Supplemental Material

Low Reward and Heightened Threat Neural Activity are Both Associated with Heightened Anhedonia: A Transdiagnostic Perspective

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This supplement presents details on study procedures, addressing missing values and data, the diagnostic interviewing procedures, the monetary incentive delay (MID) task, the Pavlovian fear learning task, galvanic skin conductance response measurement, MRI acquisition and processing, MRI regions-of-interests (ROIs), and the latent growth curve models of symptoms. In addition, it includes the results of our fMRI measurement models, analyses of galvanic skin conductance responses, and analyses of variance unique to each ROI. Finally, this supplement presents Tables showing associations of symptoms with reward generating latent variables and OFC activation during the MID and associations of symptoms with fear conditioning latent variables.

Supplemental Methods

Sampling and Participants

Participants were recruited from university and college campuses, community centers and community notice boards in Los Angeles and Chicago. Recruitment occurred as part of the larger 'Brain, Motivation and Personality Development' (BrainMAPD) study, a multi-site longitudinal project investigating positive and negative valence functioning in late adolescence to early adulthood, conducted at the University of California, Los Angeles and Northwestern University (R01 MH100117). Participants were recruited based on their scores on self-reported trait Neuroticism using the Eysenck Personality Questionnaire-Neuroticism (EPQ-N; Eysenck & Eysenck, 1975) and Reward Sensitivity using the Behavioral Activation Scale (BAS; Carver & White, 1994) from among a total of 2,461 individuals who completed screening. Participants were recruited to ensure sampling from high/mid/low ranges (tertiles) on both scales, with oversampling from the two diagonals of the bivariate space defined by the quasi-orthogonal EPQ-N and BAS scales (i.e., high EPQ-N/high BAS, low EPQ-N/low BAS, mid EPQ-N/mid BAS, high EPQ-N/low BAS and low EPQ-N/high BAS). This approach aimed to maximize variance in threat- and reward-related sensitivity within our sample to ensure diversity in symptom profiles and given that variation in threat- and reward-related sensitivity are associated with risk for mood and anxiety disorders (Nusslock, Mittal, & Alloy, 2025; Shackman & Fox, 2016). Participants were aged 18–19 years, as this is a period associated with heightened risk for internalizing psychopathology (Nusslock et al., 2024) and maturation of corticobasal ganglia and corticoamygdala circuitry (Casey et al., 2019).

Inclusion criteria were aged 18-19 years old (at the time of screening), right-handed (assessed using the Edinburgh handedness inventory; Oldfield, 1971) and fluent in English. Exclusion criteria were: (1) traumatic brain injury with evidence of neurological deficits, neurological disorders, or severe or unstable medical conditions that might be compromised by or interfere with study participation, (2) any condition that interferes with

acquisition/interpretation of fMRI data (e.g., severe claustrophobia, central nervous system illness, nonremovable metal in the body), (3) pregnancy, (4) color blindness (given the need to differentiate between colored CS stimuli, assessed using the Isihara Test), (5) lack of right-handed dominance, (6) lifetime psychotic symptoms, (7) lifetime bipolar I disorder, and (8) clinically significant substance or alcohol use disorder in the past 6 months, and (9) antipsychotic medication usage (6-9 assessed using the Structured Clinical Interview for DSM-5). To maintain ecological validity, participants taking other psychoactive medications (N = 21) were retained.

The final sample included 339 participants (see Table 1 in manuscript), of whom 272 completed the fMRI protocol. Among the 272 participants who completed fMRI, data were set to missing for the following reasons. In the MID task, data from 49 participants were set to missing due to excessive motion or poor task performance (223 retained). In the fear conditioning task, excessive motion led to missing data for 43 participants during acquisition (229 retained), 54 during extinction (218 retained), and 61 during extinction recall (211 retained). However, as discussed below in the Data Analysis section, we used full-information maximum likelihood to accommodate missing data, and thus the full sample of 339 participants was used for each analysis. Participants provided informed consent, and procedures were approved by the IRB at each institution.

Data from this sample have been published on previously (Anderson et al., 2023; Peng et al., 2023; Rosenberg et al., 2023; Young et al., 2021; Young et al., 2022). However, this study extends our prior work by modeling reward and threat neural activity within the same participants. We then examine, for the first time, whether neural correlates of the tri-level model of depression and anxiety are specific to, or shared across, reward and threat processes, as well as across broad symptom dimensions spanning both disorders.

Self-report tri-level dimensional symptom model measures. The cross-sectional analyses reported herein are embedded in a multi-year longitudinal study. Participants completed

questionnaires assessing mood and anxiety disorder symptoms at baseline (T1) and at 10, 20, and 30 months (T2, T3, and T4, respectively). T1 symptoms were assessed immediately prior to the baseline MRI scan. T2-T4 symptom assessments were used to identify the latent starting value (i.e., intercept) for T1 cross-sectional analyses, so that estimates for the starting values are corrected for measurement error, rather than sole reliance upon observed T1 values (Willett, 1988). That is, each observed score consists of both a true score component and a residual that includes measurement error. If a linear growth curve is based on at least 3 occasions or a quadratic growth curve is based on at least 4 occasions, the intercept will provide a better estimate of the true starting value than will the first observed value as the line of fit will almost never go directly through each of the observed scores (Willett, 1988). Questionnaires included the following: Fear Survey Schedule-II (Geer, 1965), Albany Panic and Phobia Questionnaire (Rapee, et al., 1994), Self-Consciousness subscale of the Social Phobia (Mattick & Clarke, 1998; Zinbarg & Barlow, 1996), Inventory to Diagnose Depression (Zimmerman & Coryell, 1987), Mood and Anxiety Symptom Questionnaire (Watson et al., 1995), Penn State Worry Questionnaire (Meyer et al., 1990), and Obsessive Compulsive-Inventory Revised (Foa et al., 2002).

