Aberrant cost-benefit integration during effort-based decision-making relates to severity of Substance Use Disorders:

Supplemental Material

Supplemental Method

Measures

Structured Clinical Interview for DSM-5 Disorders (SCID-5; First, Williams, Karg, & Spitzer, 2015). The SCID-5 assesses substance use disorders across nine substance categories. Given the polysubstance use in this sample (see Table 1 in main manuscript), we calculated an additional measure of SUD-related impairment by adding the total number of substance categories for which diagnostic criteria were met (range 0 to 9; see Anderson, Tapert, Moadab, Crowley, & Brown, 2007; Brennan, Stuppy-Sullivan, Brazil, & Baskin-Sommers, 2017; Ermer, Cope, Nyalakanti, Calhoun, & Kiehl, 2013). The SCID-5 also was used to determine lifetime diagnoses of Major Depressive Disorder (MDD). MDD was coded as a binary variable (absent vs. meets diagnosis). In Table S1 we also list other diagnoses assessed using the SCID-5 that characterized the present sample.

Addiction Severity Index (ASI; Leonhard, Mulvey, Gastfriend, & Shwartz, 2000). In order to measure the chronicity of substance use, participants were asked about their use of specific substances, including alcohol, cannabis, cocaine/crack, methamphetamines, other amphetamines, heroin, other opioids, hallucinogens, inhalants, nicotine, and other drugs. Interviewers recorded whether participants had ever tried a substance, the age at which participants first used the substance, and whether participants had regularly used the substance (three or more times per week). For participants who reported using a substance regularly, interviewers recorded age(s) when regular use started and ended to quantify the total number of years of regular use for each substance. A sum of years of regular use across substances was calculated to estimate the chronicity of cumulative use.

Power Analysis

Previous studies using the EEfRT detected three-way interactions among task variables and individual difference variables using sample sizes of 35-98 participants (Barch, Treadway, & Schoen, 2014; Treadway, Bossaller, Shelton, & Zald, 2012; Treadway, Buckholtz, Schwartzman, Lambert, & Zald, 2009). Using GLIMMPSE Statistical Software (Kreidler et al., 2013), we opted to solve for sample size with a desired power of 80%. In specifying the study model, we included individual difference variables (average SUD severity, age, and a moderator variable) as predictors and expected value (EV) as a repeated-measures variable, and we selected the option to control for a single normally distributed covariate (to account for Trial effects; the GLIMMPSE statistical package does not include an option to control for two covariates). We selected the default study design for relatively equal group sizes and identified Choice (easy vs. hard) as the response variable. Given our interest in individual differences impacting SUD severity and EV use, we specified an interaction hypothesis to include all pairwise comparisons across two predictor variables (e.g., SUD severity and delay discount rate) and EV. We used the Hotelling-Lawley Trace statistical test option and specified a Type 1 Error rate of 0.05. When inputting predicted means, we specified mean differences of 15% and 20% hard choices as a function of EV, SUD severity, and a moderator variable, based on previous studies finding 3-way interactions among an EEfRT task variable, a diagnostic variable, and an individual difference variable (Barch, Treadway, & Schoen, 2014; Treadway et al., 2012; Treadway et al., 2009). To account for variability in study variables, for EV, we specified a base correlation of

0.3 and a decay rate of 0.05, and we requested that the LEAR model correlation matrix be computed with scaled spacing values. For Choice, we specified a standard deviation of 0.05 for each response. For the covariate (Trial), we specified an expected SD of 15 trials and a correlation of -0.25 with EV. Lastly, in options, we selected to use a Quantile method and specified a Quantile value of 0.5. Based on predicted mean differences of 15% and 20% hard task choices, calculated sample sizes were estimated at 80 and 48 participants, respectively. We recruited 94 participants to power our study to base the sample size on a more conservative effect size estimate and account for potential data loss.

