**Parietal P3 and midfrontal theta prospectively predict the development of adolescent alcohol use**

***Supplemental Information***

**Methods**

**Sample**

Potential attrition effects were evaluated by comparing mean differences in age-14 task-related EEG measures (P3, and theta) between those who did (*n* = 594) or did not (*n* = 121) have complete alcohol use data for all three assessments. Differences were negligible (|Cohen’s *d*s| ≤ 0.12), indicating little evidence of meaningful attrition effects.

**Parental alcohol use disorder assessment**

As detailed in (Keyes *et al.* 2009), parents were assessed using an expanded version of the Substance Abuse Module of the Composite International Diagnostic Interview (Robins *et al.* 1987), which was administered by trained interviewers. Parents reported on alcohol use disorder symptoms covering lifetime and the past six years at the child age-11 and age-17 assessments, respectively. Diagnosis of alcohol use disorder (AUD) was defined as endorsing two or more symptoms of DSM-IV (American Psychiatric Association 1994); the psychiatric diagnostic manual at the time) alcohol dependence/abuse criteria at either assessment. This is consistent with DSM-5 (American Psychiatric Association 2013), but note that while there is high overlap between DSM-IV and DSM-5 AUD symptoms (10/11 symptoms overlap), they are not identical, and these diagnoses can be considered close proxies for DSM-5 AUD. The majority of parents were biological parents. The sample consisted of 337 families, and the breakdown of parents is as follows: age-11 assessment (*n*): biological mothers (333); biological fathers (295); stepmother (2); stepfather (7); second stepfather (1); age-17 assessment (*n*): biological mothers (327); biological fathers (265); stepmother (1); stepfather (9); second stepfather (1).

For the 337 families, 169 (50.1%) had at least one parent who met criteria for AUD at either assessment; 99 were families with paternal AUD only, 27 were families with maternal AUD only, and 43 were families with both paternal and maternal AUD. Of the 594 adolescents in this sample, 304 (51.2%) had at least one parent with lifetime AUD.

**EEG recording and processing**

At the age-14 assessment, continuous EEG was collected using a BioSemi ActiveTwo system from 61 scalp electrodes (International 10/10 montage) at 1024 Hz using an analog DC to 205 Hz band-pass filter. Vertical and horizontal electrooculogram (EOG) signals were collected using electrodes placed above and below the right eye and on the right and left temples respectively, along with left and right earlobe signals.

Signals were processed in MATLAB using EEGLAB (Delorme & Makeig, 2004) and in-house code, as described in (Harper *et al.* 2017, 2018a, 2018b). Signals were resampled at 256 Hz, highpass filtered (*firfilt* plugin; .01 Hz), and referenced to the average earlobe signals. A supervised automated pipeline detected artifacts (flat electrodes, large amplitude deviations, muscular artifacts) and inter-electrode electrolyte bridging (Tenke & Kayser, 2001) in the continuous data. Descriptives (e.g., temporal variance) were calculated across each electrode and 1 second time range; data that exceeded four normalized absolute deviations from the median (Rousseeuw & Croux, 1993) in 25% of a 1 second time range or 75% of a given electrode were removed. Ocular correction was calculated with independent components (IC) analysis (infomax; (Bell & Sejnowski, 1995). IC inverse weights and time courses were correlated with inverse weights of a stereotypical horizontal saccade or blink and the time courses of bipolar horizontal or vertical EOG signals respectively. ICs were subtracted from the data if the squared joint spatial and temporal correlations exceeded an empirically calculated threshold (Mognon *et al.* 2011). Two-second epochs flanking stimulus onset were taken and screened for the artifacts detailed above. Deleted channels were interpolated using a spherical spline method within epochs containing ≥75% original data. The mean prestimulus baseline between -200 to -1 ms was subtracted from the data. Error trials were removed.

**EEG signal analysis**

EEG analysis was performed using the Psychophysiology Toolbox (http://www.ccnlab.umd.edu/Psychophysiology\_Toolbox/) supplemented with additional in-house and external (Cohen, 2014) code.

Given a lack of evidence that target difficulty in oddball tasks has a significant interaction effect on the relationship between P3 and alcohol use (Begleiter *et al.* 1984; Hill & Steinhauer 1993; Malone *et al.* 2001), to maintain consistency with similar studies and to improve the estimation/signal-to-noise ratio of the ERP/time-frequency measures by increasing the number of trials in the averages, we collapsed across easy and hard targets in all analyses.

Subsampling (without replacement) was performed at the trial-level prior to calculating ERPs or time-frequency power averages to equate the trial numbers between target (collapsed across easy/hard trials) and standard conditions. For each participant, a random sample of standard trials was selected to match the number of available target trials (mean [SD] = 66.1 [11.8]) before calculating averages; this was repeated 25 times, and the results were averaged.

Time-frequency analysis was conducted according to our previous reports (Harper *et al.* 2017, 2019). Trial-level signals were transformed into time-frequency representations using complex Morlet wavelet convolution (Cohen, 2014), providing an estimate of total power (phase- and non-phase-locked activity). Frequencies spanning 1 to 30 Hz in 25 logarithmic steps were extracted; the number of wavelet cycles increased from 3 to 8 in 25 logarithmic steps to obtain comparable time/frequency precision across frequency bands. The resulting trial-level analytic signals (Z*t*) were temporally downsampled to 64 time bins per second. Trial-averaged power for targets and standards was separately calculated as [real(Z*t*)2 + imag(Z*t*)2] and baseline corrected (decibel transform; separately across frequencies) relative to the mean prestimulus power between -450 and -250 ms.

