


ORIGINAL ARTICLE

Sleep quality impacts the link between reactivity to uncertain threat and anxiety and alcohol use in youth

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Funding information

National Institute on Alcohol Abuse and Alcoholism, Grant/Award Number: R01AA028225

Abstract

Individual differences in reactivity to unpredictable threat (U-threat) have repeatedly been linked to symptoms of anxiety and drinking behavior. An emerging theory is that individuals who are hyper-reactive to U-threat experience chronic anticipatory anxiety, hyperarousal, and are vulnerable to excessive alcohol use via negative reinforcement processes. Notably, anxiety and alcohol use commonly relate to disruptions in sleep behavior and recent findings suggest that sleep quality may impact the link between reactivity to U-threat and psychiatric symptoms and behaviors. The aim of the current study was to examine the unique and interactive effects of reactivity to U-threat and sleep quality on anxiety symptoms and drinking behavior in a cohort of youth, ages 16–19 years. Participants ($N=112$) completed a well-validated threat-of-shock task designed to probe individual differences in reactivity to U-threat and predictable threat (P-threat). Startle eye-blink potentiation was recorded during the task as an index of aversive reactivity. Participants also completed well-validated self-report measures of anxiety and depression symptoms, lifetime alcohol use, and current sleep quality. Results revealed significant startle reactivity to U-threat by sleep quality interactions on anxiety symptoms and lifetime drinking behavior. At high levels of sleep disturbance (only), greater reactivity to U-threat was associated with greater anxiety symptoms and total number of lifetime alcoholic beverages. These results suggest that sensitivity to uncertainty and chronic hyperarousal increases anxiety symptoms and alcohol use behavior, particularly in the context of poor sleep quality.

KEYWORDS

alcohol use, anxiety, startle reactivity, uncertain threat

1 | INTRODUCTION

Converging lines of research suggest that increased reactivity to uncertain stressors or threats (U-threat) are associated with several forms of psychopathology (Gorka et al., 2017; Radoman et al., 2019). U-threat is often defined as threat that is unpredictable in its temporality, intensity, frequency, or duration. It is a specific form of

stress/threat that elicits a generalized feeling of apprehension and hypervigilance that is not associated with a clearly identifiable source, referred to as anticipatory anxiety (Barlow, 2000; Davis, 1998; Jackson et al., 2015). The U-threat is in contrast with predictable threat (P-threat), which is signaled by a discrete cue and elicits a phasic response to an identifiable stimulus that is time-locked to the threat (Barlow, 2000; Davis et al., 2010). The U-threat

and P-threat produce distinguishable aversive states that are mediated by overlapping, but separable, neural circuits (Alvarez et al., 2011; Davis, 2006). Several studies demonstrate that heightened reactivity to U-threat, but not P-threat, is an important transdiagnostic factor in the development and maintenance of a variety of disorders and behavioral issues (e.g., Barlow, 2000; Gorka et al., 2017).

Response to U-threat and P-threat has been frequently assessed in the lab using the No-Predictable-Unpredictable (NPU) paradigm (Schmitz & Grillon, 2012). The NPU paradigm is translational with three within-subjects conditions: no-shock (N), predictable electric shock (P), and unpredictable electric shock (U). The task includes loud bursts of white noise that are used to elicit and record the startle eyeblink reflex, a highly reliable cross-species index of aversive reactivity (Bradley et al., 1990; Grillon & Baas, 2003; Lang et al., 1990). Using the NPU, our group and others have demonstrated that greater startle potentiation to U-threat, but not P-threat, characterizes individuals with anxiety disorder and fear-based anxiety disorders including panic disorder, PTSD, social anxiety disorder, and specific phobias (Gorka et al., 2017; Grillon et al., 2008; Nelson et al., 2013). Studies also show that magnitude of startle reactivity to U-threat correlates with severity of current anxiety symptoms (Lieberman et al., 2017; Nelson & Hajcak, 2017) and predicts family history of anxiety psychopathology (Nelson et al., 2013). Benzodiazepines and cognitive-behavioral therapy, two efficacious therapies for anxiety, have been shown to selectively reduce startle reactivity to U-threat (Gorka et al., 2017; Grillon et al., 2006). Combined, this literature suggests that heightened U-threat response and chronic anticipatory anxiety are central to the pathophysiology of anxiety.

