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# Drinking alcohol by mid-adolescence is related to reduced reward reactivity: Novel evidence of positive valence system alterations in early initiating female youth

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#### ABSTRACT

Initiation of alcohol use at younger ages is prognostic of later drinking problems. Reward system dysfunction is theorized to contribute to early initiation and escalation of drinking, but existing evidence supports both hyposensitivity and hypersensitivity as risk-markers; research employing effective indices of reward processing is needed for clarification. The reward positivity (RewP) is a well-established neurophysiological index of hedonic "liking," an important aspect of reward processing. Adult research has yielded conflicting findings, with different studies reporting reduced, enhanced, or null associations of RewP with engagement in or risk for harmful alcohol use. No study has examined relations between RewP and multiple indices of drinking in youth. Here, we examined how RewP measured in a gain/loss feedback task related to self-reported drinking initiation and pastmonth drinking, when accounting for age along with depression and externalizing symptoms, in 250 mid-adolescent females. Analyses showed that (1) compared to not-yet drinkers, adolescents endorsing drinking initiation responded less strongly to monetary gain (RewP) but not loss feedback (FN), and (2) past-month drinking was unrelated to both RewP and FN magnitude. These findings provide evidence for reduced hedonic "liking" as a concomitant of early drinking initiation in adolescent females and warrant further research with mixed-sex adolescent samples exhibiting greater drinking variability.

Initial consumption of alcohol during adolescence is a common experience. In fact, alcohol use during adolescence is more common than experimentation with any other substance (Johnston et al., 2019). Approximately 23% of nine- to ten-year-old youth report having already sipped alcohol (Watts et al., 2021), and most youth report having consumed one full drink by age 15 (e.g., Jackson et al., 2021; Sartor et al., 2016).

Although drinking initiation in early adolescence (e.g., 14 years) is more predictive of future alcohol-related problems than initiation in later adolescence (e.g., 16 years; Morean et al., 2014), early initiation is *generally* followed by a one-to-two year delay preceding onset of later "milestones" of use (e.g., first intoxication, higher frequency of drinking; e.g., Jackson, 2010; Jackson et al., 2021; Morean et al., 2014, 2018). However, a subset of early initiating youth bypass this typical delay and escalate directly from initial use to regular drinking (e.g., once or more per month; Jackson et al., 2021; Sartor et al., 2016), and this pattern is especially prognostic of further escalation of use in later adolescence (Deutsch et al., 2017; Jackson et al., 2021). Given evidence that alcohol-related neurological changes that heighten risk for future psy-chopathology are especially evident in adolescence (e.g., Casey & Jones, 2010; Clark et al., 2008; Spear, 2016; Wiers et al., 2007), it is important to identify pre-morbid indicators that can differentiate variance in alcohol use attributable solely to early initiation from variance related to early development of regular drinking (e.g., Jackson et al., 2021). Individual difference measures of sensitivity versus insensitivity to naturally-occurring rewards could provide a means for identifying individuals likely to follow these different trajectories (e.g., Blum et al., 2022).

One of the most widely studied risk markers for substance involvement is reward system dysfunction (e.g., Baskin-Sommers & Foti, 2015; Berridge & Robinson, 2003; Destoop et al., 2019; Rádosi et al., 2021); its importance as a transdiagnostic construct also has been emphasized in

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dimensional frameworks for the study of psychopathology, such as the Research Domain Criteria (RDoC) system within "Positive Valence Systems" (e.g., Cuthbert & Insel, 2013; Insel et al., 2010). While strongly implicated in substance experimentation and harmful use, the temporal relationship between reward sensitivity and alcohol use is unclear. On one hand, some research points to heightened responsiveness of reward-related neural circuitry (e.g., Freeman et al., 2020; Morales et al., 2018; Urošević et al., 2015), reflected psychologically in traits of impulsivity and sensation seeking (e.g., Buckholtz et al., 2010; Rádosi et al., 2021; Quinn & Harden, 2013) and lower effortful control (e.g., van Hemel-Ruiter et al., 2015; Bunford et al., 2022), as a risk factor for more rapid escalation of use in adolescents, although evidence suggests these relationships may differ depending on the substance of interest (e. g., tobacco versus cannabis: see Rádosi et al., 2021). Importantly, these psychological traits all covary with the general predisposition toward externalizing behaviors more broadly (i.e., latent disinhibitory tendencies; see Krueger et al., 2009; Young et al., 2009), operationalized in adolescents via measures of rule-breaking and aggressive behavior (Achenbach & Rescorla, 2001). Thus, an important priority in addiction research is to further investigate reward sensitivity as a predictor of early drinking, over and above current externalizing symptomatology (see Hussong et al., 2017; Joyner et al., 2019).

Conversely, other research and theory indicates that hyposensitivity to naturally-occurring reward may predispose toward problematic alcohol use by prompting individuals to pursue pleasurable experience through use of pharmacological agents (e.g., Blum et al., 2000, 2011, 2022; Bowirrat & Oscar-Berman, 2005; Casement et al., 2015; Telzer et al., 2013). An explanation for these contrasting accounts may lie in the role of reward responsiveness at different points in the progression of alcohol use-from first drink, to escalation of use, to persistent heavy drinking (e.g., Carey et al., 2017; Ewing et al., 2014; Waller et al., 2019). Accordingly, a major urgency in addiction research is to clarify how reward system dysfunction unfolds early in life, prior to extensive use. Understanding the role of early reward system dysfunction could be especially important in females, given existing data suggesting a heightened proneness to quick-onset escalation following initiation of use (i.e., "telescoped" trajectories; e.g., Cheng & Anthony, 2018; Diehl et al., 2007; Hernandez-Avila et al., 2004; Menary et al., 2017) and more severe drinking-related negative consequences (e.g., social problems; illness following consumption; Foster et al., 2014; Nolen-Hoeksema, 2004; Nolen-Hoeksema & Hilt, 2006) in girls and women compared to boys and men. With this in mind, examining the extent to which individual differences in reward processing are associated with early initiation and/or frequency of alcohol use in adolescent females is a critical research priority.

The amplitude of the reward positivity (RewP), a component of the event-related brain potential (ERP) elicited by visual feedback indicating gain (vs. loss), provides an effective measure of reward system function in adolescents (e.g., Bunford et al., 2022; Kallen et al., 2020; Nelson et al., 2016). Mechanistically, RewP amplitude appears to reflect a hedonic response to the initial receipt of reward attainment (Baskin-Sommers & Foti, 2015; Cuthbert & Insel, 2013; Proudfit, 2015), and is quantified as the average brain reactivity to gain versus loss feedback, thereby reflecting neural activation distinctively associated with receipt of reward (Foti et al., 2011). In contrast, neural activation following presentation of loss feedback (vs. gain) is alternatively termed the feedback negativity (FN; e.g., Thompson et al., 2023). Evidence for construct validity of the RewP includes findings showing that it relates positively to self-report and behavioral measures of reward sensitivity (e.g., Bress & Hajcak, 2013; Liu et al., 2014; Zubovics et al., 2021) and to heightened activation in neural regions implicated in reward processing as indexed by functional neuroimaging and EEG source localization (e. g., Becker et al., 2014; Carlson et al., 2011; Ryan et al., 2022). Supporting its use as an index of individual differences, the RewP demonstrates good amplitude stability across adolescence (Burani et al., 2019; Kujawa et al., 2018). Furthermore, RewP amplitude is blunted in

adolescent girls who experience heightened dysphoric symptomatology (Bress & Hajcak, 2013) and prospectively predicts first-onset of depression in adolescents (Nelson et al., 2016). Thus, RewP amplitude shows promise as a marker for reward dysregulation posited to mark liability for substance-related pathology (e.g., Baskin-Sommers & Foti, 2015; Berridge & Robinson, 2003; Blum et al., 2022; Zubovics et al., 2021).

To date, research on reward processing—as indexed by the RewP—in relation to substance use in adolescents has been limited (but see Crowley et al., 2009; Euser et al., 2013; Hammond et al., 2021; Morie et al., 2018, 2021). Further, a recent study of adolescents that conducted a prospective regression analysis in a subsample of participants diagnosed with attention-deficit/hyperactivity disorder (ADHD; n = 84) reported a nonsignificant relationship between the RewP at baseline and between-subject increases in alcohol use at a later timepoint (Hámori et al., 2023). Critically, owing to the modest-sized sample employed in this analysis, this study may have been prevented from detecting small effects typically observed across different-modality measures, pointing to a need for larger samples to reduce the risk of Type II error (i.e., false negatives) when investigating the utility of RewP for predicting alcohol use variations.

In contrast, many studies with adults have provided evidence for hyposensitivity to reward—or reduced hedonic "liking"—as an indicator of clinically significant substance use. For example, reduced RewP amplitude to reward feedback has been found in adults exhibiting harmful substance use (e.g., Baker et al., 2011; Baker et al., 2016a; Baker et al., 2016b; Morie et al., 2016; Na et al., 2019; Parvaz et al., 2015; Sehrig et al., 2019; Zhong et al., 2020) and increased SUD symptoms (Joyner et al., 2019), as well as in those at increased familial risk for alcohol problems (Fein & Chang, 2008). On the other hand, a smaller number of studies have reported evidence for hypersensitivity to reward as a risk factor for early alcohol use. Boecker-Schlier et al. (2017), for example, reported enhanced RewP response in adults who had initiated drinking earlier in pubertal development. In 2019, Hixson et al. reported evidence that adults with a past AUD diagnosis, coupled with a current internalizing disorder diagnosis (i.e., anxiety or depressive disorder), showed a more pronounced RewP than adults with an internalizing disorder and no history of AUD (cf. Crane et al., 2023). Additionally, there have been other recent reports of enhanced RewP among abstinent adults with a history of heroin use (Zhao et al., 2017), as well as in adults engaging in occasional cannabis use (Crane et al., 2021).

With this background in mind, the current study tested for an association between RewP amplitude and both lifetime alcohol use (i.e., drinking initiation) and recent use (i.e., past 30 days) in adolescent females, over and above variance in initiation and recent use associated with depression (i.e., negative mood; anhedonia) and externalizing symptoms. Accounting for variance associated with these symptom measures is important, given that externalizing and depression relate to psychosocial factors that can, respectively, increase (e.g., via deviant peer affiliation; Achenbach & Rescorla, 2001) or decrease (e.g., via social withdrawal; Hussong et al., 2011) risk for early alcohol involvement.

Although RewP often is operationalized as a difference score (i.e., ERP elicited by monetary gain vs. loss feedback), current study analyses examined both gain and loss ERPs—indicative of RewP and FN, respectively—as concurrent predictors of drinking-related outcomes, allowing for tests of their unique contributions (see Meyer et al., 2017). Three specific hypotheses were tested. First, based on evidence indicating hyposensitivity to reward (i.e., small RewP) in individuals with a history of harmful drinking or substance use (e.g., Baker et al., 2011; Baker et al., 2016a; Baker et al., 2016b; Joyner et al., 2019) and those at increased risk for harmful use (e.g., Crowley et al., 2009; Fein & Chang, 2008), we predicted that the RewP response to monetary gain feedback—but not the FN response to loss feedback—would be smaller in adolescents who had initiated alcohol use by the time of study data collection compared to those who had not initiated. Similarly, we

predicted that the RewP would be reduced in adolescents who reported having consumed alcohol in the past 30 days. This hypothesis was advanced specifically for gain feedback based on prior work illustrating that differences in RewP amplitude are driven by variations in delta frequency band activity that are specific to gain feedback processing and that are absent in loss feedback processing (see Proudfit, 2015 for a thorough discussion). Thus, a reduction in gain feedback-specific variance ostensibly represents a central characteristic of reduced hedonic "liking" in those at risk for substance-related pathology that is argued to be well-indexed by the RewP (Baskin-Sommers & Foti, 2015). Finally, these hypothesized effects were also expected to emerge when controlling statistically for alcohol use variation attributable to age, parent-reported externalizing symptoms, and adolescent-reported depressive severity.