Multi-method tri-level model factor scores. As in prior work (Zinbarg et al., in press; Naragon-Gainey et al., 2016; Prenoveau et al., 2010), we employed a hierarchical model with three levels: a broad general factor (General Distress), two intermediate factors (Fears and Anhedonia-Apprehension), and several narrow factors. As a hierarchical model, the tri-level model allows each item to load directly on multiple uncorrelated factors (McDonald, 1999). Though hierarchical factor analysis is not without its limitations and critics (e.g., Bonifay, Lane & Reise, 2016), the specification of narrow, intermediate and broad factors that are statistically independent of one another allows for a stringent test of whether each factor is structurally necessary after accounting for the factors at the other levels (e.g., Chen, West & Sousa, 2006). The hierarchical factor model also cleanly parses variance due to a general factor versus

variance due to narrower factors when studying the correlates and predictors of the symptoms. We included both self-report indicators and interviewer-rated indicators of each factor (Zinbarg et al., in press). The latter were extracted from the Structured Clinical Interview for DSM-5 (First et al., 2015) at T1-T4, again using T2-T4 indicators to identify the latent starting value for T1 cross-sectional analyses. Model fit was tested using Mplus. (Muthen & Muthen, 2017), and factor estimates were used to represent symptom dimensions of General Distress, Fears, and Anhedonia-Apprehension.

Structured Clinical Interview for DSM-5. The Structured Clinical Interview for DSM 5, Research Version (SCID-RV; First et al., 2015) was used to assess for DSM 5 psychiatric diagnoses. All interviewers had at least a bachelor's degree and underwent extensive training and supervision, met criteria for inter-rater reliability with training materials, and interviewers presented each completed SCID at a supervision meeting led by a doctoral-level supervisor to arrive at consensus regarding final diagnoses and interviewer-rated dimensional ratings. All interviews were audio-recorded and 28 (8.3%) were randomly selected to be re-rated by an interviewer at the other site.

Based on the results of Prenoveau et al. (2010) and Naragon-Gainey et al. (2016), we developed 30 dimensional interviewer-rating variables/indicators created to be analogs of self-reported tri-level model indicators that we added to the diagnostic interview administered by our diagnostic interviewers (for more details, see Zinbarg et al., in press and the pre-registration for that article: https://osf.io/dbv2a). These dimensional variables used a 4-point rating scales (1 = absent, 2 = sub-threshold, 3 = threshold, 4 = severe). We also had an initial pool of 18 theoretically relevant Clinician Severity Ratings (CSRs) that our team has been having interviewers assign as part of our diagnostic assessments for several decades (e.g., Craske et al., 1991; Zinbarg & Barlow, 1996; Zinbarg et al., 2010). Current CSRs used the 0 to 8 response scale developed by Dinardo & Barlow (1988). Thus, scores of 1 and 2 indicate that at least some symptoms have been present in the past month but impairment and distress are sub-

clinical. A score of 3 indicates that symptoms have not only been present but may be clinically significant. A score of 4 or above indicates that symptoms associated with clinically significant distress or impairment have been present in the past month. We have previously demonstrated good inter-rater correlations for CSRs (e.g., Prenoveau et al., 2010) and for the 30-dimensional variables we added to the SCID for this investigation (Zinbarg et al., in press).

Monetary Incentive Delay reward task. Participants completed two runs of the Monetary Incentive Delay (MID) task (Samanez-Larkin et al., 2007). First, a circle cue signaling a reward trial (participant might Win $0.00, Win $1.50, or Win $5.00) or a square cue indicating a loss trial (participant might Lose $0.00, Lose $1.50, or Lose $5.00) was presented for 2 seconds. Then, a jittered fixation was presented followed by a solid white square. Participants were instructed to make a button response when the solid white square was still on the screen to either win money (reward trials) or avoid losing money (loss trials). Feedback detailing the amount of money won or lost was given for 2 seconds on each trial. Finally, a jittered fixation cross was presented for 2 seconds, 4 seconds, or 6 seconds as an intertrial interval. The initial target duration was calculated from each participant's mean hit reaction time on a practice run. The target duration then dynamically updated to maintain difficulty, so participants accurately hit the target on 66 % of trials. Each of the six trial types was presented 16 times in random order, totaling 96 trials, across two runs.

