Journal of Psychopathology and Behavioral Assessment (2022) 44:481–495
https://doi.org/10.1007/s10862-021-09941-9

Disruption in Pavlovian-Instrumental Transfer as a Function of Depression and Anxiety

Allison Metts[1] · Inna Arnaudova[2] · Lindsay Staples-Bradley[1] · Michael Sun[1] · Richard Zinbarg[3,4] · Robin Nusslock[3] · Kate M. Wassum[1] · Michelle G. Craske[1,2]

Accepted: 14 October 2021 / Published online: 8 January 2022

Abstract

The Pavlovian-Instrumental Transfer (PIT) paradigm examines probabilistic and reinforcement learning. Disruptions in mechanisms that mediate PIT (i.e., cues not triggering adaptive behaviors) are thought to be contributors to psychopathology, making the study of probabilistic and reinforcement learning clinically relevant. The current study evaluated an appetitive PIT effect and its relationship with symptom dimensions spanning depression and anxiety, with a particular focus on anhedonia. Forty young adults ranging in scores across dimensions of depression and anxiety symptoms completed the PIT paradigm and self-report symptom measures. The PIT paradigm consisted of three phases. The *instrumental phase* consisted of a contingent association in which participants squeezed a handgrip for monetary reward. The *Pavlovian phase* established a purely predictive association between three visual stimuli (CS+, CS-, baseline) and presence or absence of monetary reward. In the *transfer phase*, participants' responses allowed for examination of whether motivational characteristics of Pavlovian predictors influenced the vigor of their handgrip squeezes (instrumental action), which were formerly independent of Pavlovian associations. Analyses revealed a baseline-reward PIT effect, whereby a reward-associated Pavlovian cue enhanced instrumental responding in the transfer phase. However, there were no significant differences between CS+ and CS- or CS- and baseline cues, suggesting a disrupted interaction of Pavlovian and instrumental learning. Further, the appetitive PIT effect captured in this paradigm was not associated with anhedonia, fears, or general distress. Future work should investigate the influence of mood states using more specific appetitive PIT paradigms to further understanding of the implications of disrupted reflexive and instrumental responding.

Keywords Pavlovian-instrumental transfer · Probabilistic learning · Reward learning · Anhedonia · Depression · Anxiety

Introduction

Predictive cues influence us to take action in various day-to-day situations, such as water cues leading us to seek out and drink water when we are thirsty (Nord et al., 2018). Reward-associated cues can also alter motivation and choice in instrumental actions (i.e., acting for reward; Cartoni et al., 2016; Manglani et al., 2017). In Pavlovian-Instrumental Transfer (PIT), the vigor with which humans execute instrumental actions increases or decreases due to motivational influences arising from Pavlovian conditioned stimuli previously associated with appetitive or aversive stimuli, respectively (Manglani et al., 2017; Talmi et al., 2008).

Disruptions in the mechanisms that mediate PIT, such as cues not triggering adaptive behaviors (e.g., not drinking water when thirsty), are thought to be potential contributors to psychopathology. For example, mood-congruent biases in depression lead to over-responsiveness to negative stimuli and under-responsiveness to positive stimuli (Nord et al., 2018). Further, if reflexive approach responses to appetitive stimuli are reduced, as have been found in depression (e.g., Eshel & Roiser, 2010; Steele et al., 2007), the perceived ease and prevalence of earning reward are reduced (Huys et al., 2016). This in turn might reduce positive emotion regulation

✉ Michelle G. Craske
MCraske@mednet.ucla.edu

[1] Department of Psychology, University of California, Los Angeles, 1285 Franz Hall, Los Angeles, CA 90025, USA

[2] Department of Psychiatry, University of California, Los Angeles, 760 Westwood Plaza, Los Angeles, CA 90024, USA

[3] Department of Psychology, Northwestern University, 2029 Sheridan Road, Swift Hall 102, Evanston, IL 60208, USA

[4] The Family Institute at Northwestern University, 618 Library Place, Evanston, IL 60208, USA

strategies, result in negative cognitive distortions, or hinder problem-solving (Huys et al., 2016). Therefore, the study of reflexive and instrumental learning mechanisms is clinically relevant. The current study aimed to examine the PIT effect in young adults ranging in scores across dimensions of depression and anxiety symptoms and explore the relationship between the motivational impact of reward cues and symptoms spanning depression and anxiety.