#### 1. Method

#### 1.1. Participants

Data for this study were acquired from the two-year follow-up visit of a longitudinal project examining clinical correlates of positive affectrelated (e.g., reward; response to enjoyable pictures) electrocortical response variations in adolescent females. Participants for this project were recruited via several methods, including mailings to families identified as having an eight- to 14-year-old daughter, fliers posted in the area surrounding Stony Brook University, and word of mouth. Participants met inclusion criteria if they were fluent in English, able to comprehend and respond to questionnaires, and were lacking an intellectual disability according to parental report. During the initial lab assessment for the project, 317 adolescent females aged eight to 14 years participated with a parent. Informed consent and assent were provided by parent and adolescent participants, respectively, prior to participation in testing. Financial compensation of approximately \$20 per hour was provided at the end of each study visit. The protocol for the study was approved by the Institutional Review Board at Stony Brook University.

Two years following the initial assessment, adolescent participants and their parents returned to complete clinical interviews and questionnaires, pertaining in each case to the adolescent. During this followup assessment, adolescents also completed a battery of tasks in which EEG was continuously recorded. One of these was a simple gain/loss task—the doors choice-feedback paradigm (Proudfit, 2015). Prior analyses of data from this task and sample have investigated relations of RewP with clinical problems including stress, depression, and ADHD, and examined reliability and developmental change in this index of reward sensitivity (Burani, et al., 2021a; Burani et al., 2021b; Burani et al., 2022a; Burani et al., 2022b; Burani et al., 2019; Kallen et al., 2020; Luking et al., 2017). However, the current work is the first to examine ERPs elicited by monetary gain and loss feedback as predictors of drinking initiation and past-month use.

A total of 258 adolescent participants completed the doors task at the two-year follow-up, of whom eight were excluded from current study analyses due to inadequate EEG data based on visual inspection (n = 1) or missing data on key drinking variables (n = 7). Of note, analyses were restricted to this timepoint as drinking behavior was not assessed at the baseline visit. Thus, the final analysis sample consisted of 250 adolescents, aged 14.40 years on average at follow-up (SD = 1.82, range = 9.89-17.18); Table 1 presents other information regarding sample demographics.<sup>1</sup> Adolescents and parents (N = 249, due to missing diagnostic data for one adolescent participant) also completed a semi-structured diagnostic interview during each assessment (i.e., Kiddie Schedule for Affective Disorders and Schizophrenia - Present and

Table 1

| Samp | le c | lemographics. |
|------|------|---------------|
|------|------|---------------|

| Characteristic                       | n             | %                 | Μ       | Median  |
|--------------------------------------|---------------|-------------------|---------|---------|
| Household Income ( $n = 225$ )       | -             | -                 | 139,950 | 125,000 |
| KSADS-PL DEP and ES Dx ( $n = 249$ ) | -             | -                 | -       | -       |
| MD, DY, DEP-NOS                      | 24, 4, 2      | 9.6, 1.6,.8       | -       | -       |
| ADHD, OD, CD, DB-NOS                 | 9, 3, 0,<br>0 | 3.6, 1.2, 0,<br>0 | -       | -       |
| AA, SA, AD, SD                       | 0, 2, 0,<br>0 | 0,.8, 0, 0        | -       | -       |
| Race $(n = 242)$                     | -             | -                 | -       | -       |
| White/Caucasian                      | 209           | 86.4              | -       | -       |
| Black/African American               | 15            | 6.2               | -       | -       |
| Native Hawaiian/Pacific<br>Islander  | 1             | .4                | -       | -       |
| Mixed/Other                          | 17            | 7                 | -       | -       |
| Ethnicity                            | -             | -                 | -       | -       |
| Hispanic/Latino                      | 24            | 9.6               | -       | -       |
| Parental Education Level             | -             | -                 | -       | -       |
| Some High School                     | 1             | .4                | -       | -       |
| High School Degree or GED            | 14            | 5.6               | -       | -       |
| Some College/2 Year Degree           | 70            | 28                | -       | -       |
| 4 Year Degree                        | 82            | 32.8              | -       | -       |
| Master's Degree                      | 72            | 28.8              | -       | -       |
| Doctoral Degree                      | 11            | 4.4               | -       | -       |

Note. Dx = Diagnosis. KSADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia - Present and Lifetime version. DEP = Depression. ES = Externalizing-spectrum disorder. MD = Major depressive disorder. DY = Dysthmia. NOS = Not-otherwise-specified. ADHD = Attention-deficit/hyperactivity disorder. OD = Oppositional defiant disorder. CD = Conduct disorder. DB = Disruptive behavior disorder. AA = Alcohol abuse. SA = Substance abuse. AD = Alcohol dependence. SD = Substance dependence. Eight participants did not report their race. One participant had missing diagnostic data. Two income values presumed to be participants did not report their income. Household income is reported in U.S. dollars.

Lifetime Version [KSADS-PL: Kaufman et al., 1997]). See Table 1 for observed diagnosis rates for each KSADS-assessed externalizing-spectrum or depressive-disorder in the present analysis sample. It can be seen that lifetime prevalence rates for adolescents reaching diagnostic threshold for depressive disorders (i.e., depression not-otherwise-specified; major depressive disorder; dysthymia), and externalizing-spectrum disorders (i.e., ADHD; oppositional defiant disorder; conduct disorder; disruptive behavior disorder not-otherwise-specified; alcohol dependence; alcohol abuse; substance dependence; substance abuse) were quite low. However, our focus in the current study was on dimensional (symptom score) measures of psychopathology; therefore, diagnostic status rates for the analysis sample were not utilized in study analyses, but are presented here for descriptive purposes.

# 1.2. Measures

#### 1.2.1. Drinking behavior variables

Two items from the Youth Risk Behavior Survey (YRBS; Centers for Disease Control and Prevention) were utilized to index lifetime and pastmonth alcohol use. Lifetime alcohol consumption frequency was assessed by the following question: "During your life, on how many days have you had at least one drink of alcohol?" Response options included: "0 days," "1 or 2 days," "3–9 days," "10–19 days," "20–39 days," "40–99 days," and "100 or more days." Past-month alcohol consumption was assessed via the following item: "During the past 30 days, on how many days did you have at least one drink of alcohol?" Response options included: "0 days," "1 or 2 days," "3–5 days," "6–9 days," "10–19 days," "20–29 days," and "All 30 days." Participants were given instructions for these drinking items that stated drinking alcohol included beer, wine, wine coolers, and liquor such as rum, gin, vodka, or whiskey;

 $<sup>^{1}</sup>$  Racial distribution data utilized in the current study was assessed at the baseline study visit.

additionally, they were told that drinking alcohol does not include a few sips of wine for religious purposes.

For the lifetime number of drinking occasions variable, the frequencies of participants endorsing each ordinal response option were as follows: "0 days" (n = 179), "1 or 2 days" (n = 27), "3–9 days" (n = 18), "10–19 days" (n = 12), "20–39 days" (n = 13), and "40–99 days" (n = 1); no participant endorsed drinking on "100 or more days." For the pastmonth use variable, frequency rates for each response option were: "0 days" (n = 210), "1 or 2 days" (n = 29), "3–9 days" (n = 7), and "10–19 days" (n = 4); no participants endorsed drinking on "20–29 days," or "All 30 days."

Given limited endorsements of lifetime and past-month drinking in the current sample, n's = 71 (i.e., 28.4%) and 40 (i.e., 16%), respectively, these variables were coded in a binary fashion representing initiation versus non-initiation of use, and past-month drinking versus no past-month consumption. This dichotomized approach has been utilized in prior studies of adolescent alcohol use, for similar reasons including limited variability in substance use from community samples (e.g., Brown & Rinelli, 2010; Schleider et al., 2019). Initiation and past-month drinking status shared approximately half of their respective variance (r = .69, p < .001), thus accounting for non-redundant as well as common variance in alcohol use.

# 1.2.2. Depression and externalizing symptoms

The Children's Depression Inventory (CDI) consists of 27 self-report items that assess total depressive severity, as well as five subscales of depression in children and adolescents representing negative mood, anhedonia, negative self-esteem, ineffectiveness, and interpersonal problems (Kovacs, 1992). Each of the items are scored from zero to two, which reflect no presence of the given symptom (e.g., anhedonia; "I have fun in many things"), a mild presence of the given symptom (e.g., "I have fun in some things"), and a clinically significant presence of the symptom (e.g., "Nothing is fun at all"), respectively. The current study utilized the six-item negative mood and eight-item anhedonia subscales, as these domains represent primary depression symptom facets, and may differentially serve as predictors of adolescent drinking (see Hussong et al., 2011). The negative mood and anhedonia subscale scores showed good internal consistency ( $\alpha = .76$  and .70, respectively). Observed subscale scores ranged from zero to nine for negative mood (M = 1.84, SD = 1.98), and zero to 13 for anhedonia (M = 2.26, SD = 2.29).

The Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001) is a commonly used, 113-item parent-report measure of broadband psychopathology and includes various subscales reflecting internalizing and externalizing psychopathology. For the current study, we examined the 35-item externalizing scale raw score, which encompasses various rule-breaking and aggression-related behaviors; however, three items relating to alcohol, smoking, and drug use, respectively, were removed to avoid overlap with drinking outcomes (i.e., 32 items were employed in current analyses). Each item is rated from zero (*Not true*) to two (*Very often or often true*). Missing item-level data was accounted for using mean interpolation as long as no more than 25% of items were missing; the maximum number of missing items was seven, with 11.6% (n = 29) of subject-level cases requiring mean interpolation. Observed scores ranged from zero to 22 (M = 3.38, SD = 4.09) for the externalizing scale, and the Cronbach's alpha for complete cases (n = 221) was.84.

#### 1.2.3. Neurophysiological reward reactivity (RewP)

The doors task is a simple choice-feedback paradigm with an equal number of gain and loss trials (Proudfit, 2015). The task was administered using Presentation software (Neurobehavioral Systems, Berkeley, CA), with visual stimuli presented on a screen positioned approximately 72 cm from the participant, at eye level. At the beginning of each task trial, two identical doors appeared side by side on the screen, and participants chose either the left or the right one by pressing the left or right mouse button on a computer mouse; the doors remained on the screen until one of the two mouse buttons was pressed, indicating a choice of

one or the other door. Following this selection, a fixation cross appeared on the screen for 1500 ms, followed by the presentation of a feedback cue for 2000 ms. The feedback cue consisted of either a green arrow pointing upward (signifying a \$0.50 win), or a red arrow pointing downward (signifying a \$0.25 loss). Prior to each subsequent trial, a prompt appeared instructing the participant to "Click for next round," after which a fixation cross was presented for 1000 ms. There was a total of 60 trials in the task, comprising 30 gain and 30 loss feedback trials presented in a pseudo-random order. Participants were told they could win between zero and 15 dollars; however, all participants received eight dollars.