Pavlovian Fear Learning Task. This fMRI task was based on prior reports (Milad et al., 2009; Milad et al., 2007) and consisted of four phases: habituation, acquisition, extinction (all conducted on day 1) and recall (conducted on day 2, 1-7 days later). During habituation, participants viewed each of three conditional stimuli (CS) images for four 6-second trials, to reduce novelty. During acquisition, participants viewed images of two CS+ stimuli and one CS- stimulus. Images were office or conference rooms (context) with different colored lights (red/yellow/blue) as CS stimuli (color order and context images were counterbalanced across participants). During each trial, participants first viewed the context image (3sec), followed by

the CS embedded in the context (6sec). There were 8 trials of each CS+ (16 trials total) and 16 trials of the CS-. Five (out of eight) of the CS+ trials of each type were followed immediately by a mild electric shock applied to the left bicep. In acquisition analyses, responses to the two CS+ stimuli were combined. During extinction, participants viewed 16 trials of one CS+ (the 'extinguished' CS+ now termed the CS+E) and 16 trials of the CS-, none of which were followed by shock. During extinction recall, participants viewed 8 trials of the CS+E, 8 trials of the CS+ that were not presented during extinction (the 'unextinguished' CS+ now termed the CS+U) and 16 trials of the CS-. During all task phases, inter-trial intervals varied from 12-18sec (mean 15sec) and included a jitter of 125ms per trial to reduce slice timing bias. The task was programmed in E-Prime (version 2.0 SP1) and presented to participants using a mirror and projector system.

Shocks consisted of 10 pulses of 1ms pulse duration, delivered at 20Hz frequency (total duration = 500ms). Shocks were delivered using a DS7a constant current high voltage stimulator (Digitimer Ltd, England) at UCLA and a STMISOC constant voltage stimulator (Biopac Systems Inc, USA) at Northwestern. Shock levels were determined during a 'work-up' procedure conducted on Day 1 before scanning. In this procedure, participants were presented with shocks of increasing intensity and were asked to rate each on a pain scale of 1-10 (1 = 'not at all painful', 10 = 'most pain imaginable'). Participants were informed that we aimed to reach a level of shock that was 'uncomfortable but not painful' and 'took some effort to tolerate' (i.e., a rating of 5-6 that they were willing to tolerate for the experiment).

Contingency Awareness during the Pavlovian Fear Learning Task. At the end of each task phase, participants were asked contingency awareness questions. For each of the CS stimuli, participants rated the 'likelihood of receiving a shock if you saw this image again', on a 3-point scale, 1 'high', 2 'moderate', 3 'low'. These responses were reverse-coded during analysis so that higher scores indicated greater likelihood.

Skin conductance during the Pavlovian Fear Learning Task. Galvanic skin conductance was recorded throughout all task phases using a GSR100c amplifier (Biopac Systems Inc., USA) and was digitized using AcqKnowledge Data Acquisition and Analysis Software (Biopac Systems Inc., USA). Data were sampled at a rate of 1kHz, with a gain of 5 μS/V and further processed using the software ANSLAB. Data were visually inspected, movement artifacts were edited out (on a trial-by-trial basis) and data that still had poor quality signal following this step (i.e., technical issues with data collection, lack of variance in acquired data or excessive motion artifacts that could not be edited out; n=54) were removed, leaving *n* = 218 with usable skin conductance data. Skin conductance responses (SCR) to the CS were calculated by subtracting pre-CS baseline skin conductance level (SCL; -2 to 0s before CS onset) from the maximum CS SCL (occurring between 0 to 6s after CS onset). Data were normalized using the natural logarithm of 2+SCR.

MRI acquisition and preprocessing. Data were acquired using a Siemens Prisma 3.0 T MRI scanner with a 64-channel head coil. Identical scanners and sequences were used at the two sites. Structural 3D axial MPRAGE images were acquired (0.8 mm thick; TR = 2300 ms; TE = 3.03 ms; FOV = 256x256; Matrix = 160x160; Flip Angle = 7◦; 192 slices). Functional runs utilized a gradient echo EPI sequence covering 64 axial slices (2.0 mm thick; TR = 2050 ms for Pavlovian task; TR = 2050 ms for MID; TE = 25 ms; FOV = 208x208mm; Matrix = 104x104; Flip Angle = 76◦; Multiband acceleration Factor = 2). Functional data were first assessed for outlier volumes (75th percentile + 1.5-time interquartile range) based on framewise displacement [average of rotation and translation parameter differences, using weighted scaling (Power et al., 2012) as implemented in the fslmotionoutliers function]. Participant data with either run exceeding 10% outliers were not included in group analyses. Outlier volumes were censored in first level analyses by including a regressor with a single time point corresponding to each outlying volume. fMRI data were processed with FEAT (FMRI Expert Analysis Tool) Version

6.00nusing standard procedures. Participants with > 10 % outlier volumes in either run, as identified by the fslmotionoutliers function, were excluded.

For the MID task, first-level voxel-wise z-statistics were generated for each participant, contrasting reward anticipation (i.e., Win $1.50, Win $5.00) vs nonreward (i.e., Win $0.00), loss anticipation (i.e., Lose $1.50, Lose $5.00) vs non-loss (i.e., Lose $0.00), gain outcome vs no-gain, and loss outcome vs no-loss, in line with previous research (Samanez-Larkin et al., 2007). Guided by a meta-analysis (Oldham et al., 2018), we generated 5 mm spheres around peak activation coordinates during the MID for ventral striatal ROI analyses for anticipation and outcome periods. We used this same meta-analysis to generate OFC ROIs during the outcome period, as this region is not consistently activated during anticipation. We averaged activation across three 5 mm spheres to compute a single OFC ROI for the outcome period. We used the Harvard-Oxford anatomical atlas to generate parameter estimates for the pallidum and putamen.

