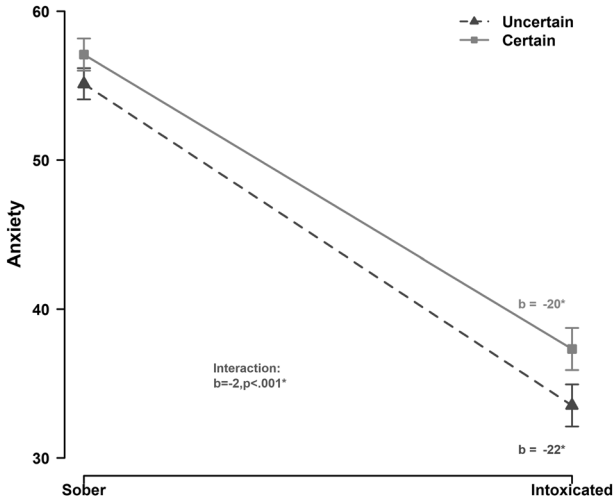

Fig. 1 Effects of stressor certainty and imagined intoxication. Confidence bars represent + one standard error for point estimates from the GLM. GLM coefficients show the simple effect of imagined intoxication for each stressor type. (*$p < 0.05$). Figure © 2023 Daniel E. Bradford, Amelia S. Dev, Angelica DeFalco, Freya Whittaker, Kiara R. Timpano under Creative Commons Attribution 4.0 International Public License CC-By.

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and/or (re)appraisal skills for decreasing stressor uncertainty specifically rather than stress-coping skills broadly.

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AUTHOR CONTRIBUTIONS

DEB, ASD, & KRT developed the study concept and design, Data collection was performed by ASD & KRT. DEB, ASD, & KRT performed the data analysis and interpretation, DEB, AD, and FW drafted the letter. ASD & KRT provided critical revisions. All authors approved the final letter.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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