#### 1.3. EEG data reduction

While participants completed the doors task, continuous EEG data were recorded using an ActiveTwo BioSemi system (BioSemi, Amsterdam, Netherlands). Data was collected with a 34-site elastic cap in line with the 10/20 system. Vertical electrooculographic (EOG) activity was recorded from two electrodes placed above and below the left eye, and horizontal EOG activity was recorded from two others placed adjacent to the outer canthi of the left and right eves. Additionally, two electrodes were placed on the left and right mastoids to serve as the offline reference. The continuous EEG signal data underwent pre-amplification at each electrode site to improve signal-to-noise ratio, and data were digitized with 24-bit resolution at a sampling rate of 1024 Hz using a lowpass fifth-order sinc filter with a half-power cutoff of 204 Hz. During online recording, active electrodes were measured with reference to a common mode sense (CMS) active electrode, with a driven right leg (DRL) passive electrode, which together replace the typical "ground" electrode in other EEG systems.

The Brain Vision Analyzer 2.2 software package (Brain Products, Gilching, Germany) was utilized for offline analysis of the continuous EEG signal data. Continuous signal data were first re-referenced to the average of the left and right mastoids, and bandpass filtered from 0.1 to 30 Hz. Next, the continuous data were segmented from 200 ms prefeedback onset to 1000 ms post-feedback onset for both gain and loss trials. Ocular correction for eyeblinks was applied using Gratton et al.'s (1983) regression-based method. An automatic artifact rejection procedure was used to exclude individual channel data for any EEG segment meeting any of the following criteria: A voltage step over 50 µV between sample points, a voltage difference of 175  $\mu V$  within any 400 ms interval, or a maximum voltage difference of less than .50 µV within any 100 ms interval. Each segment was baseline corrected using the 200 ms prestimulus period, and then averaged across nonrejected individual-trial ERP waveforms within each condition (i.e., gain and loss). In line with past published articles using data from this same participant sample (e. g., Burani et al., 2019; Kallen et al., 2020), mean feedback-locked EEG activity at electrode site FCz within a window of 250-350 ms following feedback presentation was used for scoring the RewP to gain and FN to loss-trial ERP amplitudes for each subject. The mean number of trials included in the RewP and FN ERPs were 29.82 for each (SDs = 1.19 and 1.00, respectively). Furthermore, regression-based residual scores were calculated for gain- (RewP) and loss-trial (FN) ERP scores for use in correlational analyses across study variables (see Table 3). Importantly, this allowed for direct comparisons between observed bivariate associations with study variables for mean RewP and FN values, and potential differences in observed associations when only including the unique variance in gain- and loss-trial responses that is unshared between the two (see Meyer et al., 2017). Internal consistencies of the mean-activity scores were computed separately for RewP and FN ERPs as the Spearman-Brown corrected correlation between scores for odd- versus even-numbered task trials (Levinson et al., 2017). Scores for the RewP and FN amplitudes each exhibited high internal consistency, Cronbach's  $\alpha = .92$  and .89, respectively.

#### 1.4. Data analyses

Continuous variables were examined for extreme values relative to distributional statistics computed using SPSS version 27.0 (IBM, Armonk, N.Y., USA). Univariate outliers, defined as values beyond three interquartile ranges (IQR) above or below the median, were winsorized to those thresholds. RewP values exceeded this threshold in one case (0.4%), while no FN value exceeded these numerical bounds. In addition, four anhedonia scale scores (1.6%) and two externalizing scale scores (0.8%) were winsorized; no negative mood scores exceeded three IQR from the median. Finally, all continuous variables utilized in our analyses were normally distributed, based on commonly acceptable values of - 2 to + 2 for skewness (where observed values ranged from -.54 to 1.47) and kurtosis (i.e., where observed values ranged from -.51 to 1.78).

First, bivariate correlational analyses utilizing Pearson's r were examined for all continuous study variables; point-biserial correlational coefficients were used for dichotomously coded lifetime and past-month drinking variables (0 = no drinking; 1 = any drinking over the pertinent interval). Next, as self-reported lifetime and past-month drinking status variables were coded in a binary fashion, group comparisons for each outcome were conducted utilizing hierarchical binary logistic regression models and independent samples *t*-tests with IBM SPSS Statistics (Version 27.0; IBM, Armonk, NY, 2020). Finally, each hierarchical binary logistic regression analysis was conducted utilizing mean-scores for RewP and FN as concurrent predictors, as this allowed for tests of unique variance contributed by each feedback type, which is obscured by using solely the raw mean-difference score.

All models included age as a covariate to control for the typical increase in drinking over the course of adolescence (see Jackson et al., 2021). In addition, broad externalizing symptoms and primary depressive symptoms were included as covariates given their known associations with adolescent drinking. In the first model, relations of RewP and FN with alcohol initiation status were tested with age entered at step one, followed by negative mood and anhedonia scores at step two, externalizing scores at step three, and RewP and FN mean-activity scores at step four. The use of step-wise entry highlights separable, unique contributions from each group of putative covariates and permits the last step of the analysis to reveal the incremental predictive value of reward-related ERPs, over and above those covariates. The second model, using past-month drinking status as the outcome, was specified similarly. All predictor variables in the following binary logistic regression models were standardized for ease of interpreting respective odds ratios, and to facilitate effect size comparisons in future research (e. g., Watts et al., 2021). All statistical analyses were evaluated using a

significance level of  $\alpha = .05.^2$ 

# 2. Results

Table 2 shows descriptive statistics and independent samples *t*-test results for the different study variables in initiators versus non-initiators, and in past-month drinkers versus non-drinkers. Lifetime drinking

#### Table 2

Descriptive statistics and independent samples *t*-test results for study variables comparing those who endorsed drinking and reported no drinking for their lifetime and in the past month.

| Variables     | Non-<br>Initiators<br>n = 179 | Initiators $n = 71$ | р    | Past-<br>Month<br>Non-<br>Drinkers<br>n = 210 | Past-<br>Month<br>Drinkers<br>n = 40 | р    |
|---------------|-------------------------------|---------------------|------|---|--------------------------------------|------|
| RewP (µV)     | 15.89                         | 14.42               | .281 | 15.51   | 15.25                                | .873 |
|               | (10.00)                       | (8.75)              |      | (9.79)  | (9.13)                               |      |
| FN (μV)       | 10.66                         | 10.91               | .817 | 10.73   | 10.74                                | .996 |
|               | (9.41)                        | (7.08)              |      | (9.00)  | (7.78)                               |      |
| Age           | 13.92                         | 15.62               | <    | 14.15   | 15.74                                | <    |
|               | (1.77)                        | (1.29)              | .001 | (1.80)  | (1.24)                               | .001 |
| Negative      | 1.36                          | 3.06                | <    | 1.60  | 3.15                                 | <    |
| Mood          | (1.68)                        | (2.18)              | .001 | (1.81)  | (2.33)                               | .001 |
| Anhedonia     | 1.86                          | 3.15                | <    | 2.03  | 3.29                                 | .004 |
|               | (2.02)                        | (2.30)              | .001 | (2.05)  | (2.51)                               |      |
| Externalizing | 3.23                          | 3.64                | .459 | 3.17  | 4.27                                 | .108 |
| Ū.            | (4.06)                        | (3.72)              |      | (3.99)  | (3.76)                               |      |

*Note.* N = 250. p = Significance value for independent samples *t*-test comparing the means of each variable for initiators versus non-initiators (4th column), and past-month drinkers versus past-month non-drinkers (7th column); corrected values are presented when Levene's test for equality of variances was significant (p < .05). Negative Mood = Children's Depression Inventory (CDI) negative mood subscale score. Anhedonia = Children's Depression Inventory (CDI) anhedonia subscale score. Externalizing = Child Behavior Checklist (CBCL) parent-report externalizing scale raw score with three items related to alcohol/ substance use removed. Past-Month Non-Drinkers = those who did not report consuming alcohol in the preceding 30 days. Past-Month Drinkers = those who endorsed consuming alcohol in the preceding 30 days. Non-Initiators = those who did not report consuming alcohol in their lifetime, to date. Initiators = those who endorsed consuming alcohol in their lifetime. For the ERP (RewP, FN) and questionnaire variables (externalizing, anhedonia, negative mood), raw score values falling outside the distributional boundaries of + /- three IQR from the median were winsorized to these boundaries. The number in parentheses represents the SD for each respective mean.

Binary logistic regression analysis assumes a linear relationship between continuous independent variables and the logit transformation of the outcome. This assumption was tested for the two models (lifetime initiation, past-month consumption) using the Box-Tidwell procedure (Box & Tidwell, 1962), applied to log-transformed scores for the predictor variables (age, RewP, FN, externalizing, depression). The final hierarchical step for each model was specified with the addition of a product term for each log-transformed predictor with its corresponding natural log. No product-term reached statistical significance (ps .05) in the lifetime initiation model, indicating that the linearity-of-relationship assumption was met; however, the past-month consumption model revealed a significant product term for the externalizing scale. To remedy this, an externalizing-squared (i.e., quadratic) term was added to account for non-linearity. The Box-Tidwell procedure was then re-conducted for the past-month model, and no product term reached significance following the addition of the respective quadratic term (i.e., all ps > .05). Of note, the inclusion of this quadratic term did not change the results for the corresponding model used to test associations of RewP versus FN amplitude with past-month drinking; thus, results for this hypothesis are reported for the simpler model, without inclusion of the quadratic externalizing term, for sake of consistency with the lifetime initiation model.

variability in the current sample was comparable with other recent adolescent studies (e.g., Jackson et al., 2021), with 71 participants (28.4%) endorsing some history of alcohol use. The rate of past-month drinking, on the other hand, was less than in recently published United States estimates in slightly older adolescents (i.e., 14- to 18-year-olds; Vashishtha et al., 2021), with 40 current study participants (16%) endorsing some past-month use.

Independent samples *t*-test results revealed that past-month drinkers and initiators were significantly older and endorsed more severe anhedonia and negative mood scores on the CDI than past-month nondrinkers and non-initiators, respectively. Finally, neither group comparison was significant for RewP or FN individually, nor for parentreport CBCL externalizing scores.

Bivariate correlation analyses revealed that RewP and FN scores were not correlated significantly with any of the symptom scales (i.e., externalizing; anhedonia; negative mood), although a smaller residualized RewP score was associated with an increased likelihood for drinking initiation. Moreover, older age was related to increased amplitude of both RewP and FN, as well as increased negative mood and anhedonia symptoms. Finally, anhedonia and negative mood scores showed strong positive relations with each other, and small positive relationships with externalizing scores. See Table 3 for a full matrix of correlations among the study variables, including point-biserial correlations with the dichotomous lifetime and past-month drinking outcomes.

A repeated measures analysis of variance was first conducted to confirm the presence of trial type (gain versus loss) effects for ERP responses in the doors task. As expected, gain trials (M = 15.47, SD = 9.67) were associated with significantly greater ERP-positivity within the RewP window than loss trials (M = 10.73, SD = 8.80), F[1, 249] = 181.37, p < .001,  $\eta^2 p = .42$ . Fig. 1 depicts the grand-averaged ERP waveform for the RewP, FN, and their mean-difference.

Next, the first hierarchical binary logistic regression model included RewP and FN amplitudes as separate predictors of lifetime drinking initiation. Age was entered at step one, followed by negative mood and anhedonia values at step two, externalizing at step three, and finally, RewP and FN scores at step four; all predictor variables were entered as standardized scores. Notably, both age and negative mood symptoms positively predicted increased likelihood of initiation, across all steps of the hierarchical logistic regression model. However, anhedonia and externalizing did not significantly relate to initiation at any step.

The overall model for drinking initiation was significant across steps one (i.e., age), two (i.e., addition of negative mood and anhedonia), and three (i.e., addition of externalizing); however, only age and CDIassessed negative mood contributed uniquely to prediction of initiation. Notably, the addition of RewP and FN scores at step four led to a further significant increase in variance accounted for – with reduced RewP, but not FN, accounting for this increase. Specifically, reduced positive-going RewP response to gain feedback was selectively predictive of heightened likelihood of early initiation, over and above observed effects of age and negative mood severity. Table 4 presents full results for this hierarchical model, and Fig. 2 depicts grand-averaged ERP waveforms for gain, loss, and delta RewP (mean amplitudedifference for gain-versus-loss ERPs) in initiators and non-initiators, visualizing the smaller RewP response to gain-trial feedback in initiating youth.