For the Pavlovian fear learning task, first-level analyses included regressors of interest (acquisition: context, CS+(E/U), CS− and shock; extinction: context, CS+E, CS−; extinction recall: context, CS+E, CS+U, CS−), temporal derivatives, six motion regressors, and regressors to censor outlying volumes. Region of interest (ROI) analyses defined the BNST anatomically as in prior research (Avery et al., 2014). The amygdala, anterior insula, dACC, and hippocampus ROIs were defined from the Harvard-Oxford atlas. The vmPFC was defined as a sphere (5 mm radius) around peak activations reported in a meta-analysis of human fear conditioning (Fullana et al., 2016). Analyses were conducted for each phase of fear learning using contrasts from prior fear conditioning literature (e.g., Young et al., 2021): for acquisition “CS+ vs. CS −” (all trials), for extinction “late CS+ E vs. late CS−” (last four trials of each type), and for recall “early CS+ E vs. early CS+ U” (first four trials of each type).

Latent Growth Curve Model models (LGCMs) of symptoms. For each symptom dimension (General Distress, Fears and Anhedonia-Apprehension), we fit a series of three

LGCMs to its data at T1, T2, T3 and T4. The first was an intercept-only model, the second added a linear growth factor to the model and the third added a quadratic growth factor to the model (see Supplement Figure 1). In each model, we specified an auto-regressive structure among the residuals. For each dimension, we planned to retain the intercept-only model if it did not provide a meaningfully worse fit than either of the other two. Similarly, we planned to retain the intercept plus linear growth model if it provided a meaningfully better fit than the intercept-only model but did not provide a meaningfully worse fit than the model that added a quadratic growth factor. Finally, we retained the model including quadratic growth if it provided a meaningfully better fit than both of the simpler models. As our focus in this article is on the latent starting values (i.e., the intercepts), we do not report the results for linear and quadratic growth in detail here. The most relevant aspect of the growth curve analyses for the cross-sectional focus of the present study is that basing the estimate of the intercept on all four waves of symptom data collection corrects those estimates for measurement error relative to simply using the observed T1 value as the estimate of an individual's starting level (Willett, 1988).

Measurement models for fMRI variables. fMRI latent variables and observed variables were modeled from fMRI MID and Pavlovian fear learning ROIs (see Supplement Table 1 for correlations among the MID ROIs and Supplement Table 2 for correlations among the Pavlovian fear learning ROIs). We began by identifying a priori each ROI as a reward generating, reward regulating, threat generating, or threat regulating brain region. For the MID task, the ventral striatum, pallidum, and putamen were identified as indicators of the reward-generating latent variables. For the Pavlovian fear learning task the amygdala, BNST, and anterior insula ROIs were identified as indicators of the threat generating latent variables. The MID task included two phases (Anticipation and Outcome) and the Pavlovian fear learning task included three phases (Acquisition, Extinction and Extinction Recall). A latent reward and threat generating factor was created for each phase of each task. In contrast, the reward (OFC-outcome) and threat (vmPFC, hippocampus, dACC) regulating ROIs were entered into the initial models as observed

variables that were allowed to correlate with the reward- and threat-generating latent variables, respectively. This approach was taken because the threat regulating ROIs were thought to be associated with distinct regulatory processes in the fear learning task and since there was only one reward-regulating ROI for the MID task (and a latent variable typically requires at least two indicators). If initial model fit was not adequate, our plan was to (a) re-specify the model adding all ROIs, both generating and regulating, as indicators of the latent variables, (b) consider other re-specifications based on modification indices, and (c) re-test the respecified model at T4 (our only other wave at which we measured neural activity) as a test of replicability to protect against capitalizing on sampling error.

Fit for the initial fear learning model (with 3 latent variables for generating ROIs plus observed regulatory ROIs corresponding to acquisition, extinction and extinction-recall phases) was not adequate on any index at T1 for General Distress ($\chi^2(173) = 578.285$, CFI = .76, RMSEA = .083 (.076, .091), SRMR = .127), Anhedonia-Apprehension ($\chi^2(187) = 578.223$, CFI = .71, RMSEA = .079 (.071, .086), SRMR = .130) or Fears ($\chi^2(188) = 638.807$, CFI = .68, RMSEA = .084 (.077, .091), SRMR = .134). Our respecified model added all ROIs, generating and regulating, as indicators of threat latent variables, and based on modification indices, and guided by animal research that links the amygdala and hippocampus (e.g., Greco & Liberson, 2016; Maren & Holmes, 2016), added correlated residuals between the amygdala and hippocampus ROIs for acquisition and extinction.

Fit for the initial MID ROIs model (2 latent variables for generating ROIs plus the observed regulatory OFC-outcome phase ROI) at T1 was adequate on all three fit indices for General Distress ($\chi^2(42) = 64.901$, CFI = .98, RMSEA = .040 (.019, .059), SRMR = .044) and Anhedonia-Apprehension (($\chi^2(48) = 103.400$, CFI = .92, RMSEA = .058 (.043, .074), SRMR = .068)) and on CFI and SRMR for Fears ($\chi^2(42) = 125.672$, CFI = .90, RMSEA = .076 (.061, .092), SRMR = .068) at T1. Though the MID ROIs model was not respecified based on the T1 results, we erred on the side of being conservative and tested whether it replicated at T4. Fit for

the initial MID ROIs model at T4 was adequate on all three fit indices for General Distress ($\chi^2(42) = 55.795$, CFI = .98, RMSEA = .031 (.000, .051), SRMR = .044), Anhedonia-Apprehension ($\chi^2(48) = 71.782$, CFI = .95, RMSEA = .038 (.017, .056), SRMR = .052) and Fears ($\chi^2(42) = 79.739$, CFI = .94, RMSEA = .051 (.034, .069), SRMR = .072). (See Supplement Table 3 for the factor loadings in the MID latent variable model).