**Results**

**Behavioral measure descriptive statistics**

Mean hit rate for targets was 94.7% (*SD* = 7.2). Only 80 individuals committed false alarm responses to standard stimuli (false alarm rate: mean [SD] = 5.0% [6.1]; mean across entire sample = 0.7%). Average target reaction time was 891.2 ms (*SD* = 125.9), and average intraindividual reaction time variability was 193.7 ms (*SD* = 38.3).

**Supplemental Tables**

Table S1. Quantification of alcohol use measures used in the composite drink index.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Score | Quantity | Frequency | Intoxications | Max Drinks |
| 0 | None | None | None | None |
| 1 | < 1 to 3 | < Once per month | < Once per month | < 1 to 3 |
| 2 | 4 to 6 | 1-3 times per month | 1 time per month | 4 to 6 |
| 3 | 7 to 9 | 1-2 times per week | 2-3 times per month | 7 to 9 |
| 4 | ≥ 10 | 3-4 times per week | 1-2 times per week | ≥ 10 |
| 5 |  | Every day/nearly every day | 3-4 times a week to every day |  |

Table S2. Predicting age-17 alcohol use using age-14 target P3 and theta controlling for tobacco and illicit drug use by age-14.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | *β* (95% CI) | *t* (df) | *p* | R2 |
| **Age-17**  **Drinking Index** |  |  |  | .15 |
| Target P3 | -.10  (-.18, -.03) | -2.65 (578) | .008 |  |
| Target Theta | -.11  (-.18, -.04) | -2.94 (569) | .003 |  |
| Age 11/14 Drink Index | .19  (.11, .29) | 4.36 (574) | <.001 |  |
| Parental AUD | .09  (.01, .18) | 2.11  (328) | .036 |  |
| Sex | -.06  (-.15, .03) | -1.33  (326) | .186 |  |
| Age 11/14 Tobacco | .13  (.04, .22) | 2.84  (557) | .005 |  |
| Age 11/14 Illicit Drug | .04  (-.04, .12) | 1.00  (503) | .316 |  |

*Note:* Age 11/14 tobacco initiation *n*:no = 494, yes = 92. Age 11/14 illicit drug initiation *n*: no=506, yes = 80. Including target-related theta and P3 improved model fit/prediction (Δχ2(2) = 16.83, *p* < .001; ΔR2 = .03) beyond the covariate-only model.

*Abbreviations*: CI = confidence interval; AUD = alcohol use disorder.

Table S3. Prospective analyses predicting new onset of alcohol use by age-17 using age-14 target parietal P3 and midfrontal theta controlling for tobacco/illicit drug initiation by age-14.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | New onset alcohol use behaviors at age-17 | | | | | | | | | | | |
|  | Initiation | |  | Intoxication | |  | Binge Drinking | |  | Drinking Index | | |
|  | OR | 95% CI |  | OR | 95% CI |  | OR | 95% CI |  | *β* (95% CI) | *t* (*df*) | *p* |
| Target P3 | 1.50 | 1.08-2.23 |  | 1.83 | 0.86-4.27 |  | 2.72 | 1.26-6.56 |  | -.18  (-.17, -.06) | -3.25  (462) | .002 |
| Target Theta | 1.53 | 1.10-2.32 |  | 2.91 | 1.32-7.65 |  | 2.47 | 1.18-5.82 |  | -.09  (-.18, -.001) | -1.98  (461) | .049 |
| Parental AUD | 2.16 | 1.04-5.44 |  | 3.32 | 0.48-28.47 |  | 3.08 | 0.47-24.01 |  | .11  (.01, .21) | 2.06  (281) | .041 |
| Sex | 1.80 | 0.86-4.18 |  | 1.90 | 0.27-15.07 |  | 1.19 | 0.17-8.46 |  | -.02  (-.13, .08) | -0.47  (283) | .636 |
| Age-11/14 Tobacco/Illicit Drug | 5.52 | 1.94-20.12 |  | 6.86 | 0.86-62.77 |  | 2.25 | 0.25-17.28 |  | .11  (.02, .19) | 2.48  (436) | .014 |

*Note*: Significant odds ratios above one reflect the increased odds of developing the indicated alcohol use behavior by age-17 associated with a decrease in target-related parietal P3 or midfrontal theta at age-14 (P3 and theta were multiplied by -1 to produce the inverse relationship). Note that because theta (log decibel) and P3 (linear microvolt) are measured on different scales, these measures were standardized for the logistic regressions to facilitate direct comparison of the ORs. In all cases, including target-related theta and P3 improved model fit/prediction (Δχ2(2) ≥ 10.41, *p* ≤ .006) beyond the covariate-only model. R2 for the drinking index model was .06 (ΔR2 after adding theta and P3 = .03).

Because of low endorsement of initiation for either substance among alcohol-naïve age-14 individuals, tobacco (*n*: no = 442, yes= 26) and illicit drug (*n*: no = 436, yes = 32) were combined into a single binary variable for this analysis (*n*: no = 420, yes = 48).

*Abbreviations*: OR = odds ratio; CI = confidence interval.

**Supplemental References**

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