The second and final hierarchical binary logistic regression model examined RewP and FN as predictors of past-month drinking, over and above covariates of age, depression subscales, and externalizing entered at steps one, two, and three, respectively. In line with the results for drinking initiation likelihood, older age and increased negative mood severity were each uniquely predictive of past-month drinking, while main effects for externalizing and anhedonia did not reach significance.

As for initiation likelihood, the overall model for past-month drinking was significant across all four hierarchical steps. Additionally, both the inclusion of age at step one, and of depressive symptom subscales at step two, led to a significant increase in the level of model-predicted variance for past-month drinking; however, neither externalizing, nor RewP or FN responses, were significantly related to drinking over the past month. Table 5 presents full results for this model.<sup>3</sup>

## 3. Discussion

The current study sought to clarify how reward sensitivity—quantified using a well-established neural index of hedonic "liking," the neural response to monetary gain feedback (vs. loss) (i.e., RewP; Baskin-Sommers & Foti, 2015)—relates to early drinking initiation and past-month drinking in adolescent females, when accounting for current externalizing and depressive symptomatology, as well as exact age at the time of assessment. Results suggested that (1) adolescent females who had reported drinking initiation by the point of study assessment were characterized by a smaller RewP response to monetary gain—but FN response not loss—feedback; and, (2) these observed RewP amplitude reductions for initiators were independent of both self-reported depressive (i.e., negative mood; anhedonia) and parent-reported externalizing symptom severity, as well as the adolescents age at the point of assessment. However, RewP and FN mean-activity scores were unrelated to past-month drinking in the current community sample.

An appreciable body of research points to a role for altered reward sensitivity in the harmful use of substances, including alcohol (e.g., Baskin-Sommers & Foti, 2015; Blum et al., 2022; Casey & Jones, 2010; Crane et al., 2023; Rádosi et al., 2021). However, diverging theoretical perspectives exist as to the relative importance of reward hypersensitivity versus hyposensitivity. The current finding of reduced neural response to reward feedback in alcohol-initiating youth aligns with the reward deficiency hypothesis (e.g., Blum et al., 2000, 2011, 2022; Bowirrat & Oscar-Berman, 2005; Casement et al., 2015; Telzer et al., 2013), which posits that biological risk for drinking initiation is associated with blunted hedonic "liking" of natural reinforcers. This association being separate from variations in drinking initiation uniquely accounted for by age and negative mood symptoms highlights the utility of reward-related ERPs—particularly the RewP—as a distinct indicator of substance-related risk.

Current study results also accord with findings from prior research showing smaller RewP in adults exhibiting problematic substance use relative to controls (e.g., Baker et al., 2011; Baker et al., 2016a; Baker et al., 2016b; Morie et al., 2016; Na et al., 2019; Parvaz et al., 2015; Sehrig et al., 2019; Zhong et al., 2020), and prior work reporting inverse associations of RewP magnitude with dimensional representations of SUD severity (Joyner et al., 2019) and familial risk for harmful alcohol use (Fein & Chang, 2008). The present findings extend this prior work in two important ways. First, by demonstrating an association in young adolescents with limited alcohol exposure history, our data suggest that blunted reward reactivity is a premorbid liability for, rather than a consequence of, problematic drinking. Second, given that the RewP indexes latent biological risk not tapped by observable characteristics such as parent- and self-reported disinhibitory tendencies (e.g., externalizing behaviors; Achenbach & Rescorla, 2001; Joyner et al., 2019) or

<sup>&</sup>lt;sup>3</sup> All binary logistic regression analyses were also conducted with the mean RewP-difference scores (i.e., delta RewP: gain – loss amplitude at site FCz, from 250 ms to 350 ms post-feedback), to confirm consistency of results across differential ERP quantification methods (see Meyer et al., 2017). Importantly, all results from models utilizing the delta RewP scores were identical to those from analyses reported in the main text utilizing RewP and FN as separate predictors. In particular, the delta RewP was significantly smaller for initiators compared to non-initiators (b = -.44, OR = .65, 95% CI = .45 to .93, p = .017), whereas no difference in delta RewP amplitude was found between past-month drinkers and non-drinkers (p = .915), over and above the model covariates (i.e., age; parent-reported CBCL externalizing behavior; adolescent-reported CDI negative mood and anhedonia).

#### Table 3

Zero-order correlations between study variables.

|                         | 1.                        | 2.                        | 3.                        | 4.                    | 5.                        | 6.                       | 7.                        | 8.             | 9.                        |  |
|-------------------------|---------------------------|---------------------------|---------------------------|-----------------------|---------------------------|--------------------------|---------------------------|----------------|---------------------------|--|
| 1. Age                  | -                         | -                         | -                         | -                     | -                         | -                        | -                         | -              | -                         |  |
| 2. Negative Mood        | .30 <sup>(&lt;.001)</sup> | -                         | -                         | -                     | -                         | -                        | -                         | -              | -                         |  |
| 3. Anhedonia            | .33 <sup>(&lt;.001)</sup> | .64(<.001)                | -                         | -                     | -                         | -                        | -                         | -              | -                         |  |
| 4. Externalizing        | 02 <sup>(.723)</sup>      | .25(<.001)                | .25(<.001)                | -                     | -                         | -                        | -                         | -              | -                         |  |
| 5. RewP (μV)            | .25(<.001)                | 04 <sup>(.555)</sup>      | .02 <sup>(.762)</sup>     | 07 <sup>(.273)</sup>  | -                         | -                        | -                         | -              | -                         |  |
| 6. Res.RewP (µV)        | $.08^{(.211)}$            | 05 <sup>(.481)</sup>      | $01^{(.936)}$             | .04 <sup>(.532)</sup> | .57 <sup>(&lt;.001)</sup> | -                        | -                         | -              | -                         |  |
| 7. FN (μV)              | .25(<.001)                | 02 <sup>(.818)</sup>      | .03 <sup>(.671)</sup>     | 11 <sup>(.077)</sup>  | .82(<.001)                | $.00^{(1)}$              | -                         | -              | -                         |  |
| 8. Res. FN (μV)         | .08 <sup>(.217)</sup>     | .03 <sup>(.654)</sup>     | $.02^{(.759)}$            | $10^{(.128)}$         | $.00^{(1)}$               | 82 <sup>(&lt;.001)</sup> | .57 <sup>(&lt;.001)</sup> | -              | -                         |  |
| 9. Drinking Initiation  | .42(<.001)                | .39(<.001)                | .27 <sup>(&lt;.001)</sup> | .05 <sup>(.459)</sup> | 07 <sup>(.281)</sup>      | 14 <sup>(.028)</sup>     | .01 <sup>(.837)</sup>     | $.12^{(.054)}$ | -                         |  |
| 10. Past-Month Drinking | .32(<.001)                | .29 <sup>(&lt;.001)</sup> | $.21^{(<.001)}$           | .10 <sup>(.108)</sup> | 01 <sup>(.873)</sup>      | 02 <sup>(.774)</sup>     | < .0 <sup>(.996)</sup>    | $.02^{(.811)}$ | .69 <sup>(&lt;.001)</sup> |  |

*Note.* N = 250. Negative Mood = Children's Depression Inventory (CDI) negative mood subscale score. Anhedonia = Children's Depression Inventory (CDI) anhedonia subscale score. Externalizing = Child Behavior Checklist (CBCL) parent-report externalizing scale raw score with three items related to alcohol/substance use removed. Drinking Initiation (0 = no reported lifetime drinking, to date; 1 = reported lifetime drinking). Past-Month Drinking (0 = no past-month drinking; 1 = past-month drinking). Res. RewP = standardized unique variance remaining in RewP after removing shared variance with FN. Res. FN = standardized unique variance remaining in FN after removing shared variance with RewP. For the ERP (RewP, FN) and questionnaire variables (externalizing, anhedonia, negative mood), raw score values falling outside the distributional boundaries of + /- three IQR from the median were winsorized to these boundaries. Number in parentheses is *p*-value for respective bivariate association. Point-biserial correlation coefficients are reported for all effects including binary drinking outcomes; Pearson's *r* is reported otherwise.

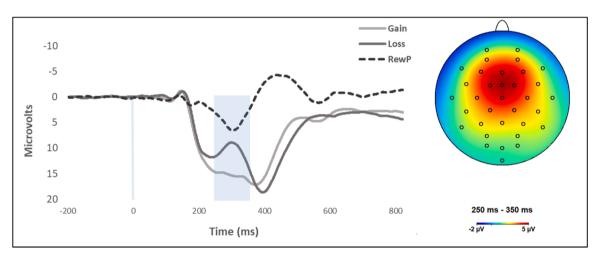


Fig. 1. Grand-average feedback-locked ERP waveforms for gain, loss and delta RewP (gain ERP – loss ERP). Note. N = 250. Left side: Depiction of sample-average, stimulus-locked ERP waveforms for gain (light gray line) and loss (dark gray line) trials, and the delta RewP (i.e., difference in mean EEG activity for gain trials minus loss trials; dashed black line), at site FCz. Right side: Color headmap represents the scalp topography for the delta RewP from 250–350 ms post-feedback onset (shaded region) at site FCz.

self-reported depressive symptoms (e.g., negative mood, anhedonia), the present findings demonstrate the incremental utility of psychophysiological assessment of reward sensitivity for better understanding variability in youth risk trajectories.

Unexpectedly, anhedonia and externalizing symptoms did not uniquely relate to either drinking outcome in this sample. It may be that variance in early drinking patterns expected for anhedonic symptoms might be suppressed by simultaneous protective (e.g., social withdrawal) and risk-related (e.g., seeking substances for pleasurable experience) aspects of the construct; future work should examine this possibility. Alternatively, it may be that adolescents with more severe anhedonia-driven alcohol use (see Blum et al., 2022) were underrepresented in the present sample. In particular, each CDI item is rated from zero (i.e., no presence of the given symptom) to two (i.e., clinically significant presence of the respective symptom); as expected for a community sample, mean sum-scores for current study participants on the CDI-Anhedonia subscale were generally low (M = 2.26; range = zero to 13). In addition, it is possible that externalizing symptoms relate more strongly to drinking in male compared to female youth (e.g., Chassin et al., 2002; King et al., 2004), or that main effects of externalizing might be less apparent in community adolescent samples with low levels of disinhibitory tendencies (Kendler et al., 2011).