Reinforcement sensitivity theory presumes individual differences in one's sensitivity to rewards and punishments (Corr, 2004). Anhedonia—which is related to deficits in reward sensitivity—could therefore be considered at the extreme end of these individual differences. Anhedonia is characterized by loss of enjoyment or desire to engage in pleasurable activities and diminished interest to previously-rewarding stimuli (American Psychiatric Association, 2013). Anhedonia is associated with disrupted anticipation, consumption, and learning of reward above and beyond symptoms of depression (Chung & Barch, 2015; Craske et al., 2016; Epstein et al., 2006; Greenberg et al., 2015; Stoy et al., 2011; Ubl et al., 2015; Yang et al., 2014). Anhedonia is also a transdiagnostic feature of both depression and anxiety. Whereas evidence from earlier models claim that anhedonia is exclusively linked to depression relative to anxiety (e.g., Brown et al., 1998; Clark & Watson, 1991), more recent evidence demonstrates that significant variation in both anxiety and depression symptoms are explained by features of anhedonia, including positive affect (Kashdan, 2007; Prenoveau et al., 2010). Research also demonstrates hedonic impairments in populations with anxiety (Kashdan et al., 2011; Srivastava et al., 2003) and similar effect sizes between anxiety and positive affect and depression and positive affect (Khazanov & Ruscio, 2016; Kotov et al., 2010).

The PIT paradigm captures two key constructs specified in the positive valence symptom domain of the NIMH research domain criteria that are related to the experience of positive affect: approach motivation and responsiveness to reward (Craske et al., 2016). Approach motivation involves mechanisms that regulate the direction and maintenance of approach behavior influenced by factors such as preexisting tendencies and learning. Approach behavior can consist of both goal-directed and Pavlovian-conditioned responses. Component processes include effort valuation and willingness to work for reward (Craske et al., 2016). Responsiveness to reward refers to mechanisms that are associated with hedonic responses (e.g., behavioral response; subjective experience) and reward seeking (Craske et al., 2016). Individuals with deficits in positive affect display loss of enjoyment of pleasurable activities (responsiveness) as well as loss of desire to engage in pleasurable activities (approach motivation; Snaith, 1993; American Psychiatric Association, 2013). Given this relationship, anhedonia may be expected to alter the strength of a PIT effect using appetitive stimuli.

Research by Talmi et al. (2008) demonstrated PIT in a healthy sample of 16 adults (mean age = 31) using an appetitive PIT paradigm that included the same Pavlovian and instrumental outcomes as the current study. This PIT paradigm is unique compared to other PIT paradigms in that it captures both specific (i.e., cues enhancing specific actions association with the same outcome as the cue) and general (i.e., cues enhancing specific actions paired with both same and different outcomes; Cartoni et al., 2016) mechanisms in the overall PIT effect. There was evidence for a PIT effect such that a predictor of the noncontingent delivery of monetary reward induced participants to squeeze a handgrip more vigorously to earn money (a robust secondary reinforcer). Specifically, handgrip frequency, but not force, was higher in response to the CS + cue (fractal image associated previously with monetary reward) compared to the CS- cue (fractal image associated with reward non-delivery) and baseline cue (fractal image never associated with (non-) delivery). CS- and baseline cues did not differ. We aimed to examine whether there was evidence for this PIT effect (CS + vs. CS-) in a community sample of young adults ranging in scores across dimensions of depression and anxiety symptoms to gain a better understanding of how disruptions in mechanisms mediating PIT contribute to psychopathology.

Only a handful of recent studies to our knowledge have investigated the PIT effect in relation to depression and anxiety (Huys et al., 2016; Krypotos & Engelhard, 2020; Nord et al., 2018; Quail et al., 2017). One study examined a general PIT effect in a paradigm capturing both appetitive and aversive PIT in 25 depressed patients and 40 healthy controls (mean age = 27.7; Huys et al., 2016). This study did not find group differences in appetitive or aversive PIT. However, it was found that currently depressed patients lacked action specificity (i.e., CS positively related to active response in approach and negatively related to active response during withdrawal) whereas healthy controls displayed action specificity. In a separate study, the same PIT paradigm was used in 26 depressed patients and 28 healthy volunteers (mean age = 27.4; Nord et al., 2018). Patients were found to be more strongly influenced by aversive Pavlovian stimuli than healthy volunteers. There was a significant positive correlation between the aversive, but not appetitive, PIT effect, and symptoms of depression and anhedonia. There was no effect of anxiety on the PIT effect.