In addition to anxiety, studies show that individuals with current and past AUD exhibit increased startle reactivity to U-threat, but not P-threat, compared with controls (Gorka et al., 2020; Gorka & Shankman, 2017; Moberg et al., 2017). Magnitude of startle reactivity to U-threat (only) correlates with measures of problem alcohol use and coping-oriented motives for drinking behavior (Gorka et al., 2020). These findings align with previous work that demonstrates that alcohol intoxication selectively and effectively dampens startle reactivity to U-threat (Bradford et al., 2013). Studies show that as threat uncertainty increases, so does the magnitude of alcohol's acute stress-dampening effects (Hefner et al., 2013). Alcohol therefore targets the biological, affective and/or cognitive processes engaged by threat uncertainty (Gorka et al., 2018). An emerging hypothesis is that those who are most sensitive and reactive to uncertain threat, and thus experience chronic heightened anticipatory anxiety, are particularly motivated to consume alcohol to dampen their distress.

This sets the stage for negative reinforcement processes to drive excessive, continuous alcohol use.

Taken together, existing research study indicates that increased reactivity to U-threat and chronic anticipatory anxiety can drive the development of anxiety and alcohol use behavior. Importantly, however, not all individuals who are sensitive to U-threat develop anxiety symptoms nor engage in alcohol use. There are likely important moderators that impact the associations between individual differences in U-threat, anxiety symptoms, and alcohol use behavior. It is important we identify these moderators to understand who is most-at risk. Moderators also shed light on potential prevention and intervention targets and improve mechanistic understanding of risk pathways. Individuals with anxiety and alcohol use problems commonly report experiencing disordered sleep including shorter sleep duration, frequent awakenings, and difficulty falling asleep (Koob & Colrain, 2020). Evidence indicates there are bidirectional relationships between sleep disturbance, anxiety, and alcohol use. For instance, increased daytime arousal has been shown to lead to poorer nighttime sleep quality, whereas improvements in sleep quality correlates with improvements in anxiety symptom severity (Talbot et al., 2014). Meanwhile, difficulty falling asleep has been linked to subsequent alcohol use (Wong et al., 2010), whereas daily alcohol use relates to poorer sleep quality (Chueh et al., 2019). Given that disordered sleep increases state anxiety levels and arousal (Pires et al., 2016), we hypothesize that individuals who are sensitive to U-threat *and* experience poor sleep quality are particularly vulnerable to chronic hyperarousal and thus symptoms of anxiety and alcohol use. To date, no prior study has directly examined this hypothesis and explored the unique and interactive effects of sensitivity to U-threat and sleep quality on anxiety and/or drinking behavior.

The current study aimed to examine the moderating impact of sleep disturbance on the established links between startle reactivity to U-threat, anxiety symptoms, and alcohol use behavior in a cohort of youth aged 16–19 years old. Late adolescence and young adulthood are developmental periods marked by the emergence of anxiety symptoms, alcohol use behavior, and sleep changes (Baum et al., 2014; Masten et al., 2009). Testing the current study hypotheses in a youth cohort affords the opportunity to better understand potential links between these symptoms and constructs as they develop, and perhaps before they escalate to clinical levels of severity. All participants completed a well-validated battery of questionnaires and the NPU threat paradigm to probe startle eyeblink reactivity to U- and P-threat. We hypothesized that disordered sleep would moderate the associations between startle reactivity to U-threat and (1) anxiety symptoms and (2) alcohol use behavior. More specifically, we speculated that

at high levels of disordered sleep, reactivity to U-threat would be robustly associated with anxiety symptoms and alcohol use in youth. At low levels of disordered sleep, there would be a moderate link between these variables.