Fit at T1 for the re-specified threat latent variable model (with 3 latent variables corresponding to acquisition, extinction and extinction-recall) was adequate on RMSEA and CFI for General Distress ($\chi^2(200) = 378.874$, CFI = .91, RMSEA = .051 (.043, .059), SRMR = .082), RMSEA for Anhedonia-Apprehension ($\chi^2(205) = 383.336$, CFI = .89, RMSEA = .051 (.043, .058), SRMR = .084) and for Fears($\chi^2(200) = 427.585$, CFI = .87, RMSEA = .058 (.050, .066), SRMR = .086). Fit at T4 for the re-specified threat latent variable model was adequate on all three fit indices for General Distress ($\chi^2(200) = 318.277$, CFI = .91, RMSEA = .042 (.033, .050), SRMR = .072) and on RMSEA and SRMR for Anhedonia-Apprehension ($\chi^2(205) = 333.535$, CFI = .87, RMSEA = .043 (.034, .051), SRMR = .071) and Fears ($\chi^2(200) = 319.546$, CFI = .89, RMSEA = .042 (.033, .050), SRMR = .077). (See Supplement Table 4 for the factor loadings in the re-specified threat latent variable model).

SCR Results. SCR was significantly higher in the last 4 trials of the acquisition phase for CS+ (M =.15, sd = .44; t = 3.64, df = 207, p < .001) and CS+E (M = .18, sd = .58; t = 3.99, df = 222, p < .001) than for CS- (.04, sd = .17). In contrast, SCR activation did not significantly different for CS+ and CS+E (t = -0.60, df = 207, p = .551). This pattern of results is consistent with fears being acquired to CS+ and CS+E (and without evidence for differential acquisition to CS+ and CS+E).

During the last four trials of the extinction phase, CS+E did show a significant reduction in SCR ($M_{reduction}$ = .10, sd = .66; t = 2.17, df = 206, p = .03) compared to the last four trials of the acquisition phase as well as a significantly greater reduction than CS- ($M_{reduction}$ = -.03, sd = .27; t = 2.97, df = 206, p = .003). In addition, SCR during the last four trials of the extinction phase

did not significantly differ between CS+E (M = .08, sd = .31) and CS- (M = .08, sd = .26; t = 0.11, df = 218, p = .917). This pattern of results is consistent with fears being extinguished to CS+E.

Supplemental Results

Adjusting for potential covariates. We considered site, current psychotropic medication use and sex as potential covariates. There are two reasons why one might enter a covariate in an analysis: (1) it is correlated with the dependent variable and so might increase power by removing error variance in the dependent variable or (2) it is correlated with both the dependent variable and the predictor of interest and so might be a confounder. Thus, we began by associating our potential covariates with our dependent variables (the symptom intercepts) and with our predictor variables (the brain latent variables and OFC-outcome activation). Those covariates that correlated significantly with a symptom intercept were included in analyses to potentially increase power. And those that correlated significantly with a symptom intercept and approached significance ($p \leq .20$) in correlating with a predictor variable were included in analyses to adjust for potential confounders (we adopted a lenient p-value for the associations with predictors to make sure we didn't miss a potential confounder). Sex correlated significantly with the intercept of Anhedonia-Apprehension (r = .16, p = .013) and the intercept of General Distress (r = .22, p = .000). And sex approached significance in correlating with the MID Outcome latent variable (r = -.12, p = .101) and the OFC-Outcome activation ROI (r = .09, p = .185). Current medication use correlated significantly with the intercept of General Distress (r = .26, p = .000). And current medication use approached significance in correlating with the MID Anticipation latent variable (r = -.13, p = .063) and the Fear Extinction Recall latent variable (r = .13, p = .069). Therefore, we conducted one set of reanalyses for Anhedonia-Apprehension entering sex as a covariate. And we conducted two sets of reanalyses for General Distress – in one we entered sex as a covariate and in the other we entered current medication use as a covariate.

93.4% of the association of Anhedonia-Apprehension with the threat latent variable during Extinction was retained with sex as a covariate (b = .20, se = .063, p = .002). 80.0% of the association of Anhedonia-Apprehension with OFC Activation during the MID was retained with sex as a covariate (b = -.27, se = .142, p = .055). 92.5% of the association of Anhedonia-Apprehension with the unique variance in the ventral striatum during Reward Anticipation was retained with sex as a covariate (b = -.49, se = .208, p = .018). With current psychotropic medication use and sex as covariates in the analyses of General Distress, all associations with brain variables remained non-significant. Thus, none of the covariates we considered (site, current psychotropic medication use and sex) appreciably altered associations of the symptom latent intercepts with the threat latent variables during the fear learning task, reward generating latent variables or OFC activation during the MID.