Supplemental Results

Differentiating willingness to expend effort from ability to execute effortful tasks

To ensure that findings related to EV integration and SUD severity were driven by an individual's willingness to exert effort to obtain rewards and not their ability to complete effortful tasks, we examined the completion rate across all trials for each subject. We found that all subjects completed between 80%-100% of trials. Additionally, there was no relationship between completion rate and average SUD severity, $r(78) = -.02$, $p = .833$.

We also considered the possibility that the decreased willingness to exert effort in response to EV among individuals with SUDs could reflect a decreased desire to spend time considering the effort-based decisions themselves. To examine whether individuals with SUDs were less likely to use EV information when accounting for time spent to consider effortful tasks, we included choice reaction time (RT) as a covariate in the main analysis. The interaction between EV and average SUD severity remained significant ($p= 0.001$, 95% CI = -.221, -.060).

Therefore, the association between diminished integration of EV and average SUD severity appeared independent from the time spent considering effort-based decisions.

It is also possible that the diminished EV integration among individuals with greater average SUD severity actually reflects poor cognitive abilities or reduced fluency with numbers. To examine whether the EV by SUD severity interaction remained when controlling for individual differences in cognitive ability or numeracy, we ran separate models including scores from several neuropsychological measures as covariates (Part B of the Trail Making Task; natural-log transformed and z-scored; Reitan, 1958; Digits Backwards from the Wechsler Digit Span Test; z-scored; Wechsler, 1945; IQ from the Shipley Institute of Living Scale; z-scored; Zachary, 1986). Results from these models indicate that the diminished use of EV associated with SUD severity appeared independent from neuropsychological functioning scores (Trails B: $p = 0.001$, 95% CI = -.217, -.056; Digits Backwards: $p = 0.001$, 95% CI = -.220, -.059; IQ: $p = 0.001$, 95% CI = -.220, -.059).

Individuals with a greater number of SUDs show diminished cost-benefit integration during effort-based choice

To assess whether findings were robust to the clinical measure of SUD severity, we used an additional mixed-effect logistic regression model to determine whether sensitivity to EV during effort-based choice varied as a function of the total number of SUDs across substance categories. Consistent with our SUD severity finding, individuals with a greater number of SUD diagnoses appeared less likely to use EV to modulate effort expenditure ($B = -0.087$, $SE = 0.027$, 95% CI = -0.141, -0.034, $z = -3.20$, $p = 0.001$), suggesting diminished use of EV is robustly related to SUD clinical impairment. This pattern of results is consistent with the notion that individuals with greater SUD-related impairment demonstrate a deficit in the capacity to integrate available decisions variables to modulate action valuation and selection during cost-benefit decisions involving effort allocation.

More chronic substance use is associated with diminished cost-benefit integration during effort-based choice

Beyond diagnostic measures of SUD severity, which estimate the level of clinical impairment associated with substance use, metrics such as the chronicity of substance use provide broadband estimates of problematic substance use. We found that individuals with more chronic substance use appeared less likely to use EV to modulate effort expenditure (B = -.011, SE = 0.002, 95% CI = -.014, -.008, z = -6.91, p < 0.001). Together with the main analyses, these results suggested that impaired use of EV information to modulate effort expenditure is robustly related to substance misuse, from measures tapping clinical impairment to measures tapping substance use chronicity.

Delay discounting is associated with diminished use of probability, but not reward magnitude, during effort-based choice

To explore whether delay-discounting-linked differences in the use of EV information during effort-based choice reflected blunted sensitivity to one or both of the decision variables used to calculate EV, we completed a follow-up analysis to explore the two-way interactions between each decision variable and delay discounting. When we examined a model including the main effects of reward magnitude, probability, and ln$k$ as well as the two-way interactions between the two task variables and ln$k$ as continuous fixed-effect predictors, only sensitivity to probability was blunted in individuals with higher levels of delay discounting (Probability x ln*k*: B = -0.486, SE = 0.104, 95% C.I. = -0.690, -0.282, z = -4.67, $p < 0.001$). By contrast, sensitivity to reward magnitude of the hard task was intact among these individuals (Reward Magnitude x ln*k*: B = -0.022, SE = 0.036, 95% C.I. = -0.092, -0.048, z = -0.62, $p = .535$). These findings suggest that the relationship between delay discounting and effort-based decision-making may be specific to the use of probability information, rather than a deficit integrating multiple decision variables (i.e., reward and probability).