2 | METHODS

2.1 | Participants

One hundred and fifteen participants were recruited from the community as part of a larger study examining neurobiological mechanisms underlying the association between trauma exposure, psychiatric symptoms, and alcohol use. Individuals were recruited via social media advertisements and flyers posted in the Columbus, Ohio community including nearby high school and college campuses. Participants were required to be between the ages of 16 and 19, as this age often reflects the initial emergence and escalation of alcohol use and co-occurring psychopathology. Participants were enrolled into one of two groups: (1) lifetime history of interpersonal trauma exposure (i.e., physical assault, sexual assault, or immediate family violence) or (2) no lifetime history of interpersonal trauma exposure. Given that the aims of the larger study included prediction of initial onset of alcohol use disorder, participants were required to have had minimal alcohol exposure at enrollment (i.e., self-reported consuming >1 but <100 standard alcoholic drinks in their lifetime), but be at risk for the development of alcohol problems by virtue of self-reporting affiliation with risky peers and having access to alcohol. Exclusionary criteria included any major active medical or neurological illness, lifetime history of manic/psychotic symptoms, active suicidal intent, deafness, traumatic brain injury, current psychotropic medication use, lifetime history of alcohol or substance use disorder, and pregnancy. Individuals were instructed to abstain from drugs and alcohol at least 24 h prior to the lab assessments, which was verified via screening of urine and breath alcohol. All study procedures were approved by the Ohio State University Institutional Review Board. Participants provided written informed consent or assent with parental consent. Participants were monetarily compensated for their time. Three individuals were missing startle eyeblink data resulting in a final sample size of 112 youth.

2.2 | Self-report measures

Participants completed an initial screening session involving a battery of validated self-report measures. Sleep quality was assessed using the “gold-standard” Pittsburgh

Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI includes 19-items capturing seven components of sleep: quality, onset latency, duration, efficiency, disturbance, use of sleep medication, and daytime dysfunction. Participants were instructed to think of a typical night during the previous month for each item. Each component is scored from 0 to 3, with higher scores indicating worse sleep quality. The seven component scores are summed for a global score ranging from 0 to 21.

Current anxiety and depression symptoms were assessed using the Beck Anxiety Inventory (BAI; Beck et al., 1988) and the Beck Depression Inventory-II (BDI-II; Beck et al., 1996). The BAI is comprised of 21 self-report items scored on a four-point scale from 0 (“not at all”) to 3 (“severely”). Participants are asked about the past week with total scores ranging from 0 to 63. The BDI-II is also comprised of 21 self-report items scored on a four-point scale from 0 to 3. Participants are asked about the past two weeks with total scores ranging from 0 to 63.

2.3 | NPU task and startle data processing

The NPU startle task and procedures have been extensively described by our group (Gorka, 2020; Gorka & Shankman, 2017). Shock electrodes were first placed on participants' left wrist, and a shock work-up procedure was completed to identify the level of shock intensity each participant described as “highly annoying but not painful” (i.e., 1–5 mA). Participants then completed a 2-min startle habituation task involving presentation of six acoustic startle probes. The task itself was modeled after Grillon and colleagues' NPU threat task and included three within-subject conditions: no shock (N), predictable shock (P), and unpredictable shock (U). Text at the bottom of the computer monitor informed participants of the current condition. Each condition lasted 145 s, during which a 4-s visual countdown (CD) was presented six times. The interstimulus intervals (ISIs; i.e., time between CDs) ranged from 15 s to 21 s, during which only the text describing the condition was on the screen. No shocks were delivered during the N condition. A shock was delivered every time the CD reached 1 during the P condition. Shocks were delivered at random during the U condition. Startle probes were administered during both the CD and ISI. Each condition was presented two times in a randomized order, counterbalanced. Participants received 24 total electric shocks (12 in P, 12 in U) and 60 total startle probes (20 in N, 20 in P, 20 in U).

Startle data were acquired using BioSemi Active Two system (BioSemi; Amsterdam, The Netherlands) and stimuli were administered using Presentation (Albany,

CA). Electric shocks lasted 400 ms, and acoustic startle probes, which consisted of 103-dB bursts of white noise lasting 40 ms presented via headphones. Startle responses were recorded from two 4-mm Ag/AgCl electrodes placed over the orbicularis oculi muscle below the left eye. The ground electrode was located at the frontal pole (Fpz) of an electroencephalography cap that participants wore as part of the larger study. Data were collected using a bandpass filter of DC–500 Hz at a sampling rate of 2000 Hz.