Supplemental Discussion

In addition, we chose to use a hierarchical, rather than a higher-order, dimensional symptom model and hierarchical models tend to overfit data that is actually generated by a higher-order model (i.e., Bonifay & Cai, 2017; Reise, Kim, Mansolf, & Widaman, 2016; Snyder, Young, & Hankin, 2017). Given this limitation, we would *not* argue that the items have direct associations with the general factor rather than associations with the general factor that are mediated by the group factors as specified in a higher-order representation. Fortunately, however, this question is not central to our primary aims. We used the hierarchical model to permit a clean decomposition of variance due to factors of differing levels of breadth (i.e., general/broad, intermediate and narrow).

Supplemental References

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Supplement Table 1. Correlations among the Regions-of-Interest (ROIs) in the Monetary Incentive Delay (MID) reward task

	2	3	4	5	6	7
1 APall	.75	.53	.06	.02	.07	-.03
2 APut	-					
3 AVS	.51	-				
4 OPall	.06	.17	-			
5 OPut	.07	.12	.68	-		
6 OVS	.06	.14	.43	.58	-	
7 OOFC	-.09	.01	.20	.28	.33	-

Note: APall = Pallidum activation during the anticipation phase, APut = Putamen activation during the anticipation phase, AVS = Ventral striatum activation during the anticipation phase, OPall = Pallidum activation during the outcome phase, OPut = Putamen activation during the outcome phase, OVS = Ventral striatum activation during the outcome phase, OOFC = Orbitofrontal cortex activation during the outcome phase.

Supplement Table 2. Correlations among the Regions-of-Interest (ROIs) in the Pavlovian Fear Learning Task

	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1. AdACC	.01	.51	.28	.66	.22	.04	.04	.04	.07	-.01	.01	-.15	-.01	-.13	-.16	-.04	-.17
2. AvmPFC	-																
3. ABNST	.19	-															
4. AAmyg	.42	.31	-														
5. AAnt	.12	.53	.34	-													
6. AHipp	.46	.32	.76	.27	-												
7. EdACC	-.02	-.04	-.17	.03	-.17	-											
8. EvmPFC	.08	-.05	-.01	.01	-.07	.31	-										
9. EBNST	.02	.03	-.02	.09	.04	.47	.28	-									
10. EAmyg	.14	.12	.00	.02	.00	.41	.41	.26	-								
11. EAnt	-.01	.08	-.11	.01	-.09	.70	.38	.47	.47	-							
12. EHipp	.13	.04	-.03	.03	-.02	.51	.54	.32	.76	.56	-						
13. RdACC	.04	-.15	.06	.17	.08	-.10	-.15	-.03	.06	-.14	-.12	-					
14. RvmPFC	-.05	-.02	-.01	.04	.02	-.02	-.04	-.04	.02	-.05	-.09	.26	-				
15. RBNST	.03	-.15	-.05	-.13	-.08	-.02	-.15	-.16	-.08	-.04	-.12	.23	.23	-			
16. RAmyg	.10	-.12	.16	-.16	.06	-.15	-.23	-.09	.06	-.15	-.14	.45	.44	.33	-		
17. RAnt	-.03	-.03	.08	-.04	.07	-.11	-.18	-.05	.07	-.15	-.19	.54	.31	.32	.43	-	
18. RHipp	.04	-.10	.08	-.17	-.01	-.03	-.19	.01	-.01	-.06	-.10	.43	.55	.32	.74	.42	-

Note. AdACC = Dorsal anterior cingulate cortex in the acquisition phase, AvmPFC = Ventromedial prefrontal cortex in the acquisition phase, ABNST = Bed nucleus of the stria terminalis in the acquisition phase, AAmyg = Amygdala in the acquisition phase, AAnt =

Anterior insula in the acquisition phase, AHipp = Hippocampus in the acquisition phase, EdACC = Dorsal anterior cingulate cortex in the extinction phase, EvmPFC = Ventromedial prefrontal cortex in the extinction phase, EBNST = Bed nucleus of the stria terminalis in the extinction phase, EAmyg = Amygdala in the extinction phase, EAnt = Anterior insula in the extinction phase, EHipp = Hippocampus in the extinction phase, RdACC = Dorsal anterior cingulate cortex in the extinction recall phase, RvmPFC = Ventromedial prefrontal cortex in the extinction recall phase, RBNST = Bed nucleus of the stria terminalis in the extinction recall phase, RAmyg = Amygdala in the extinction recall phase, RAnt = Anterior insula in the extinction recall phase, RHipp = Hippocampus in the extinction recall phase.

Supplement Table 3. Standardized Factor Loadings of the Emotion-Generating Regions-of-Interest (ROIs) in the Monetary Incentive Delay (MID) reward task on Emotion-Generating Latent Variables and Correlations of the Latent Variables with Emotion-Regulating ROIs

	Factor	
ROI	Anticipation	Outcome
APall	.85**	
APut	.88**	
AVS	.61**	
OPall		.72**
OPut		.94**
OVS		.62**
OOFC	-.09	.32**

Note: ** = $p \leq .001$. APall = Pallidum activation during the anticipation phase, APut = Putamen activation during the anticipation phase, AVS = Ventral striatum activation during the anticipation phase, OPall = Pallidum activation during the outcome phase, OPut = Putamen activation during the outcome phase, OVS = Ventral striatum activation during the outcome phase, OOFC = Orbitofrontal cortex activation during the outcome phase.

