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ISTART: Neural Monetary Reward Anticipation in Substance Use and Anhedonia (#32737)

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1) Have any data been collected for this study already?
No, no data have been collected for this study yet.

2) What's the main question being asked or hypothesis being tested in this study?
We aim to quantify the relation between reward function, substance use and anhedonia, by testing the following hypotheses:
H1. More severe self-report (Temporal Experience of Pleasure Scale; TEPS) and interviewer-rated (Structured Clinical Interview for DSM-5; SCID-5) overall anhedonia will be associated with smaller differences in relative motivation, defined as the difference in reaction time (RT) for large relative to small incentive cues (irrespective of reward and loss) in the Monetary Incentive Delay (MID) task.
H2a: Reward-hyposensitive individuals (i.e., scoring < 15th percentile on the Behavioral Activation Scale and Sensitivity to Reward Questionnaire among 1,000 online responders) will exhibit blunted striatal responses to reward anticipation (i.e., cues of potential monetary reward) compared to individuals with moderate sensitivity (i.e., 16-84th percentile). Reward-hypersensitive individuals (i.e., > 85th percentile) will exhibit enhanced striatal responses to reward anticipation compared to individuals with moderate sensitivity.
H2b: Both enhanced and blunted striatal responses to reward anticipation will be associated more strongly with the self-report and interviewer-rated motivational anhedonia (i.e., a deficit in feeling motivated) than hedonic anhedonia (i.e., a deficit in experiencing pleasure). Both enhanced and blunted striatal response to reward anticipation will be associated with more current problematic substance use.
H3a. Reward-hyposensitive individuals will exhibit enhanced corticostriatal connectivity with the orbitofrontal cortex (OFC) and the Default Mode Network (DMN) compared to individuals with moderate sensitivity. Reward-hypersensitive individuals will exhibit blunted corticostriatal connectivity with OFC and the DMN relative to individuals with moderate sensitivity.
H3b. Both enhanced/blunted corticostriatal connectivity with the OFC and DMN would be associated with current problematic substance use, and will both be associated more strongly with motivational than hedonic anhedonia.

3) Describe the key dependent variable(s) specifying how they will be measured.
Behavioral: RT to reward and loss in the MID task, self-report assessments of reward sensitivity, self-report and interviewer-rated substance use and anhedonia. Neural: Task-evoked (MID task) BOLD response during the fMRI scans, and connectivity analysis (network-based psychophysiological interaction analysis [nPPI]).

4) How many and which conditions will participants be assigned to?
Between Subjects Factors: Reward Sensitivity (self-report and behavioral), Substance Use (self-report and diagnostic interview), and Anhedonia (self-report and diagnostic interview). Within Subjects Factors: Magnitude of monetary gain and loss (i.e., large, small, or neutral) and Outcome (hit or miss) in the MID task.

We will exclude individuals with a past-month mood disorder, a past-12-month substance use disorder that includes symptoms of physical dependence (i.e., tolerance or withdrawal), or past-month psychotropic medication use (i.e., mood stabilizers, SSRIs, epilepsy, psychosis, anti-anxiety and pain medications) from participation. Age, sex, history of alcohol use and non-alcohol substance use disorders, head motion, and handedness will be included as covariates in the primary analyses if they are significantly correlated with the dependent variables.

5) Specify exactly which analyses you will conduct to examine the main question/hypothesis.
H1a: We will conduct a one-way ANCOVA to compare relative motivation for reward (RT for small minus large rewards) vs. for loss avoidance (RT for small minus large losses) in the MID task.
H2a: Region of interest (ROI) analyses will be conducted using the ventral striatum (as anatomically defined via the Oxford-GSK-Imanova Structural–anatomical Striatal Atlas) as an a priori ROI, and we will conduct an ANCOVA comparing anticipation response in the ROIs between high (one standard deviation above the mean)/low (one standard deviation below the mean) and moderate (at the mean level) self-report reward sensitivity groups.
H2b: A polynomial regression will assess the quadratic fit for striatal responses to reward anticipation and motivational anhedonia. A polynomial regression will assess the quadratic fit for striatal responses to reward anticipation and hedonic anhedonia. We will also conduct a polynomial regression comparing high (one standard deviation above the mean)/low (one standard deviation below the mean) relative to moderate (at the mean level) striatal responses as a function of current problematic substance use.
H3a. Task-based connectivity analysis (i.e., nPPI) using the ventral striatum as a seed will examine effective connectivity of reward-related circuits during the MID task. The striatal-OFC connectivity will use the Oxford-GSK-Imanova Structural–anatomical Striatal Atlas (ventral striatum) and the FSL Harvard-Oxford cortical atlas (OFC). We will conduct an ANCOVA comparing high (one standard deviation above the mean) /low (one standard deviation below the mean) vs. moderate (at the mean level) reward sensitivity on the connectivity parameters.

H3b. We will conduct a quadratic regression on the aforementioned connectivity parameters and current problematic substance use. We will also run correlations between the connectivity metrics and motivational vs. hedonic anhedonia, and use r-to-Z transformation to assess the significance of the difference between the two correlation coefficients.

6) Describe exactly how outliers will be defined and handled, and your precise rule(s) for excluding observations.
Participants will be excluded as outliers for demonstrating poor neuroimaging data quality (as assessed with MRIQC and FMRIPREP). We will remove runs based on the efc, fber, tsnr, fd_mean, or gsr_y IQMs from MRIQC. Outlier runs will be defined as runs with efc, fd_mean, or gsr_y values exceeding 1.5 times the inter-quartile range above the 75th percentile, as well as those with fber and tsnr values lower than 1.5 times the lower bound minus the 25th percentile. Additionally, participants who miss more than 20% of task trials on any runs will be excluded.

7) How many observations will be collected or what will determine sample size? No need to justify decision, but be precise about exactly how the number will be determined.
We will aim to recruit 100 18-22 year-old participants, but we note that data collection will terminate in June of 2020 regardless of our sample size at that point in time.

8) Anything else you would like to pre-register? (e.g., secondary analyses, variables collected for exploratory purposes, unusual analyses planned?)
Our exploratory analyses will focus on three goals:
1. To examine whether the associations between substance use, reward sensitivity, and neural measures of reward on the MID task are stronger for anticipation (presentation of cues of potential reward) responses than consumption (presentation of reward) responses.

2. To investigate whether enhanced (i.e., one standard deviation above the mean) /blunted (i.e., one standard deviation below the mean) striatal response to reward anticipation and corticostriatal connectivity with the OFC and DMN would predict more future depressive episodes and substance use symptoms compared to moderate (i.e., at the mean level) neural response.

3. To explore the relationship between different facets of reward-related function and neural measures of reward on the MID task and substance use and anhedonia. These facets include:
a. Temporal discounting of reward value – via the Delay Discounting Task (using area under the curve with monetary values on the y axis and temporal delay on the x axis)
b. Effort-based decision-making for rewards – via the Effort-Expenditure for Rewards Task (the proportion of making hard relative to easy choice among all trials in which a task difficulty choice is made)
c. Reward responsiveness – via the Card Arranging Reward Responsivity Objective Test (change in amount of time taken to sort cards as a function of monetary reward values)
d. Anticipatory and consummatory components of the experience of pleasure – via the Temporal Experience of Pleasure Scale and SCID-5, and
e. Risk taking – via the Balloon Analogue Risk Task (average number of pumps on unexploded balloons)