Importantly, our finding of reduced reward reactivity in adolescent

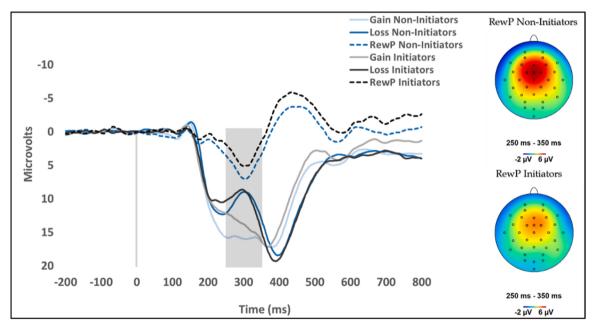
initiators runs contrary to some adult work reporting enhanced RewP relative to controls in individuals with a history of AUD and a current (Hixson et al., 2019) or past-internalizing disorder (Crane et al., 2023), compared to adults with a current internalizing disorder only, or remitted diagnosis for either an internalizing disorder or AUD, respectively. The present findings also contrast with those of Boecker-Schlier et al. (2017), who found a large RewP to be predictive of earlier pubertal initiation of drinking assessed via retrospective report, a risk marker that also related to increased severity of AUD symptoms assessed concurrently. These diverging findings point to a need for further clarification of the direction of association between reward sensitivity and alcohol use, and whether this association might vary according to developmental stage or alcohol exposure history. For example, a recent study of risk-based reward responding in adolescent females (Freeman et al., 2020) reported a positive association between behaviorally assessed risk-taking and RewP; however, this effect was present among older (15-19 years) but not younger-aged (10-14 years) individuals. These findings suggest that hypersensitivity to reward may relate in particular to late-adolescent risky behavior, including early escalation of substance use following initiation (e.g., Buckholtz et al., 2010; Freeman et al., 2020; Morales et al., 2018; Quinn & Harden, 2013; Urošević et al., 2015; van Hemel-Ruiter et al., 2015). By contrast, during mid-adolescence - a developmental period in which initiation of drinking is less atypical (see

#### Table 4

Prediction of drinking initiation in a four-step hierarchical binary logistic regression model.

|               | 2      | 2        |       | , ,   | -     |      |     |       |      |               |        |
|---------------|--------|----------|-------|-------|-------|------|-----|-------|------|---------------|--------|
|               | $R^2$  | $\chi^2$ | Spec. | Sens. | Acc.  | В    | SE  | Wald  | OR   | 95% CI for OR | р      |
| Step 1        | .28    | 54.48    | 89.9% | 45.1% | 77.2% |      |     |       |      |               | < .001 |
| Age           |        |          |       |       |       | 1.35 | .22 | 36.51 | 3.87 | 2.50-6.01     | <.001  |
| Step 2        | .37*** | 74.13    | 91.1% | 52.1% | 80%   |      |     |       |      |               | <.001  |
| Age           |        |          |       |       |       | 1.24 | .23 | 28.11 | 3.46 | 2.19-5.48     | <.001  |
| Negative Mood |        |          |       |       |       | .79  | .21 | 14.30 | 2.20 | 1.46-3.31     | <.001  |
| Anhedonia     |        |          |       |       |       | 14   | .20 | .51   | .87  | .59-1.28      | .476   |
| Step 3        | .37    | 74.27    | 92.2% | 52.1% | 80.8% |      |     |       |      |               | <.001  |
| Age           |        |          |       |       |       | 1.23 | .24 | 27.63 | 3.44 | 2.17-5.44     | <.001  |
| Negative Mood |        |          |       |       |       | .80  | .21 | 14.22 | 2.23 | 1.47-3.39     | <.001  |
| Anhedonia     |        |          |       |       |       | 13   | .20 | .44   | .87  | .59-1.30      | .507   |
| Externalizing |        |          |       |       |       | 07   | .18 | .14   | .94  | .66-1.33      | .712   |
| Step 4        | .41**  | 83.86    | 88.8% | 50.7% | 78%   |      |     |       |      |               | <.001  |
| Age           |        |          |       |       |       | 1.37 | .25 | 30.81 | 3.95 | 2.43-6.42     | <.001  |
| Negative Mood |        |          |       |       |       | .76  | .22 | 12.26 | 2.15 | 1.40-3.29     | <.001  |
| Anhedonia     |        |          |       |       |       | 11   | .21 | .27   | .90  | .60-1.35      | .604   |
| Externalizing |        |          |       |       |       | 07   | .18 | 1.34  | .94  | .66-1.33      | .715   |
| RewP (µV)     |        |          |       |       |       | 88   | .33 | 7.04  | .42  | .2279         | .008   |
| FN (μV)       |        |          |       |       |       | .45  | .32 | 2.00  | 1.56 | .84-2.91      | .158   |

*Note.*  $R^2$  = Nagelkerke Pseudo- $R^2$ . Spec. = Specificity value representing the percent of correctly predicted zero values (i.e., denied drinking). Sens. = Sensitivity value representing the percent of correctly predicted nonzero values (i.e., endorsed drinking). Acc. = Overall accuracy for the model in predicting observed values on the respective outcome. Negative Mood = Children's Depression Inventory (CDI) negative mood subscale score. Anhedonia = Children's Depression Inventory (CDI) anhedonia subscale score. Externalizing = Child Behavior Checklist (CBCL) parent-report externalizing scale raw score with three items related to alcohol/substance use removed. OR = odds ratio. Wald. = Wald chi-square value. Each step is in prediction of drinking initiation (0 = no reported lifetime drinking, to date; 1 = reported lifetime drinking). All predictor variables are standardized in the model, and have raw score values falling outside the distributional boundaries of + /- three IQR from the median winsorized to these boundaries. \* \* p < .01 for  $\Delta R^2$ , \* \*\* p < .001 for  $\Delta R^2$ .



**Fig. 2.** Feedback-locked waveforms for gain, loss, and delta RewP group averages in initiators and non-initiators. *Note.* ns = 179 ("Non-Initiators"; zero values, those did not report lifetime drinking, to date), 71 ("Initiators"; nonzero values, those who reported lifetime drinking). Figure depicts a smaller RewP—but not FN—in those who have initiated drinking versus those who have not, which parallels results from binary logistic regression analyses. Waveforms represent group-averaged ERP response for gain trials, loss trials, and delta RewP (i.e., difference in mean EEG activity for gain trials minus loss trials at FCz) for all individuals within each group; color headmaps represents the scalp topography for the delta RewP from 250 ms to 350 ms post-feedback onset (shaded region) at site FCz for each group.

Jackson et al., 2021) – indices of reward sensitivity may relate more specifically to this drinking "milestone."

These complicated patterns of risk for adolescent harmful substance use may partially explain prior reports of null relations of RewP with adolescent substance use (or risk for use), including findings of nonsignificant results from healthy controls versus current users of tobacco or cannabis (Hammond et al., 2021; Morie et al., 2021), individuals with a parental history of a SUD (Euser et al., 2013), prenatal cocaine exposure (PCE; Morie et al., 2018; but see Crowley et al., 2009, for a sex-specific smaller RewP amplitude in males with PCE), or for prospective prediction of alcohol use in adolescents with ADHD (Hámori et al., 2023). However, it is also possible that correlates of adolescent drinking initiation or past-month drinking may differ from adolescent smoking engagement (e.g., Rádosi et al., 2021), genetic risk for SUDs, or risk arising from prenatal substance exposure – highlighting this as a direction for future studies testing RewP differences in relation to other substances (e.g., nicotine, cannabis). Finally, concerning the nonsignificant relationship between RewP and later alcohol use reported by Hámori et al. (2023), it may be that an increase in sample size would have provided adequate statistical power to detect small effect sizes in

#### Table 5

Prediction of past-month drinking status in a four-step hierarchical binary logistic regression model.

|               | $R^2$ | $\chi^2$ | Spec. | Sens. | Acc.  | В    | SE  | Wald  | OR   | 95% CI for OR | р      |
|---------------|-------|----------|-------|-------|-------|------|-----|-------|------|---------------|--------|
| Step 1        | .20   | 31.78    | 100%  | 0%    | 84%   |      |     |       |      |               | < .001 |
| Age           |       |          |       |       |       | 1.28 | .27 | 21.92 | 3.60 | 2.11-6.15     | < .001 |
| Step 2        | .25*  | 40.11    | 97.6% | 15%   | 84.4% |      |     |       |      |               | < .001 |
| Age           |       |          |       |       |       | 1.14 | .28 | 16.23 | 3.12 | 1.79-5.42     | < .001 |
| Negative Mood |       |          |       |       |       | .52  | .22 | 5.76  | 1.69 | 1.10 - 2.59   | .016   |
| Anhedonia     |       |          |       |       |       | 06   | .22 | .06   | .95  | .61-1.46      | .803   |
| Step 3        | .26   | 40.89    | 97.1% | 12.5% | 83.6% |      |     |       |      |               | < .001 |
| Age           |       |          |       |       |       | 1.16 | .28 | 16.71 | 3.20 | 1.83 - 5.58   | < .001 |
| Negative Mood |       |          |       |       |       | .49  | .22 | 4.78  | 1.63 | 1.05 - 2.51   | .029   |
| Anhedonia     |       |          |       |       |       | 08   | .22 | .12   | .93  | .60-1.43      | .725   |
| Externalizing |       |          |       |       |       | .17  | .19 | .79   | 1.19 | .81-1.74      | .373   |
| Step 4        | .27   | 42.40    | 97.6% | 15%   | 84.4% |      |     |       |      |               | < .001 |
| Age           |       |          |       |       |       | 1.24 | .29 | 17.91 | 3.45 | 1.94-6.11     | < .001 |
| Negative Mood |       |          |       |       |       | .47  | .22 | 4.35  | 1.60 | 1.03-2.48     | .037   |
| Anhedonia     |       |          |       |       |       | 06   | .22 | .08   | .94  | .61-1.45      | .774   |
| Externalizing |       |          |       |       |       | .16  | .19 | .68   | 1.17 | .80-1.71      | .410   |
| RewP (µV)     |       |          |       |       |       | 12   | .37 | 1.06  | .89  | .43-1.82      | .744   |
| FN (μV)       |       |          |       |       |       | 14   | .36 | .16   | .87  | .43-1.75      | .689   |

*Note.*  $R^2$  = Nagelkerke Pseudo- $R^2$ . Spec. = Specificity value representing the percent of correctly predicted zero values (i.e., denied past-month drinking). Sens. = Sensitivity value representing the percent of correctly predicted nonzero values (i.e., endorsed past-month drinking). Acc. = Overall accuracy for the model in predicting observed values on the respective outcome. Negative Mood = Children's Depression Inventory (CDI) negative mood subscale score. Anhedonia = Children's Depression Inventory (CDI) anhedonia subscale score. Externalizing = Child Behavior Checklist (CBCL) parent-report externalizing scale raw score with three items related to alcohol/substance use removed. OR = odds ratio. Wald. = Wald chi-square value. Each step is in prediction of past-month drinking (0 = no past-month drinking; 1 = past-month drinking). All predictor variables are standardized in the model, and have raw score values falling outside the distributional boundaries of + /- three IQR from the median winsorized to these boundaries. \* p < .05 for  $\Delta R^2$ .

this study.

Finally, novel findings of smaller RewP response to monetary gain feedback among adolescent drinking initiators are best considered in relation to theories that posit a transdiagnostic role for reward sensitivity in the etiology of psychopathology more broadly. Along this line, Baskin-Sommers and Foti (2015) proposed that physiological indices of reward processing, such as RewP, can serve as transdiagnostic biological markers of appetitive-system processes (e.g., initial receipt of reward, as described in the RDoC framework; Cuthbert & Insel, 2013; Insel et al., 2010). In addition, RewP amplitude was specifically posited as a proxy for hedonic "liking" that contributes to different "profiles" of reward dysfunction, which each present with unique patterns of depressive and substance-related symptomatology. Two primary "profiles" presented were termed "Primarily Anhedonic," and "Primarily Hyperthymic," which distinctly entail normative "wanting" (i.e., attribution of salience to potential rewards) but diminished "liking," and normal-range "liking" but hypersensitive "wanting," respectively. As such, ERP-based indices of "wanting" and subsequent reward-learning dysfunction in youth may highlight avenues for future research that can continue blending psychophysiological methodologies with dimensional psychopathology approaches (see Perkins et al., 2020).