Blinks were processed and scored according to published guidelines (Blumenthal et al., 2005): Applied using a 28 Hz high-pass filter, rectified, and then smoothed using a 40 Hz low-pass filter. Peak amplitude was defined within 20–150 ms following the probe onset relative to baseline (i.e., average activity for the 50-ms preceding the probe onset). Each peak was identified by software but examined by hand to ensure acceptability. Blinks were scored as nonresponses if activity during the post stimulus timeframe did not produce a peak that was visually differentiated from baseline. Blinks were scored as missing if the baseline period was contaminated with noise, movement artifact, or if a spontaneous or voluntary blink began before minimal onset latency. In the current sample, startle magnitude during N_{CD} was highly correlated with startle magnitude during U_{CD} ($r = 0.89$, $p < .001$) and P_{CD} ($r = 0.91$, $p < .001$). As discussed in Meyer et al. (2017), traditional subtraction-based difference measures are problematic for highly correlated variables. Therefore, to quantify the difference between threat and no-threat trials, we calculated a standardized residual score for U-threat ($U_{threat_{resid}}$) and P-threat ($P_{threat_{resid}}$) by saving the variance left-over (i.e., the amount of variability in a dependent variable [DV] that is not explained by an independent variable [IV]) in two simple linear regressions, where the N_{CD} (IV) was entered to separately predict the U_{CD} and P_{CD} (DVs). The U_{CD} residual score was used as the primary independent variable.¹

2.4 | Data analysis plan

To test our hypotheses, we performed a series of hierarchical linear regression analyses. In all models, biological sex (dummy coded) was included as a covariate and

¹We also calculated traditional startle potentiation scores by subtracting startle magnitude during N_{CD} from U_{CD} . To examine the reliability of our findings across various methods for quantifying U-threat reactivity, we re-ran our analyses with startle potentiation to U-threat as the independent variable. Results indicated that the pattern of results was identical.

entered in Step 1. Biological sex was assessed via self-report and included because there are well-established sex differences in anxiety symptoms and alcohol use (Pleil & Skelly, 2018; Zilberman et al., 2003). Presence of interpersonal trauma (yes = 1, no = 0) was also included in Step 1 given that subjects were enrolled into the study in one of two groups and trauma exposure is associated with psychopathology (McLaughlin & Lambert, 2017). The main effects of startle reactivity to U-threat and sleep disturbance (PSQI) were entered in Step 2. The interaction term was entered in Step 3. All continuous variables were first mean-centered.

Separate models were run for each outcome. Although the focus of the study was on anxiety and alcohol use, consistent with prior literature, we also tested our model with depression symptoms. Depression was highly prevalent in the sample (see Table 1) and often co-occurs with anxiety and alcohol use. In the Supplemental Materials, we also present models examining the role of startle reactivity to P-threat on our outcomes. Significant two-way interactions were followed up using a standard simple slopes approach (Aiken et al., 1991). Specifically, the moderator (i.e., PSQI) was re-centered at 1 SD above the mean for “high sleep disturbance” and 1 SD below the mean for “low sleep disturbance”. Two new interaction terms were created and post-hoc additional follow-up linear regression models were run at high and low sleep disturbance. All analyses were conducted using SPSS v27 (IBM).

3 | RESULTS

Results of the hierarchical linear regression analyses are presented in Table 2. For the anxiety model, there was a main effect of PSQI such that greater sleep disturbance was associated with greater anxiety. This main effect was qualified by a significant reactivity to U-threat by the PSQI interaction. At high levels of sleep disturbance, greater reactivity to U-threat was associated with greater anxiety ($\beta = .22$, $t = 2.01$, $p = .047$). At low levels of sleep disturbance, there was no association between the reactivity to U-threat and anxiety ($\beta = -.12$, $t = -1.04$, $p = .299$) (Figure 1a).

For the alcohol use model, there was a main effect of reactivity to U-threat such that greater startle potentiation to U-threat was associated with greater number of lifetime alcoholic drinks. This main effect was qualified by a significant reactivity to U-threat by PSQI interaction. At high levels of sleep disturbance, greater reactivity to U-threat was associated with greater lifetime alcohol use ($\beta = .45$, $t = 3.50$, $p < .001$). At low levels of sleep disturbance, there was no association between reactivity to U-threat

TABLE 1 Participant demographics and characteristics.