Quail et al. (2017) used an appetitive PIT paradigm to examine whether self-reported anxiety and depression symptoms related to specific or general PIT effects in 24 healthy undergraduates (mean age = 20.4). Whereas depression did not relate to specific or general PIT, anxiety was significantly negatively correlated with general PIT (i.e., higher anxiety, weaker PIT). High anxiety individuals were found to respond more to non-rewarding cues, whereas low anxiety individuals appropriately suppressed responses to the

nonrewarding cue. Lastly, an avoidance-related PIT effect was examined in 48 individuals with subclinical levels of OCD (mean age = 20.42; Krypotos & Engelhard, 2020). It was found that individuals with low levels of OCD displayed stronger specific PIT than individuals with high levels of OCD. There was no evidence for general PIT in this sample. In sum, existing studies on depression and anxiety in relation to the PIT effect are limited in number and inconclusive. Therefore, more research exploring PIT in relation to depression and anxiety is needed.

Existing work on PIT in the context of depression and anxiety uses response rate via button clicks as the PIT outcome. Because of the ease of executing a button click, this measure of effort may not capture the reduced willingness to expend effort for rewards that is characteristic of trait anhedonia (Treadway et al., 2009). A more effortful measure (handgrip squeeze) of response vigor might have greater potential to capture individual differences in appetitive behavior. It could be that a lack of relation between anhedonia and the appetitive PIT effect in Nord et al. (2018) was a function of the instrumental response measure not requiring high effort. Further, existing work has yet to explore influences of symptoms of depression and anxiety in a paradigm that captures both specific and general mechanisms of PIT, which is presumed to be more powerful as it captures both processes in the overall PIT effect (Talmi et al., 2008). With regard to motivational aspects, anhedonia has previously been linked to decreased motivation on effortful motor tasks for monetary reward (e.g., Treadway et al., 2009, 2012), it is possible that a PIT paradigm using monetary reward may capture an association between anhedonia and decreased motivation on effortful motor tasks. The current study aimed to investigate the strength of appetitive PIT in relation to self-reported transdiagnostic symptoms of depression and anxiety using both frequency and force metrics to measure effort to obtain monetary reward.

The Present Study

The goals of the present study were two-fold. First, we aimed to examine whether there was evidence for the PIT effect (CS + vs. CS-) observed in sample of healthy adults using a validated PIT paradigm (Talmi et al., 2008) in a sample of young adults ranging in scores across dimensions of depression and anxiety symptoms. Second, we aimed to examine the relationship of the PIT effect with transdiagnostic symptoms of depression and anxiety, particularly anhedonia. Despite the lack of significant relationships between appetitive PIT and anhedonia in a prior study (Nord et al., 2018), we hypothesized a significant negative association between the strength of the PIT effect and anhedonia given other evidence to suggest a relationship with anhedonia and reduced effort when working for reward and use of reward information to guide behavior (Treadway et al., 2012).

Method

Participants

Participants aged 18–19 years old were recruited from a larger sample of 157 young adults in a longitudinal study of positive and negative valence systems (Brain, Motivation, and Personality Development project; BrainMAPD (NIMH R01 MH100117-01; UCLA site). Participants were recruited from colleges and the community in the greater Los Angeles area and participated for compensation for a bonus behavioral session of the parent study ($45 + winnings from task, which ranged from $4–8). Participants were recruited for the parent study based on self-reported trait Neuroticism as measured by the 12-item Eysenck Personality Questionnaire-Neuroticism scale (EPQ-N; Eysenck & Eysenck, 1975)[1] and Reward Sensitivity as measured by the Behavioral Activation Sensitivity (BAS; Carver & White, 1994). Sampling procedures were designed to recruit participants 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). Other inclusion criteria were between 18–19 years ago, right-handed and English fluency. Exclusion criteria were a history of a DSM-5 criteria for lifetime diagnosis of bipolar disorder or psychotic disorder, or current, severe substance use disorder (per diagnostic interview), a moderate or greater traumatic brain injury/neurological disorder, MRI contraindications (e.g., severe claustrophobia), and color-blindness.