Some limitations of the current study warrant mention. First, the study sample consisted solely of females from families endorsing a predominately above-average socio-economic status, thus reducing generalizability of the findings, and precluding tests for differences by sex or level of financial hardship. Nevertheless, research focusing on female-specific risk for harmful substance use is important given that females historically have been excluded from alcohol-related research (see White, 2020), given evidence for more rapid movement toward heavy drinking following first use (i.e., "telescoped" trajectories; Cheng & Anthony, 2018; Diehl et al., 2007; Hernandez-Avila et al., 2004; Menary et al., 2017), and more adverse alcohol-related consequences across time (Foster et al., 2014; Nolen-Hoeksema, 2004; Nolen-Hoeksema & Hilt, 2006) among females compared to males. Additionally, the current sample was at the stage of mid-adolescence on average (mean age = 14.40), with most participants identifying their race as White (86.4%), which precluded testing for different patterns of association at later stages of adolescence (e.g., Freeman et al., 2020) or as a function of race (e.g., Sartor et al., 2016).

Notwithstanding these limitations, the current study was the first to evaluate RewP as an indicator of early drinking initiation, and pastmonth alcohol use, as pre-morbid risk markers of problem drinking in adolescent-aged females. Our analyses revealed an association for smaller RewP to monetary gain feedback with early initiation of drinking in this target group, independently of variance attributable to age and clinical-symptom variables. This finding adds to data from prior research with adolescent females showing smaller RewP to be predictive of longitudinal increases in dysphoria (Bress & Foti, Kotov, et al., 2013), ADHD symptoms (Bunford et al., 2022; Kallen et al., 2020), and increased risk for first-onset major depressive episodes (Nelson et al., 2016). The present findings add to an evidence base suggesting a role for deficient "liking" in proneness to clinical problems of different types (Baskin-Sommers & Foti, 2015; Proudfit, 2015), and support the utility of physiological indicators such as RewP for identifying children at risk for early initiation of drinking (Bunford et al., 2022). Given the paucity of existing research examining reward-related ERPs (e.g., RewP) as a correlate of use (or risk for use) in adolescents, and heightened sex-specific risk for females compared to males, continued understanding of transdiagnostic factors that contribute to initiation and escalation of use in youth can help to inform strategies for early intervention and prevention.

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### CRediT authorship contribution statement

Alexander M. Kallen: Conceptualization, Formal analysis, Writing – original draft, Visualization, Methodology.; Christopher J. Patrick: Conceptualization, Methodology, Writing – review & editing, Supervision.; Bruce D. Bartholow: Methodology, Writing – review & editing, Supervision.; Greg Hajcak: Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Investigation, Data curation, Funding acquisition, Project administration.

#### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### **Data Availability**

Data will be made available on request.

#### References

- Achenbach, T. M., & Rescorla, L. (2001). Manual for the ASEBA school-age forms & profiles: An integrated system of multi-informant assessment. Aseba Burlington. VT: University of Vermont Research Center for Children, Youth, & Families.
- Baker, T. E., Stockwell, T., Barnes, G., Haesevoets, R., & Holroyd, C. B. (2016a). Reward sensitivity of ACC as an intermediate phenotype between DRD4-521 T and substance misuse. *Journal of Cognitive Neuroscience*, 28(3), 460–471. https://doi.org/ 10.1162/jocn a 00905
- Baker, T. E., Stockwell, T., Barnes, G., & Holroyd, C. B. (2011). Individual differences in substance dependence: At the intersection of brain, behaviour and cognition. *Addiction Biology*, 16(3), 458–466. https://doi.org/10.1111/j.1369-1600.2010.00243.x
- Baker, T. E., Wood, J. M. A., & Holroyd, C. B. (2016b). Atypical valuation of monetary and cigarette rewards in substance dependent smokers. *Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology*, 127(2), 1358–1365. https://doi.org/10.1016/j.clinph.2015.11.002
- Baskin-Sommers, A. R., & Foti, D. (2015). Abnormal reward functioning across substance use disorders and major depressive disorder: Considering reward as a transdiagnostic mechanism, 2 International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology, 98(Pt 2), 227–239. https://doi.org/ 10.1016/j.ijpsycho.2015.01.011.
- Becker, M. P. I., Nitsch, A. M., Miltner, W. H. R., & Straube, T. (2014). A single-trial estimation of the feedback-related negativity and its relation to BOLD responses in a time-estimation task. *Journal of Neuroscience*, 34(8), 3005–3012. https://doi.org/ 10.1523/JNEUROSCI.3684-13.2014
- Berridge, K. C., & Robinson, T. E. (2003). Parsing reward. Trends in Neurosciences, 26(9), 507–513. https://doi.org/10.1016/S0166-2236(03)00233-9
- Blum, K., Braverman, E. R., Holder, J. M., Lubar, J. F., Monastra, V. J., Miller, D., Lubar, J. O., Chen, T. J., & Comings, D. E. (2000). Reward deficiency syndrome: A biogenetic model for the diagnosis and treatment of impulsive, addictive, and compulsive behaviors. *Journal of Psychoactive Drugs*, 32(i–iv), 1–112. https://doi. org/10.1080/02791072.2000.10736099
- Blum, K., Chen, A. L. C., Oscar-Berman, M., Chen, T. J. H., Lubar, J., White, N., Lubar, J., Bowirrat, A., Braverman, E., Schoolfield, J., Waite, R. L., Downs, B. W., Madigan, M., Comings, D. E., Davis, C., Kerner, M. M., Knopf, J., Palomo, T., Giordano, J. J., & Bailey, J. A. (2011). Generational association studies of dopaminergic genes in reward deficiency syndrome (RDS) Subjects: selecting appropriate phenotypes for reward dependence behaviors (Article) International Journal of Environmental Research and Public Health, 8(12), 12. https://doi.org/10.3390/ijerph8124425.
- Blum, K., Elman, I., Dennen, C. A., McLaughlin, T., Thanos, P. K., Baron, D., Gold, M. S., & Badgaiyan, R. D. (2022). "Preaddiction" construct and reward deficiency syndrome: genetic link via dopaminergic dysregulation. *Annals of Translational Medicine*, 10(21), 1181. https://doi.org/10.21037/atm-2022-32
- Boecker-Schlier, R., Holz, N. E., Hohm, E., Zohsel, K., Blomeyer, D., Buchmann, A. F., Baumeister, S., Wolf, I., Esser, G., Schmidt, M. H., Meyer-Lindenberg, A., Banaschewski, T., Brandeis, D., & Laucht, M. (2017). Association between pubertal stage at first drink and neural reward processing in early adulthood. Addiction Biology, 22(5), 1402–1415. https://doi.org/10.1111/adb.12413
- Bowirrat, A., & Oscar-Berman, M. (2005). Relationship between dopaminergic neurotransmission, alcoholism, and reward deficiency syndrome. *American Journal* of Medical Genetics Part B: Neuropsychiatric Genetics, 132B(1), 29–37. https://doi.org/ 10.1002/ajmg.b.30080
- Box, G. E. P., & Tidwell, P. W. (1962). Transformation of the independent variables. *Technometrics*, 4(4), 531–550. https://doi.org/10.1080/00401706.1962.10490038
- Bunford, N., Kujawa, A., Dyson, M., Olino, T., & Klein, D. N. (2022). Examination of developmental pathways from preschool temperament to early adolescent ADHD symptoms through initial responsiveness to reward. *Development and Psychopathology*, 34(3), 841–853. https://doi.org/10.1017/S0954579420002199
- Bress, J. N., Foti, D., Kotov, R., Klein, D. N., & Hajcak, G. (2013). Blunted neural response to rewards prospectively predicts depression in adolescent girls. *Psychophysiology*, 50 (1), 74–81. https://doi.org/10.1111/j.1469-8986.2012.01485.x
- Bress, J. N., & Hajcak, G. (2013). Self-report and behavioral measures of reward sensitivity predict the feedback negativity. *Psychophysiology*, 50(7), 610–616. https://doi.org/10.1111/psyp.12053
- Brown, S. L., & Rinelli, L. N. (2010). Family structure, family processes, and adolescent smoking and drinking. *Journal of Research on Adolescence*, 20, 259–273. https://doi. org/10.1111/j.1532-7795.2010.00636.x
- Buckholtz, J. W., Treadway, M. T., Cowan, R. L., Woodward, N. D., Li, R., Ansari, M. S., Baldwin, R. M., Schwartzman, A. N., Shelby, E. S., Smith, C. E., Kessler, R. M., &

Zald, D. H. (2010). Dopaminergic network differences in human impulsivity. *Science* (*New York*, *N York*), 329(5991), 532. https://doi.org/10.1126/science.1185778

- Burani, K., Brush, C. J., Gallyer, A., Joiner, T., Nelson, B., & Hajcak, G. (2021a). Maternal suicidality interacts with blunted reward processing to prospectively predict increases in depressive symptoms in 8-to-14-year-old girls. *International Journal of Psychophysiology*, 170, 67–74. https://doi.org/10.1016/j.ijpsycho.2021.10.002
- Burani, K., Klawohn, J., Levinson, A. R., Klein, D. N., Nelson, B. D., & Hajcak, G. (2021b). Neural response to rewards, stress and sleep interact to prospectively predict depressive symptoms in adolescent girls. *Journal of Clinical Child & Adolescent Psychology*, 50(1), 131–140. https://doi.org/10.1080/15374416.2019.1630834
- Burani, K., Mulligan, E. M., Klawohn, J., Luking, K. R., Nelson, B. D., & Hajcak, G. (2019). Longitudinal increases in reward-related neural activity in early adolescence: Evidence from event-related potentials (ERPs). *Developmental Cognitive Neuroscience*, 36, Article 100620. https://doi.org/10.1016/j.dcn.2019.100620
- Burani, K., Brush, C., Shields, G., Klein, D., Nelson, B., Slavich, G., & Hajcak, G. (2022a). Cumulative lifetime acute stressor exposure interacts with reward responsiveness to predict longitudinal increases in depression severity in adolescence. *Psychological Medicine*, 1–10. https://doi.org/10.1017/S0033291722001386
- Burani, K., Brush, C. J., Shields, G. S., Klein, D. N., Nelson, B. D., Slavich, G. M., & Hajcak, G. (2022b). Greater cumulative lifetime stressor exposure predicts blunted reward positivity in adolescent girls followed for 2 years. *Biological Psychiatry Cognitive Neuroscience and Neuroimaging*, 7(10), 1017–1024. https://doi.org/ 10.1016/j.bpsc.2022.05.011
- Carey, C. E., Knodt, A. R., Conley, E. D., Hariri, A. R., & Bogdan, R. (2017). Rewardrelated ventral striatum activity links polygenic risk for attention-deficit/ hyperactivity disorder to problematic alcohol use in young adulthood. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 2(2), 180–187. https://doi.org/ 10.1016/j.bpsc.2016.10.003
- Carlson, J. M., Foti, D., Mujica-Parodi, L. R., Harmon-Jones, E., & Hajcak, G. (2011). Ventral striatal and medial prefrontal BOLD activation is correlated with rewardrelated electrocortical activity: A combined ERP and fMRI study. *NeuroImage*, 57(4), 1608–1616. https://doi.org/10.1016/j.neuroimage.2011.05.037
- Casement, M. D., Shaw, D. S., Sitnick, S. L., Musselman, S. C., & Forbes, E. E. (2015). Life stress in adolescence predicts early adult reward-related brain function and alcohol dependence. Social Cognitive and Affective Neuroscience, 10(3), 416–423. https://doi. org/10.1093/scan/nsu061
- Casey, B. J., & Jones, R. M. (2010). Neurobiology of the adolescent brain and behavior: Implications for substance use disorders. *Journal of the American Academy of Child & Adolescent Psychiatry*, 49(12), 1189–1201. https://doi.org/10.1016/j. jaac.2010.08.017
- Chassin, L., Pitts, S. C., & Prost, J. (2002). Binge drinking trajectories from adolescence to emerging adulthood in a high-risk sample: Predictors and substance abuse outcomes. *Journal of Consulting and Clinical Psychology*, 70(1). https://doi.org/10.1037/0022-006X.70.1.67
- Cheng, H. G., & Anthony, J. C. (2018). Male-female differences in the onset of heavy drinking episode soon after first full drink in contemporary United States: From early adolescence to young adulthood. *Drug and Alcohol Dependence, 190*, 159–165. https://doi.org/10.1016/j.drugalcdep.2017.12.035
- Clark, D. B., Thatcher, D. L., & Tapert, S. F. (2008). Alcohol, psychological dysregulation, and adolescent brain development. Alcoholism: Clinical and Experimental Research, 32 (3), 375–385. https://doi.org/10.1111/j.1530-0277.2007.00601.x