Demographics	
Age in years	18.09 (0.97)
Sex (% female)	66.07%
Ethnicity (% Hispanic)	8.93%
Education level (years)	12.09 (0.91)
Trauma group (yes)	53.57%
Race	
White	66.96%
Black	13.39%
Asian	8.04%
American Indian or Alaskan Native	0.00%
More than one race	9.82%
Unknown	1.79%
Baseline DSM-5 diagnoses	
Lifetime Major Depressive Disorder	51.79%
Current Major Depressive Disorder	7.14%
Lifetime Generalized Anxiety Disorder	8.93%
Current Generalized Anxiety Disorder	7.14%
Lifetime Social Anxiety Disorder	17.86%
Current Social Anxiety Disorder	9.82%
Lifetime Panic Disorder	0.89%
Current Panic Disorder	0.00%
Lifetime Specific Phobia	2.68%
Current Specific Phobia	1.79%
Lifetime Post-Traumatic Stress Disorder	19.64%
Current Post-Traumatic Stress Disorder	3.57%
Lifetime Alcohol Use Disorder	0.00%
Current Alcohol Use Disorder	0.00%
Lifetime Substance Use Disorder	0.00%
Current Substance Use Disorder	0.00%
Self-reported behaviors and clinical symptoms	
Average Pittsburgh Sleep Quality Index score	6.48 (2.97)
Depression Symptom Severity (BDI-II total score)	12.38 (9.18)
Anxiety Symptom Severity (BAI total score)	13.82 (10.10)
No. lifetime alcoholic drinks	33.87 (26.72)
Daily cigarette smoker (% yes)	0.00%

Abbreviations: BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II.

and lifetime alcohol use ($\beta = -.07$, $t = -0.51$, $p = .613$) (Figure 1b).

For the depression symptom model, there was a main effect of PSQI such that greater sleep disturbance was associated with greater depression. There was no main effect of startle reactivity to U-threat or two-way interaction.

4 | DISCUSSION

Studies show that reactivity to U-threat may be a risk factor for anxiety and problem alcohol use; though not all individuals who are sensitive to U-threat exhibit anxiety symptoms nor engage in drinking behavior. Theory and research suggest that sleep quality may impact the link between reactivity to U-threat and psychiatric symptoms and behaviors. The aim of the study was to directly test this hypothesis in a sample of youth at high-risk for psychopathology and substance use. Consistent with our hypotheses, results revealed significant startle reactivity to U-threat by sleep quality interactions on anxiety symptoms and lifetime drinking behavior. At high levels of sleep disturbance (only), greater reactivity to U-threat was associated with greater anxiety symptoms and total number of lifetime alcoholic beverages. Broadly, these results support theory suggesting that sensitivity to uncertainty and chronic hyperarousal increases anxiety symptoms and alcohol use behavior, particularly in the context of poor sleep quality.

Findings from the current study supported our overarching hypotheses. Specifically, we found evidence to suggest that the relationship between reactivity to U-threat and anxiety and alcohol use was observed at high, but not low, levels of sleep disturbance. Individuals who are sensitive to U-threat tend to experience increased anticipatory anxiety and chronic hyperarousal (Lieberman et al., 2017). Poor sleep quality is known to exacerbate daytime arousal and response to stress, which can then maintain sleep disruptions (Han et al., 2012). Those who are sensitive to U-threat, and inherently prone to sustained hyperarousal, may be particularly vulnerable to the deleterious effects of disrupted sleep and experience exaggerated levels of psychophysiological distress. Over time, the interactive influences between sensitivity to U-threat and poor sleep quality may manifest as anxiety symptoms and motivate the desire for relief/escape via alcohol use. Although alcohol may acutely dampen anticipatory anxiety and arousal, there are robust rebound effects and repeated alcohol use worsens anxiety and sleep quality (Stein & Friedmann, 2006). We therefore speculate that sensitivity to U-threat in the context of sleep disturbance promotes a vicious feedback loop contributing to anxiety symptoms and the motivation to use alcohol.

The current study did not yield significant results when examining the interactive effects of reactivity to U-threat and sleep quality on depressive symptoms. This null interaction is consistent with the broader literature suggesting that individual differences in reactivity to U-threat are not related to the onset and maintenance of depression. For example, our lab and others have shown that individuals with major depressive disorder (MDD)

TABLE 2 Results of hierarchical linear regression analyses.