A total of 60 participants recruited into the study completed the current task. Of those 60 participants, 55 had usable task data (i.e., complete data in all task phases). Of those 55 participants, 40 had available symptom data that fell within one month (max 31 days) of task completion (24 female, mean age = 18.47 years, standard deviation (*SD*) = 0.51), see Table 1 for racial/ethnic composition and BAS and EPQ-N descriptive statistics of the final current sample of 40 young adults). Participants included in analyses did not differ from participants who completed the PIT task but were not included in analyses on gender, minority group status, screener EPQ-N or BAS, or symptoms

[1] A modified EPQ-N was used in the present study such that participants responded to items on a 0 (Not at all) to 3 (Very much) Likert scale instead of answering Yes or No.

Table 1 Screener variables, demographics, and diagnostic statuses of participants included in this study

	N	%
Screener Classification		
Low BAS/Low EPQ-N	8	20.0
Low BAS/Med EPQ-N	2	5.0
Low BAS/High EPQ-N	6	15.0
Med BAS/Low EPQ-N	0	0
Med BAS/Med EPQ-N	8	20.0
Med BAS/High EPQ-N	5	12.5
High BAS/Low EPQ-N	5	12.5
High BAS/Med EPQ-N	2	5.0
High BAS/High EPQ-N	4	10.0
Race		
White	21	52.5
Black or African American	2	5.0
Asian	15	37.5
American Indian or Alaska Native	1	2.5
None by choice	1	2.5
Ethnicity		
Not Hispanic or Latinx	**25**	**62.5**
Hispanic or Latinx	**15**	**37.5**
Diagnoses		
Current Anxiety Disorder	12	30
Current Depressive Disorder	6	15
Current Depressive and Anxiety Disorder	6	15
	M (range)	*SD*
Screener Variable		
BAS-Drive	11.37 (9–14)	1.444
BAS-Reward Responsiveness	17.40 (14–20)	1.823
BAS-Fun Seeking	11.85 (7–16)	2.082
BAS Total	40.63 (32–47)	3.946
Neuroticism (EPQ-N)	18.55 (7–34)	7.338

BAS = Behavioral Activation Sensitivity (BAS; Carver & White, 1994). EPQ-N = Eysenck Personality Questionnaire-Neuroticism scale (Eysenck & Eysenck, 1975). 12 participants total met for an anxiety or a depressive disorder diagnoses (6 with both diagnoses; 6 with anxiety only; 0 with depression only). Anxiety disorders included agoraphobia, generalized anxiety disorder, panic disorder, separation anxiety, social anxiety disorder, and specific phobia. Depressive disorders included major depressive disorder and persistent depressive disorder. Depressive and anxiety disorders reported here include those that met for full diagnostic criteria or otherwise specified criteria for a given disorder. Disorders are referred to as "diagnoses and possible diagnoses" to reflect the rating of at least a 3 (probable diagnosis) on the Clinical Severity Rating scale (Di Nardo & Barlow, 1988)

($ps \geq 0.25$ across comparisons). All study procedures were approved by Institutional Review Board at the University of California–Los Angeles (protocol #13–001,606).

Although this study was designed to use a dimensional approach to investigate broad symptom domains, diagnostic interviews were also conducted for the current sample. Participants were assessed using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; First et al., 2016), a semi-structured diagnostic interview. The diagnoses reported were rated as 3 or above on the 0 to 8 Clinical Severity Rating (CSR) Scale (Di Nardo & Barlow, 1988). This range of scores represents cases on the boundary between sub-clinical presentation and "caseness" (rating of 3) and those that met threshold for the definition of "caseness" according to clinically significant impairment/interference with functioning and/or significant distress. "Disorders and possible disorders" reflect this CSR coding. The proportions of individuals who met for current anxiety and depressive disorders and possible disorders are reported in Table 1. 30% of participants met criteria for a current depressive or anxiety disorder.