Crane, N. A., Funkhouser, C. J., Burkhouse, K. L., Klumpp, H., Phan, K. L., & Shankman, S. A. (2021). Cannabis users demonstrate enhanced neural reactivity to reward: An event-related potential and time-frequency EEG study. Addictive Behaviors, 113, Article 106669. https://doi.org/10.1016/j.addbeh.2020.106669

- Crane, N. A., Li, L. Y., Brooks, J. M., & Shankman, S. A. (2023). Preliminary evidence that individuals with remitted alcohol use disorder and major depressive disorder exhibit enhanced neural responses to reward: An EEG study. Addictive Behaviors, 143, Article 107712. https://doi.org/10.1016/j.addbeh.2023.107712
- Crowley, M. J., Wu, J., Crutcher, C., Bailey, C. A., Lejuez, C. W., & Mayes, L. C. (2009). Risk-taking and the feedback negativity response to loss among at-risk adolescents. *Developmental Neuroscience*, 31(1–2), 137–148. https://doi.org/10.1159/000207501
- Cuthbert, B. N., & Insel, T. R. (2013). Toward the future of psychiatric diagnosis: the seven pillars of RDoC. BMC Medicine, 11(1), 126. https://doi.org/10.1186/1741-7015-11-126
- Destoop, M., Morrens, M., Coppens, V., & Dom, G. (2019). Addiction, anhedonia, and comorbid mood disorder. A narrative review. *Frontiers in Psychiatry*, 10, 311. https:// doi.org/10.3389/fpsyt.2019.00311

Deutsch, A. R., Slutske, W. S., Lynskey, M. T., Bucholz, K. K., Madden, P. A. F., Heath, A. C., & Martin, N. G. (2017). From alcohol initiation to tolerance to problems: Discordant twin modeling of a developmental process. *Development and Psychopathology*, 29(3), 845–861. https://doi.org/10.1017/S0954579416000523

- Diehl, A., Croissant, B., Batra, A., Mundle, G., Nakovics, H., & Mann, K. (2007). Alcoholism in women: Is it different in onset and outcome compared to men? *European Archives of Psychiatry and Clinical Neuroscience*, 257(6), 344–351. https:// doi.org/10.1007/s00406-007-0737-z
- Euser, A. S., Greaves-Lord, K., Crowley, M. J., Evans, B. E., Huizink, A. C., & Franken, I. H. A. (2013). Blunted feedback processing during risky decision making in adolescents with a parental history of substance use disorders, 4 *Development and Psychopathology*, 25(Pt 1), 1119–1136. https://doi.org/10.1017/ S0954579413000412.
- Ewing, S. W. F., Sakhardande, A., & Blakemore, S.-J. (2014). The effect of alcohol consumption on the adolescent brain: a systematic review of MRI and fMRI studies of alcohol-using youth. *NeuroImage Clinical*, *5*, 420–437. https://doi.org/10.1016/j. nicl.2014.06.011

Fein, G., & Chang, M. (2008). Smaller feedback ERN amplitudes during the BART are associated with a greater family history density of alcohol problems in treatmentnaïve alcoholics. *Drug and Alcohol Dependence*, 92(1), 141–148. https://doi.org/ 10.1016/j.drugalcdep.2007.07.017

- Foster, K. T., Hicks, B. M., Iacono, W. G., & McGue, M. (2014). Alcohol use disorder in women: risks and consequences of an adolescent onset and persistent course. *Psychology of Addictive Behaviors*, 28(2), 322–335. https://doi.org/10.1037/ a0035488
- Foti, D., Weinberg, A., Dien, J., & Hajcak, G. (2011). Event-related potential activity in the basal ganglia differentiates rewards from nonrewards: Temporospatial principal components analysis and source localization of the feedback negativity. *Human Brain Mapping*, 32(12), 2207–2216. https://doi.org/10.1002/hbm.21182
- Freeman, C., Dirks, M., & Weinberg, A. (2020). Neural response to rewards predicts risktaking in late but not early adolescent females. *Developmental Cognitive Neuroscience*, 45, Article 100808. https://doi.org/10.1016/j.dcn.2020.100808
- Hammond, C. J., Wu, J., Krishnan-Sarin, S., Mayes, L. C., Potenza, M. N., & Crowley, M. J. (2021). Co-occurring tobacco and cannabis use in adolescents: Dissociable relationships with mediofrontal electrocortical activity during reward feedback processing. *NeuroImage: Clinical*, 30, Article 102592. https://doi.org/ 10.1016/j.nicl.2021.102592
- Hámori, G., File, B., Fiáth, R., Pászthy, B., Réthelyi, J. M., Ulbert, I., & Bunford, N. (2023). Adolescent ADHD and electrophysiological reward responsiveness: a machine learning approach to evaluate classification accuracy and prognosis. *Psychiatry Research*, 323, Article 115139. https://doi.org/10.1016/j. psychres.2023.115139
- Hernandez-Avila, C. A., Rounsaville, B. J., & Kranzler, H. R. (2004). Opioid-, cannabisand alcohol-dependent women show more rapid progression to substance abuse treatment. *Drug and Alcohol Dependence*, 74(3), 265–272. https://doi.org/10.1016/j. drugalcdep.2004.02.001
- Hixson, H., Burkhouse, K. L., Gorka, S. M., & Klumpp, H. (2019). A preliminary examination of the relation between neural sensitivity to reward and history of alcohol use disorder among adults with internalizing psychopathologies. *Neuroscience Letters*, 690, 17–22. https://doi.org/10.1016/j.neulet.2018.10.003
- Hussong, A. M., Jones, D. J., Stein, G. L., Baucom, D. H., & Boeding, S. (2011). An internalizing pathway to alcohol use and disorder. *Psychology of Addictive Behaviors*, 25(3), 390–404. https://doi.org/10.1037/a0024519
- Hussong, A. M., Ennett, S. T., Cox, M. J., & Haroon, M. (2017). A systematic review of the unique prospective association of negative affect symptoms and adolescent substance use controlling for externalizing symptoms. *Psychology of Addictive Behaviors*, 31(2), 137–147. https://doi.org/10.1037/adb0000247
- Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., Sanislow, C., & Wang, P. (2010). Research domain criteria (RDoC): Toward a new classification framework for research on mental disorders. *The American Journal of Psychiatry*, 167 (7), 748–751. https://doi.org/10.1176/appi.ajp.2010.09091379
- Jackson, K. M. (2010). Progression through early drinking milestones in an adolescent treatment sample. Addiction, 105(3), 438–449. https://doi.org/10.1111/j.1360-0443.2009.02800.x
- Jackson, K. M., Marceau, K., Colby, S. M., Barnett, N. P., Rogers, M. L., & Hayes, K. L. (2021). Trajectories of early alcohol use milestones: Interrelations among initiation and progression. Alcoholism: Clinical and Experimental Research, 45(11), 2294–2308. https://doi.org/10.1111/acer.14723
- Johnston, L.D., Miech, R.A., O'Malley, P.M., Bachman, J.G., Schulenberg, J.E., Patrick, M.E., 2019. Monitoring the Future national survey results on drug use, 1975–2018: Overview, key findings on adolescent drug use. In *Institute for Social Research*. Institute for Social Research. (https://eric.ed.gov/?id=ED594190).
- Joyner, K. J., Bowyer, C. B., Yancey, J. R., Venables, N. C., Foell, J., Worthy, D. A., Hajcak, G., Bartholow, B. D., & Patrick, C. J. (2019). Blunted reward sensitivity and trait disinhibition interact to predict substance use problems. *Clinical Psychological Science*, 7(5), 1109–1124. https://doi.org/10.1177/2167702619838480
- Kallen, A. M., Perkins, E. R., Klawohn, J., & Hajcak, G. (2020). Cross-sectional and prospective associations of P300, RewP, and ADHD symptoms in female adolescents. *International Journal of Psychophysiology*, 158, 215–224. https://doi.org/10.1016/j. ijpsycho.2020.08.017
- Kaufman, J., Birmaher, B., Brent, D., Rao, U. M. A., Flynn, C., Moreci, P., & Ryan, N. (1997). Schedule for affective disorders and schizophrenia for school-age childrenpresent and lifetime version (K-SADS-PL): Initial reliability and validity data. *Journal* of the American Academy of Child & Adolescent Psychiatry, 36(7), 980–988. https:// doi.org/10.1097/00004583-199707000-00021
- Kendler, K. S., Gardner, C., & Dick, D. M. (2011). Predicting alcohol consumption in adolescence from alcohol-specific and general externalizing genetic risk factors, key environmental exposures and their interaction (Article) *Psychological Medicine*, 41 (7), 7. https://doi.org/10.1017/S003329171000190X.
- King, S. M., Iacono, W. G., & McGue, M. (2004). Childhood externalizing and internalizing psychopathology in the prediction of early substance use (Article) *Addiction*, 99(12), 12. https://doi.org/10.1111/j.1360-0443.2004.00893.x.

Kovacs, M. , 1992. Children's depression inventory: Manual. Multi-Health Systems North Tonawanda, NY.