Individuals with more severe SUDs show diminished cost-benefit integration during effort-based choice independent of major depressive disorder

Aberrations in willingness to exert effort to obtain rewards is considered a transdiagnostic marker of psychiatric risk and illness (Reitan, 1958). In fact, the EEfRT has been used extensively in populations diagnosed with MDD (Cuthbert, 2014). Given the substantial comorbidity between SUDs and MDD (e.g., Treadway et al., 2012; Treadway et al., 2009), we examined whether MDD would impact the relationship between EV and SUD severity.

MDD was added to the SUD severity logistic regression model and the two-way interaction between EV and MDD and the three-way interaction among EV, SUD severity, and MDD were included. Neither the two-way interaction between EV and MDD (p =.664) nor the three-way interaction among EV, SUD severity, and MDD was significant (p=.438). Additionally, when including MDD as a covariate, the interaction between EV and SUD severity (p = 0.001, 95% CI = -0.220, -0.060) remained significant. Therefore, the association between diminished integration of EV and SUD severity appeared independent from MDD status.

Table S1. Other Psychiatric Diagnoses Present in Current Sample

Diagnosis	Number of Participants Meeting Criteria
Major Depressive Disorder	26
Bipolar Disorder	0
Panic Disorder	5
Agoraphobia	2
Social Anxiety Disorder	3
Specific Phobia	2
Generalized Anxiety Disorder (Current/Past)	3/0
Obsessive-Compulsive Disorder	3
Bulimia Nervosa	0
Binge Eating Disorder	0
Attention Deficit/Hyperactivity Disorder	2
Acute Stress Disorder	0
Posttraumatic Stress Disorder	14
Narcissistic Personality Disorder	2
Borderline Personality Disorder	6
Antisocial Personality Disorder	20

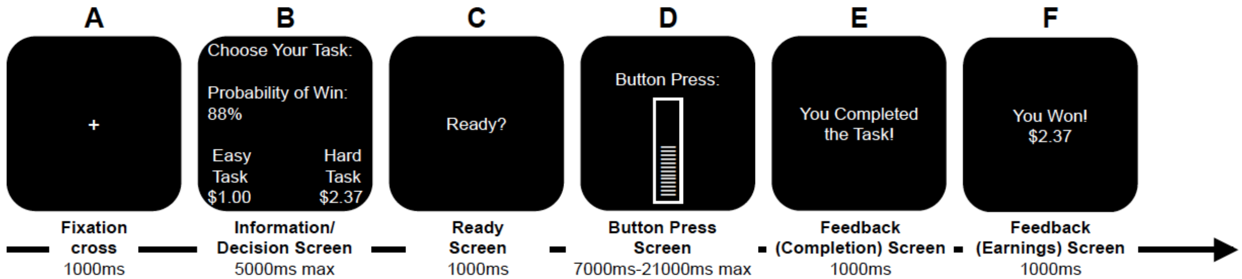

Fig. S1. Sample of trial sequence for the EEfRT. Each trial began with (**A**) a fixation cross (1000ms) followed by (**B)** a screen in which information about the probability of earning a reward and the reward magnitude for completing each task was presented (up to 5000ms), and individuals were asked to make a decision via button press. After either a choice was made or the allotted decision time was up, (**C)** a ready screen was presented briefly (1000ms), followed by (**D)** a button press screen, which marked each button press the participant made during the allotted task time (up to 7000ms or 21000ms). After the task was completed or the allotted task time had passed, participants saw (**E)** a feedback screen indicating whether they successfully completed the task (1000ms) and, if they completed the task, (**F)** a second feedback screen indicating the reward amount, if any, they earned for completing the task (1000ms).

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