Power Analysis

A sample of 40 participants allowed us to detect an effect size of $f = 0.21$ (i.e., medium effect size), for alpha of 0.05, one group, three measurements, and a power of 0.80. Given that Talmi et al. (2008) detected a large effect ($f = 0.64$) in a sample of 16 healthy adults, we concluded that our sample was sufficiently powered for our analyses.

Apparatus and Stimuli

Instrumental responding data were collected from a hand dynamometer (Vernier; Beaverton, OR) plugged into an Arduino RedBoard V-21 (SparkFun Electronics; Niwot, CO). The dynamometer measures the exerted force of a participant's hand squeeze in volts. Visual stimuli were presented using Matlab (R2014a, Mathworks) and Psychtoolbox (version 3011) on a 17-inch computer screen placed approximately 20 inches in front of participants. The visual cues were images of colored rectangles with fractal patterns. The instrumental and baseline cues (comparison stimuli) were gray and blue, respectively. The CS + and CS- were counterbalanced to be green or purple hues. Visual feedback during instrumental responding was represented by a picture of a thermometer containing "mercury" that responded in proportion to the amount of effort exerted. An American dollar sign ($) appeared on the screen represented a monetary reward in the amount of 5 cents. A red X over this image indicated no reward. A colored rectangular representing a given cue was presented behind these images in all phases.

Measures

Appetitive Responding

Subjective ratings of valence and arousal for conditional stimuli were collected at the end of the Pavlovian phase. Participants were instructed to use the arrow keys to move the indicators on the displayed scales to enter their responses. The valence scale was described to participants to be an indicator of feeling very negative (e.g., unhappy, upset; numerically coded as 1) to very positive (e.g., happy, pleased; numerically coded as 7). The middle was described as feeling neutral (i.e., neither positive nor negative; numerically coded as 4). The arousal scale was described to participants to be an indicator of low arousal (e.g., unaroused, slow; numerically coded as 1) to high arousal (e.g., very alert, aroused; numerically coded as 7). The middle was described as moderate arousal (numerically coded as 4).

Symptoms of Anxiety and Depression

Anxiety and depression symptoms were assessed in a dimensional framework, using factor analytic methods to generate factor score estimates across distinct dimensions of symptoms. Previous research has identified a tri-level model of anxiety and depression based on factor analyses of symptoms in studies of adolescents and adults (Naragon-Gainey et al., 2016; Prenoveau et al., 2010). These analyses identified a "broad" factor (general distress) and two "intermediate" factors (fears and anhedonia-apprehension). General distress represents symptoms common to anxiety and depression. Anhedonia-apprehension (referred to as "anhedonia" in the present study) represents symptoms once thought to be specific to depression but since shown to also be elevated in some forms of anxiety, especially social anxiety. Specifically, this factor explains covariation among symptoms of positive affect, anhedonia, depression and social fears not explained by narrower group factors or the general distress factor. Fears represents symptoms more specific to anxiety disorder diagnoses and explains covariation among social fears, fears of specific stimuli, fears of interoceptive sensations and agoraphobia fears that was not explained by narrower factors or general distress (Prenoveau et al., 2010).

Participants completed 101 questionnaire items selected from self-report depression and anxiety symptom measures. Sixty-seven of these items were used in the Prenoveau et al. (2010) tri-level hierarchical model, which originated from five self-report measures: the Fear Survey Schedule-II (FSS; Geer, 1965), the Albany Panic and Phobia Questionnaire (APPQ; Rapee et al., 1994), the Self-Consciousness subscale of the Social Phobia Scale (SPS; Mattick & Clarke, 1998; Zinbarg & Barlow, 1996), the Inventory to Diagnose Depression (IDD; Zimmerman et al., 1986), and the Mood and Anxiety Symptom Questionnaire (MASQ; Watson et al., 1995).

The FSS (Geer, 1965) consists of 50 items that examine symptoms representative of specific phobia. The FSS asks participants to identify how much fear they would experience if they encountered a particular situation or stimulus on a 0 (none) to 6 (terror) scale. Participants answered only the seven items used by Prenoveau et al. (2010).