Supplement Table 4. Standardized Factor Loadings of the Regions-of-Interest (ROIs) in the Pavlovian Fear Learning Task

	Factor		
ROI	**Acq**	Ext	Recall
AdACC	.78**		
AvmPFC	.16*		
ABNST	.65**		
AAmyg	.40**		
AAnt	.83**		
AHipp	.34**		
EdACC		.80**	
EvmPFC		.48**	
EBNST		.55**	
EAmyg		.54**	
EAnt		.86**	
EHipp		.67**	
RdACC			.55**
RvmPFC			.57**
RBNST			.40**
RAmyg			.83**
RAnt			.54**
RHipp			.86**

Note: * = p ≤ .05, ** = p ≤ .001. AdACC = Dorsal anterior cingulate cortex during the acquisition phase, AvmPFC = Ventromedial prefrontal cortex during the acquisition phase, ABNST = Bed nucleus of the stria terminalis during the acquisition phase, AAmyg = Amygdala during the acquisition phase, AAnt = Anterior insula during the acquisition phase, AHipp = Hippocampus

during the acquisition phase, EdACC = Dorsal anterior cingulate cortex during the extinction phase, EvmPFC = Ventromedial prefrontal cortex during the extinction phase, EBNST = Bed nucleus of the stria terminalis during the extinction phase, EAmyg = Amygdala during the extinction phase, EAnt = Anterior insula during the extinction phase, EHipp = Hippocampus during the extinction phase, RdACC = Dorsal anterior cingulate cortex during the extinction recall phase, RvmPFC = Ventromedial prefrontal cortex during the extinction recall phase, RBNST = Bed nucleus of the stria terminalis during the extinction recall phase, RAmyg = Amygdala during the extinction recall phase, RAnt = Anterior insula i during the extinction recall phase, RHipp = Hippocampus during the extinction recall phase, Acq = Acquisition latent brain activation factor, Ext = Extinction latent brain activation factor, Recall = Extinction Recall latent brain activation factor.

Supplement Table 5. Correlations of Time 1 Symptom Scores and Regions-of-Interest (ROIs) in the Monetary Incentive Delay Reward Task

		T1 Symptoms	
ROI	GD	An	Fears
APall	.04	-.02	-.07
APut	.06	-.09	-.07
AVS	.05	-.15*	-.07
OPall	.02	-.06	.01
OPut	.03	-.03	.01
OVS	-.05	.06	.02
OOFC	.04	-.14	.15^

Note. * = $p \leq .05$. ^ = $p \leq .10$. APall = Pallidum activation during the anticipation phase, APut = Putamen activation during the anticipation phase, AVS = Ventral striatum activation during the anticipation phase, OPall = Pallidum activation during the outcome phase, OPut = Putamen activation during the outcome phase, OVS = Ventral striatum activation during the outcome phase, OOFC = Orbitofrontal cortex activation during the outcome phase, GD = General Distress, An = Anhedonia-Apprehension.

Supplement Table 6. Correlations of Time 1 Symptom Scores and Regions-of-Interest (ROIs) in the Pavlovian Fear Learning Task

		T1 Symptoms	
ROI	GD	An	Fears
AdACC	-.03	.14	-.02
AvmPFC	-.05	.06	-.11
ABNST	-.12	.10	-.08
AAmyg	.13	.02	.01
AAnt	-.07	.08	-.07
AHipp	.03	.09	.02
EdACC	-.08	.15*	-.04
EvmPFC	.08	.17*	-.06
EBNST	.03	.14	-.06
EAmyg	-.06	.12	-.07
EAnt	.03	.18*	-.09
EHipp	.00	.11	-.02
RdACC	.04	.05	.10
RvmPFC	-.07	.09	.02
RBNST	-.04	-.18*	.12
RAmyg	-.04	-.14	.03
RAnt	-.04	-.04	.09
RHipp	-.01	-.07	.02

Note. * = $p \leq .05$. AdACC = Dorsal anterior cingulate cortex activation during the acquisition phase, AvmPFC = Ventromedial prefrontal cortex activation during the acquisition phase, ABNST = Bed nucleus of the stria terminalis activation during the acquisition phase, AAmyg = Amygdala activation during the acquisition phase, AAnt = Anterior insula activation during the

acquisition phase, AHipp = Hippocampus activation during the acquisition phase, EdACC = Dorsal anterior cingulate cortex activation during the extinction phase, EvmPFC = Ventromedial prefrontal cortex activation during the extinction phase, EBNST = Bed nucleus of the stria terminalis activation during the extinction phase, EAmyg = Amygdala activation during the extinction phase, EAnt = Anterior insula activation during the extinction phase, EHipp = Hippocampus activation during the extinction phase, RdACC = Dorsal anterior cingulate cortex activation during the extinction recall phase, RvmPFC = Ventromedial prefrontal cortex activation during the extinction recall phase, RBNST = Bed nucleus of the stria terminalis activation during the extinction recall phase, RAmyg = Amygdala activation during the extinction recall phase, RAnt = Anterior insula activation during the extinction recall phase, RHipp = Hippocampus activation during the extinction recall phase, GD = General Distress, An = Anhedonia-Apprehension.

Supplement Table 7. Associations of Symptom Dimensions with Reward Generating Latent Variable and Orbitofrontal Cortical Activation during the Monetary Inventive Delay (MID) Reward Task.