Predictors	β	t	p -value	Adjusted R^2	ΔR^2	F for ΔR^2
Model 1: Anxiety symptoms						
Step 1				.07	.08*	4.91
Sex	0.26*	2.67	.009			
Trauma group (yes/no)	0.07	0.71	.480			
Step 2				.28	.23*	17.50
Startle to U-threat	0.06	0.69	.493			
PSQI	0.47*	5.71	<.001			
Step 3				.31	.03*	4.73
Startle \times PSQI	0.18*	2.18	.032			
Model 2: Lifetime drinks						
Step 1				.01	.02	1.27
Sex	-0.13	-1.29	.201			
Trauma group (yes/no)	-0.05	-0.48	.633			
Step 2				.03	.04	2.12
Startle to U-threat	0.20*	2.06	.042			
PSQI	-0.03	-0.32	.754			
Step 3				.09	.07*	8.08
Startle \times PSQI	0.28*	2.84	.005			
Model 3: Depression symptoms						
Step 1				.05	.07*	4.01
Sex	0.10	0.98	.330			
Trauma group (yes/no)	0.22*	2.21	.029			
Step 2				.36	.32*	27.82
Startle to U-threat	-0.03	-0.37	.711			
PSQI	0.57	7.43	<.001			
Step 3				.37	<.01	1.06
Startle \times PSQI	0.08	1.03	.306			

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; U-threat, unpredictable threat.

* $p < .05$.

and healthy controls demonstrate comparable levels of startle reactivity to U-threat during the NPU paradigm (Gorka et al., 2014; Shankman et al., 2013). Sensitivity to U-threat relates to several forms of psychopathology, but not all forms of psychopathology, and there is something specific about the associations between reactivity to U-threat, anxiety, and alcohol use behavior. Even in the context of disrupted sleep, increased reactivity to U-threat does not necessarily drive increased depressive symptoms. This lends further support to our theory regarding the role of hyperarousal (specifically) in anxiety and alcohol use outcomes.

Results of the current study suggest sleep quality is an important moderator of the association between reactivity to U-threat, anxiety symptoms, and alcohol use. Notably, there was no significant main effect of U-threat reactivity on anxiety symptoms in the omnibus model, which points

to a more nuanced relationship between these variables than previously considered. It is unclear to what extent sleep disturbance contributed to prior anxiety and U-threat reactivity findings given that these associations have not been investigated. With this in mind, it is remarkable that sleep quality is a relatively modifiable factor and numerous cognitive and behavioral strategies have been shown to improve sleep quality in youth (Åslund et al., 2018). It is possible that targeting sleep quality in adolescents and young adults could help disrupt negative reinforcement cycles of anxiety and alcohol use during a critical developmental period marked by onset and escalation of psychiatric symptoms and risk behavior. Given that reactivity to U-threat has at least some trait-like properties (Gorka et al., 2016), targeting sleep may be a more viable and impactful youth prevention initiative. First, however, longitudinal studies are needed to elucidate the directional