- Krueger, R. F., Hicks, B. M., Patrick, C. J., Carlson, S. R., Iacono, W. G., & McGue, M. (2009). Etiologic connections among substance dependence, antisocial behavior, and personality: Modeling the externalizing spectrum (p. 88). American Psychological Association. https://doi.org/10.1037/11855-003
- Kujawa, A., Carroll, A., Mumper, E., Mukherjee, D., Kessel, E. M., Olino, T., Hajcak, G., & Klein, D. N. (2018). A longitudinal examination of event-related potentials sensitive to monetary reward and loss feedback from late childhood to middle adolescence. *International Journal of Psychophysiology: Official Journal of the International*

Organization of Psychophysiology, 132(Pt B), 323–330. https://doi.org/10.1016/j. ijpsycho.2017.11.001

- Levinson, A. R., Speed, B. C., Infantolino, Z. P., & Hajcak, G. (2017). Reliability of the electrocortical response to gains and losses in the doors task (Article) *Psychophysiology*, 54(4), 4. https://doi.org/10.1111/psyp.12813.
- Liu, W., Wang, L., Shang, H., Shen, Y., Li, Z., Cheung, E. F. C., & Chan, R. C. K. (2014). The influence of anhedonia on feedback negativity in major depressive disorder. *Neuropsychologia*, 53, 213–220. https://doi.org/10.1016/j. neuropsychologia.2013.11.023
- Luking, K. R., Nelson, B. D., Infantolino, Z. P., Sauder, C. L., & Hajcak, G. (2017). Internal consistency of functional magnetic resonance imaging and electroencephalography measures of reward in late childhood and early adolescence. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 2(3), 289–297. https://doi.org/10.1016/j. bpsc.2016.12.004
- Menary, K. R., Corbin, W. R., & Chassin, L. (2017). Associations between early internalizing symptoms and speed of transition through stages of alcohol involvement. *Development and Psychopathology*, 29(4), 1455–1467. https://doi.org/ 10.1017/S0954579417000384
- Meyer, A., Lerner, M. D., De Los Reyes, A., Laird, R. D., & Hajcak, G. (2017). Considering ERP difference scores as individual difference measures: Issues with subtraction and alternative approaches. *Psychophysiology*, 54(1), 114–122. https://doi.org/10.1111/ psyp.12664
- Morales, A. M., Jones, S. A., Ehlers, A., Lavine, J. B., & Nagel, B. J. (2018). Ventral striatal response during decision making involving risk and reward is associated with future binge drinking in adolescents (Article) *Neuropsychopharmacology*, 43(9), 9. https://doi.org/10.1038/s41386-018-0087-8.
- Morean, M. E., Kong, G., Camenga, D. R., Cavallo, D. A., Connell, C., & Krishnan-Sarin, S. (2014). First drink to first drunk: Age of onset and delay to intoxication are associated with adolescent alcohol use and binge drinking. Alcoholism: Clinical and Experimental Research, 38(10), 2615–2621. https://doi.org/10.1111/acer.12526
- Morean, M. E., L'Insalata, A., Butler, E. R., McKee, A., & Krishnan-Sarin, S. (2018). Age at drinking onset, age at first intoxication, and delay to first intoxication: Assessing the concurrent validity of measures of drinking initiation with alcohol use and related problems. Addictive Behaviors, 79, 195–200. https://doi.org/10.1016/j. addbeh.2017.12.017
- Morie, K. P., De Sanctis, P., Garavan, H., & Foxe, J. J. (2016). Regulating task-monitoring systems in response to variable reward contingencies and outcomes in cocaine addicts. *Psychopharmacology*, 233(6), 1105–1118. https://doi.org/10.1007/s00213-015-4191-8
- Morie, K. P., Wu, J., Landi, N., Potenza, M. N., Mayes, L. C., & Crowley, M. J. (2018). Feedback processing in adolescents with prenatal cocaine exposure: An electrophysiological investigation. *Developmental Neuropsychology*, 43(3), 183–197. https://doi.org/10.1080/87565641.2018.1439945
- Morie, K. P., Wu, J., Potenza, M. N., Krishnan-Sarin, S., Mayes, L. C., Hammond, C. J., & Crowley, M. J. (2021). Daily cannabis use in adolescents who smoke tobacco is associated with altered late-stage feedback processing: a high-density electrical mapping study. *Journal of Psychiatric Research*, 139, 82–90. https://doi.org/ 10.1016/j.jpsychires.2021.05.022
- Na, E., Jang, K.-M., & Kim, M.-S. (2019). An event-related potential study of decisionmaking and feedback utilization in female college students who binge drink. *Frontiers in Psychology*, 10. (https://www.frontiersin.org/article/10.3389 /fpsyc.2019.02606).
- Nelson, B. D., Perlman, G., Klein, D. N., Kotov, R., & Hajcak, G. (2016). Blunted neural response to rewards as a prospective predictor of the development of depression in adolescent girls. *American Journal of Psychiatry*, 173(12), 1223–1230. https://doi. org/10.1176/appi.ajp.2016.15121524
- Nolen-Hoeksema, S. (2004). Gender differences in risk factors and consequences for alcohol use and problems. *Clinical Psychology Review*, 24(8), 981–1010. https://doi. org/10.1016/j.cpr.2004.08.003
- Nolen-Hoeksema, S., & Hilt, L. (2006). Possible contributors to the gender differences in alcohol use and problems. *The Journal of General Psychology*, 133(4), 357–374. https://doi.org/10.3200/GENP.133.4.357-374
- Parvaz, M. A., Konova, A. B., Proudfit, G. H., Dunning, J. P., Malaker, P., Moeller, S. J., Maloney, T., Alia-Klein, N., & Goldstein, R. Z. (2015). Impaired neural response to negative prediction errors in cocaine addiction. *The Journal of Neuroscience*, 35(5), 1872–1879. https://doi.org/10.1523/JNEUROSCI.2777-14.2015
- \*Perkins\*, E. R., Joyner\*, K. J., Patrick, C. J., Bartholow, B. D., Latzman, R. D., DeYoung, C. G., Kotov, R., Reininghaus, U., Cooper, S. E., Afzali, M. H., Docherty, A. R., Dretsch, M. N., Eaton, N. R., Goghari, V. M., Haltigan, J. D., Krueger, R. F., Martin, E. A., Michelini, G., Ruocco, A. C., & Zald, D. H. (2020). Neurobiology and the Hierarchical Taxonomy of Psychopathology: Progress toward ontogenetically informed and clinically useful nosology. *Dialogues in Clinical Neuroscience*, 22(1), 51–63. https://doi.org/10.31887/DCNS.2020.22.1/eperkins
- Proudit, G. H. (2015). The reward positivity: From basic research on reward to a biomarker for depression. *Psychophysiology*, 52(4), 449–459. https://doi.org/ 10.1111/psyp.12370
- Quinn, P. D., & Harden, K. P. (2013). Differential changes in impulsivity and sensation seeking and the escalation of substance use from adolescence to early adulthood. *Development and Psychopathology*, 25(1), 223–239. https://doi.org/10.1017/ S0954579412000284
- Rádosi, A., Pászthy, B., Welker, T.É., Zubovics, E. A., Réthelyi, J. M., Ulbert, I., & Bunford, N. (2021). The association between reinforcement sensitivity and substance use is mediated by individual differences in dispositional affectivity in adolescents. *Addictive Behaviors*, 114, Article 106719. https://doi.org/10.1016/j. addbeh.2020.106719

Ryan, J., Pouliot, J. J., Hajcak, G., & Nee, D. E. (2022). Manipulating reward sensitivity using reward circuit-targeted transcranial magnetic stimulation. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 7(8), 833–840. https://doi.org/ 10.1016/j.bpsc.2022.02.011

- Sartor, C. E., Jackson, K. M., McCutcheon, V. V., Duncan, A. E., Grant, J. D., Werner, K. B., & Bucholz, K. K. (2016). Progression from first drink, first intoxication, and regular drinking to alcohol use disorder: a comparison of African American and European American youth. Alcoholism: Clinical and Experimental Research, 40(7), 1515–1523. https://doi.org/10.1111/acer.13113
- Schleider, J. L., Ye, F., Wang, F., Hipwell, A. E., Chung, T., & Sartor, C. E. (2019). Longitudinal reciprocal associations between anxiety, depression, and alcohol use in adolescent girls. *Alcoholism: Clinical and Experimental Research*, 43(1), 98–107. https://doi.org/10.1111/acer.13913
- Sehrig, S., Weiss, A., Miller, G. A., & Rockstroh, B. (2019). Decision- and feedback-related brain potentials reveal risk processing mechanisms in patients with alcohol use disorder. *Psychophysiology*, 56(12), Article e13450. https://doi.org/10.1111/ psyp.13450
- Spear, L. P. (2016). Alcohol consumption in adolescence: a translational perspective. Current Addiction Reports, 3(1), 50–61. https://doi.org/10.1007/s40429-016-0088-9
- Telzer, E. H., Fuligni, A. J., Lieberman, M. D., & Galván, A. (2013). Ventral striatum activation to prosocial rewards predicts longitudinal declines in adolescent risk taking. *Developmental Cognitive Neuroscience*, 3, 45–52. https://doi.org/10.1016/j. dcn.2012.08.004
- Thompson, B., Santopetro, N. J., Brush, C. J., Foti, D., & Hajcak, G. (2023). Neural deficits in anticipatory and consummatory reward processing are uniquely associated with current depressive symptoms during adolescence. *Psychophysiology*., Article e14257. https://doi.org/10.1111/psyp.14257
- Urošević, S., Collins, P., Muetzel, R., Schissel, A., Lim, K. O., & Luciana, M. (2015). Effects of reward sensitivity and regional brain volumes on substance use initiation in adolescence. *Social Cognitive and Affective Neuroscience*, 10(1), 106–113. https:// doi.org/10.1093/scan/nsu022
- van Hemel-Ruiter, M. E., de Jong, P. J., Ostafin, B. D., & Wiers, R. W. (2015). Reward sensitivity, attentional bias, and executive control in early adolescent alcohol use. Addictive Behaviors, 40, 84–90. https://doi.org/10.1016/j.addbeh.2014.09.004
- Vashishtha, R., Pennay, A., Dietze, P., Marzan, M. B., Room, R., & Livingston, M. (2021). Trends in adolescent drinking across 39 high-income countries: Exploring the timing

and magnitude of decline. European Journal of Public Health, 31(2), 424–431. https://doi.org/10.1093/eurpub/ckaa193

- Waller, R., Murray, L., Shaw, D. S., Forbes, E. E., & Hyde, L. W. (2019). Accelerated alcohol use across adolescence predicts early adult symptoms of alcohol use disorder via reward-related neural function. *Psychological Medicine*, 49(4), 675–684. https:// doi.org/10.1017/S003329171800137X
- Watts, A. L., Wood, P. K., Jackson, K. M., Lisdahl, K. M., Heitzeg, M. M., Gonzalez, R., Tapert, S. F., Barch, D. M., & Sher, K. J. (2021). Incipient alcohol use in childhood: Early alcohol sipping and its relations with psychopathology and personality. *Development and Psychopathology*, 33(4), 1338–1350. https://doi.org/10.1017/ S0954579420000541
- White, A. M. (2020). Gender differences in the epidemiology of alcohol use and related harms in the United States. Alcohol Research: Current Reviews, 40(2). https://doi.org/ 10.35946/arcr.v40.2.01
- Wiers, R. W., Bartholow, B. D., van den Wildenberg, E., Thush, C., Engels, R. C. M. E., Sher, K. J., Grenard, J., Ames, S. L., & Stacy, A. W. (2007). Automatic and controlled processes and the development of addictive behaviors in adolescents: a review and a model. *Pharmacology Biochemistry and Behavior*, 86(2), 263–283. https://doi.org/ 10.1016/j.pbb.2006.09.021
- Young, S. E., Friedman, N. P., Miyake, A., Willcutt, E. G., Corley, R. P., Haberstick, B. C., & Hewitt, J. K. (2009). Behavioral disinhibition: liability for externalizing spectrum disorders and its genetic and environmental relation to response inhibition across adolescence. *Journal of Abnormal Psychology*, *118*(1), 117–130. https://doi.org/ 10.1037/a0014657
- Zhao, Q., Li, H., Hu, B., Wu, H., & Liu, Q. (2017). Abstinent heroin addicts tend to take risks: ERP and source localization. *Frontiers in Neuroscience*, 11. (https://www.front iersin.org/article/10.3389/fnins.2017.00681).
- Zhong, N., Chen, T., Zhu, Y., Su, H., Ruan, X., Li, X., Tan, H., Jiang, H., Du, J., & Zhao, M. (2020). Smaller feedback-related negativity (FRN) reflects the risky decision-making deficits of methamphetamine dependent individuals. *Frontiers in Psychiatry*, 11. (htt ps://www.frontiersin.org/article/10.3389/fpsyt.2020.00320).
- Zubovics, E. A., Fiáth, R., Rádosi, A., Pászthy, B., Réthelyi, J. M., Ulbert, I., & Bunford, N. (2021). Neural and self-reported reward responsiveness are associated with dispositional affectivity and emotion dysregulation in adolescents with evidence for convergent and incremental validity. *Psychophysiology*, 58(2), Article e13723. https://doi.org/10.1111/psyp.13723