Variable	B (β)	se	z	p
		General Distress		
Anticipation LV	.05 (.06)	.074	0.692	.489
Outcome LV	.00 (.00)	.078	0.041	.968
OOFC	.08 (.04)	.171	0.485	.628
		Anhedonia-Apprehension		
Anticipation LV	-.09 (-.14)	.067	-1.333	.182
Outcome LV	.05 (.07)	.070	0.658	.510
OOFC	-.34 (-.23)	.147	-2.312	.021
		Fears		
Anticipation LV	-.16 (-.37)	.083	-1.917	.055
Outcome LV	.03 (.07)	.090	0.335	.738
OOFC	.04 (.04)	.182	0.212	.832

Note. Anticipation LV = Anticipation Latent Variable, Outcome LV = Outcome Latent Variable, OOFC = Orbitofrontal cortical activation during the outcome phase, b = unstandardized regression coefficient, β = standardized regression coefficient, se = standard error, z = z-test value.

Supplement Table 8. Associations of the Unique Variances for Individual Regions-of-Interest (ROIs) within the Threat Latent Variable with Anhedonia-Apprehension during the Extinction Phase of the Pavlovian Fear Learning Task.

ROI	b (β)	se	z	p
dACC	.04 (-.05)	.130	0.309	.757
vmPFC	.07 (-.13)	.054	1.326	.185
BNST	.06 (-.06)	.105	0.578	.563
Amyg	-.05 (.04)	.113	-0.404	.686
Ant	-.21 (.22)	.214	-0.970	.332
Hipp	-.06 (.05)	.153	-0.402	.687

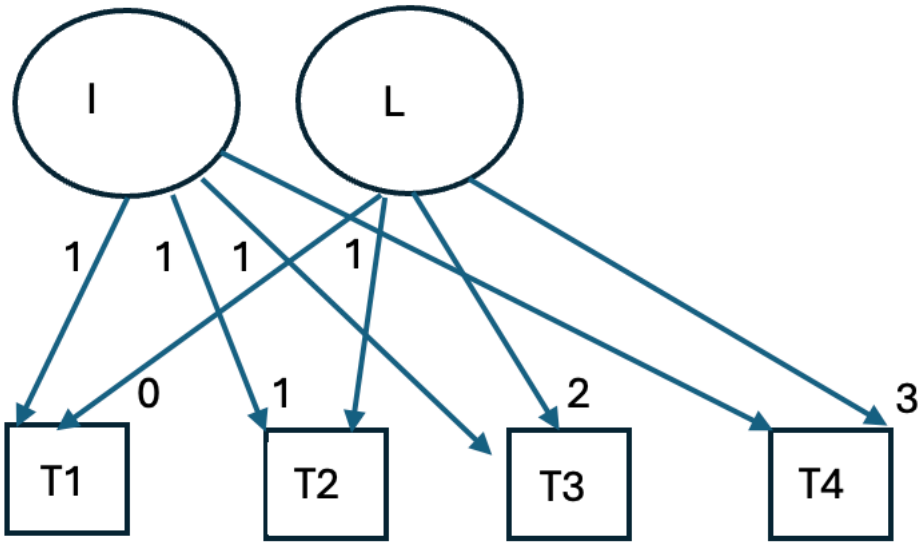
Note. To model unique variances, these associations adjust for the threat latent variable during the extinction phase. dACC = Dorsal anterior cingulate cortex activation in the extinction phase, vmPFC = Ventromedial prefrontal cortex activation in the extinction phase, BNST = Bed nucleus of the stria terminalis activation in the extinction phase, Amyg = Amygdala activation in the extinction phase, Ant = Anterior insula activation in the extinction phase, Hipp = Hippocampus activation in the extinction phase, b = unstandardized regression coefficient, β = standardized regression coefficient, se = standard error, z = z-test value.

Supplement Table 9. Associations of Symptom Dimensions with Threat Latent Variables during the Pavlovian Fear Learning Task.

Latent Variable	B (β)	se	z	p
		General Distress		
Acquisition	-.08 (-.10)	.074	-1.054	.292
Extinction	-.01 (-.01)	.075	-0.117	.907
Extinction Recall	-.05 (-.06)	.074	-0.672	.501
		Anhedonia-Apprehension		
Acquisition	.07 (-.11)	.068	1.093	.274
Extinction	.21 (-.32)	.066	3.184	.001
Extinction Recall	-.02 (.02)	.069	-0.225	.822
		Fears		
Acquisition	-.06 (-.14)	.077	-0.834	.404
Extinction	-.05 (-.10)	.077	-0.578	.563
Extinction Recall	-.03 (-.06)	.083	-0.353	.724

Note. b = unstandardized regression coefficient, β = standardized regression coefficient, se = standard error, z = z-test value.

Supplement Figure 1. Schematic of Latent Growth Curve Model for Identifying the Latent Starting Value (i.e., Latent Intercept) for General Distress, Fears, and Anhedonia-Apprehension at T1.



Note. I = Intercept factor, L = linear growth factor. The latent starting value (i.e., latent intercept) for General Distress, Fears, and Anhedonia-Apprehension were used as the symptom data for all T1 cross-sectional analyses. The benefit of this approach is that the estimates of T1 starting values or latent intercepts (i.e., the symptom data for this paper), account for measurement error and do not solely rely on observed T1 scores. The General Distress and Fears final models each also included a quadratic growth factor - not depicted for legibility - with loadings of 0, 1, 4 and 9.