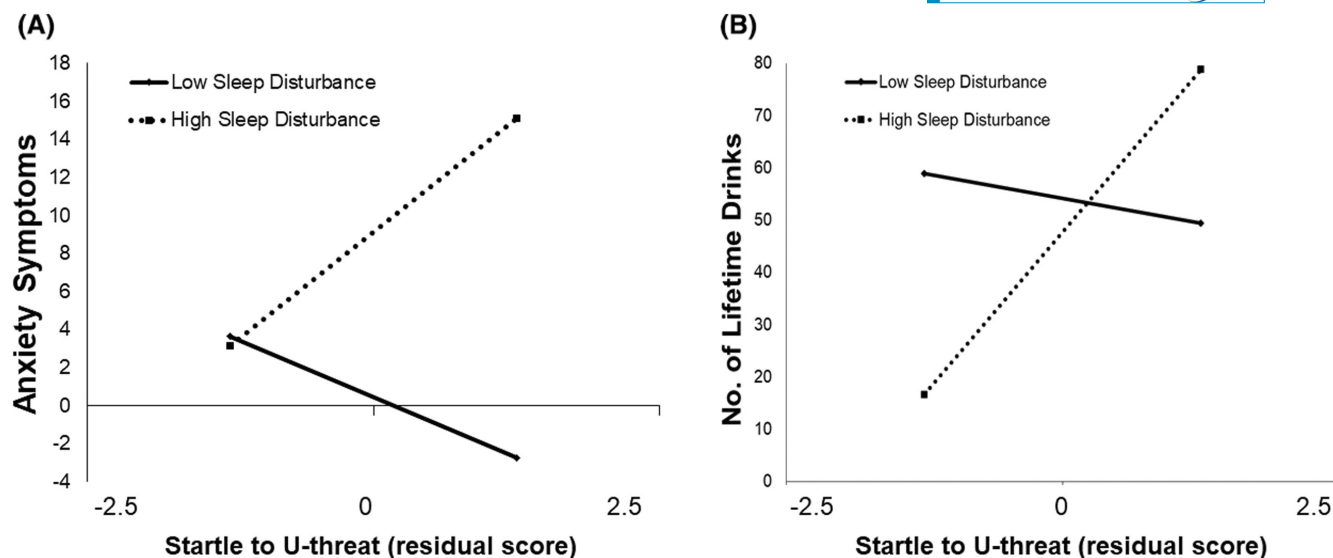


FIGURE 1 The moderating effect of sleep disturbance on the association between startle reactivity to unpredictable threat (U-threat) and anxiety symptoms (a) and the number of lifetime alcoholic beverages (b).

influences and mechanisms contributing to the observed pattern of results. If further supported, screening youth for poor sleep quality and high levels of sensitivity to U-threat may be a way to identify high-risk youth for early intervention efforts.

The present study has multiple strengths including the large youth cohort, use of well-validated measures, and objective measurement of reactivity to U-threat. The study also has several limitations. First, the inclusion/exclusion criteria were dictated by the design of the larger study and included youth with and without a history of trauma who were at risk for subsequent alcohol use and not currently taking psychotropic medication. Given the characteristics of the sample, it is unclear whether the findings generalize to other youth cohorts. Second, the sample reflects a non-clinical, non-treatment seeking cohort and it is unknown whether the findings would generalize to groups with higher levels of anxiety symptoms and/or problem alcohol use. Future longitudinal studies with a more heterogeneous sample are needed to account for potential study confounds and determine direction of effects.

It is important to note that our study is the first to test the interactive effects of sensitivity to U-threat and sleep quality on anxiety and/or drinking behavior. In summary, this study provides important findings suggesting that reactivity to U-threat is associated with anxiety and alcohol use behavior in the context of high, but not low, disrupted sleep. Broadly, these results provide support for existing theory and research suggesting that exaggerated anticipatory anxiety and chronic hyperarousal increase distress and the motivation for alcohol use. Sleep quality may be a meaningful factor in these associations and produce

bidirectional influences that contribute to and/or maintain anxiety and alcohol use. Given that sleep quality is an often over-looked modifiable factor in youth, future studies should explore the utility of targeting sleep quality in the context of preventive mental health-based strategies.

AUTHOR CONTRIBUTIONS

Kathryn Jenkins: Conceptualization; formal analysis; visualization; writing – original draft. **Jordan Difatta:** Data curation; investigation; writing – review and editing. **Emily Jones:** Data curation; project administration; supervision; writing – review and editing. **Kayla Kreutzer:** Project administration; supervision; writing – review and editing. **Baldwin Way:** Conceptualization; methodology; writing – review and editing. **K. Luan Phan:** Investigation; project administration; writing – review and editing. **Stephanie M. Gorka:** Funding acquisition; investigation; methodology; project administration; supervision; writing – review and editing.

FUNDING INFORMATION

The study was supported by the National Institute of Alcohol Abuse and Alcoholism, grant/award number R01AA028225 (principal investigator: S. M. Gorka).

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available at The National Institute of Mental Health Data Archive (NDA).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Data S1. Supporting Information.

Table S1. Results of hierarchical linear regression analyses testing unique and interactive effects of p-threat reactivity and sleep disturbance.

How to cite this article: Jenkins, K. C., Difatta, J., Jones, E. E., Kreutzer, K. A., Way, B. M., Phan, K. L., & Gorka, S. M. (2024). Sleep quality impacts the link between reactivity to uncertain threat and anxiety and alcohol use in youth. *Psychophysiology*, 61, e14490. <https://doi.org/10.1111/psyp.14490>