The APPQ (Rapee et al., 1994) consists of 22 items that examine fear of sensation-producing activities along with agoraphobic scenarios. Like the FSS, the original version of this questionnaire asks participants how much fear they would feel in each of the listed experiences from 0 (no fear) to 8 (extreme fear). Participants answered only the 10 questions used by Prenoveau et al. (2010).

The Self-Consciousness subscale of the SPS (Mattick & Clarke, 1998; Zinbarg & Barlow, 1996) consists of 13 items that examine sensitivity to social evaluation. This sensitivity is a key component of social phobia. The original version of this questionnaire asks how typical a statement is of the participant from 0 (not typical of me) to 4 (extremely typical of me). Participants in this study answered only the eight items used by Prenoveau et al. (2010).

The IDD (Zimmerman et al., 1986) consists of 21 items that assess depression symptoms such as anhedonia and hopelessness. Each IDD item contains five statements. The participants decide which of the statements best reflect how they have been feeling in the past week. Participants in this study answered only the eight items used by Prenoveau et al. (2010).

The MASQ (Watson et al., 1995) consists of 90 items that assess symptoms of a broad range of anxiety and depressive disorders. The original MASQ asks participants to describe to what extent they have had certain symptoms over the past week from 1 (not at all) to 5 (extremely). Participants in this study answered only the 34 items used in Prenoveau et al. (2010).

The remaining 34 items used to generate these factor scores were the full scales of the Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990) and the Obsessive–Compulsive Inventory Revised (OCIR; Foa et al., 2002), which were used in Naragon-Gainey et al. (2016) and Kramer et al. (2019). These items were included to better characterize symptoms of generalized anxiety disorder and obsessive–compulsive disorder (Young et al., 2020).

The PSWQ (Meyer et al., 1990) contains 16 items that assess worry. Participants identified how typical a given statement is of their life in general on a 1 (not at all typical) to 5 (very typical) scale. All items were used.

The 18-item OCI-R (Foa et al., 2002) self-report measure examines key symptoms of OCD. Participants assess how prevalent OCD symptoms are in their lives on a 0 (not at all) to 4 (extremely) scale. All items were used.

Confirmatory factory analysis on these tri-level factors was previously conducted in a larger sample of participants from the parent study using baseline depression and anxiety symptom data sample and provided good fit to the self-reported symptom data across key indices (Kramer et al., 2019). Evidence of face validity of these tri-level factors from a larger sample of participants from the parent study (i.e., correlations between factor scores and diagnostic status) reported here can be found in Young et al. (2020).

Procedure

Participants completed self-report questionnaire measures in a separate testing session prior to the bonus behavioral session where the PIT paradigm of the present study was administered. The time between the self-report questionnaires and the bonus behavioral session was capped at 31 days ($M = 13.300$, $SD = 6.896$). The 30-min PIT task was completed fourth in a series of eight tasks that comprised the 90-min bonus behavioral session.

The PIT task began with a baseline measure of handgrip strength during which the participant held the handgrip without exerting any pressure. A calibration trial followed in which participants were asked to squeeze the handgrip as hard as possible to determine individual maximum handgrip strength. Throughout the rest of the experiment, required handgrip strength randomly oscillated between 50 and 70% of the participant's maximum handgrip strength, to control for individual differences in handgrip strength. Participants were seated in front of a computer monitor and were provided with a chinrest for collection of eye-tracking data using an Eye-Trac 6 unit (Applied Science Laboratories, Waltham, MA). Eye-tracking data were not analyzed. Figure 1 displays all task phases.

For the *instrumental conditioning phase*, the instrumental response of squeezing the handgrip was followed by monetary reward. Participants were instructed that the reward stimulus ($) represented real money. Participants were also told that they should perform quick squeezes and use their judgment to decide when to squeeze to obtain the reward to maximize their profit. The instrumental phase included 24 12-s trials of the handgrip strength indicator overlaid atop a fractal cue, both centered on the screen. Participants received a reward (cued with the $ symbol) if the exerted handgrip strength reached the maximum required handgrip strength for the trial during two one-second randomly selected windows when reward was available. The one-second reward windows were not signaled in any way. Each trial was followed by a 4–12 s intertrial interval (ITI), during which a fixation cross was presented.

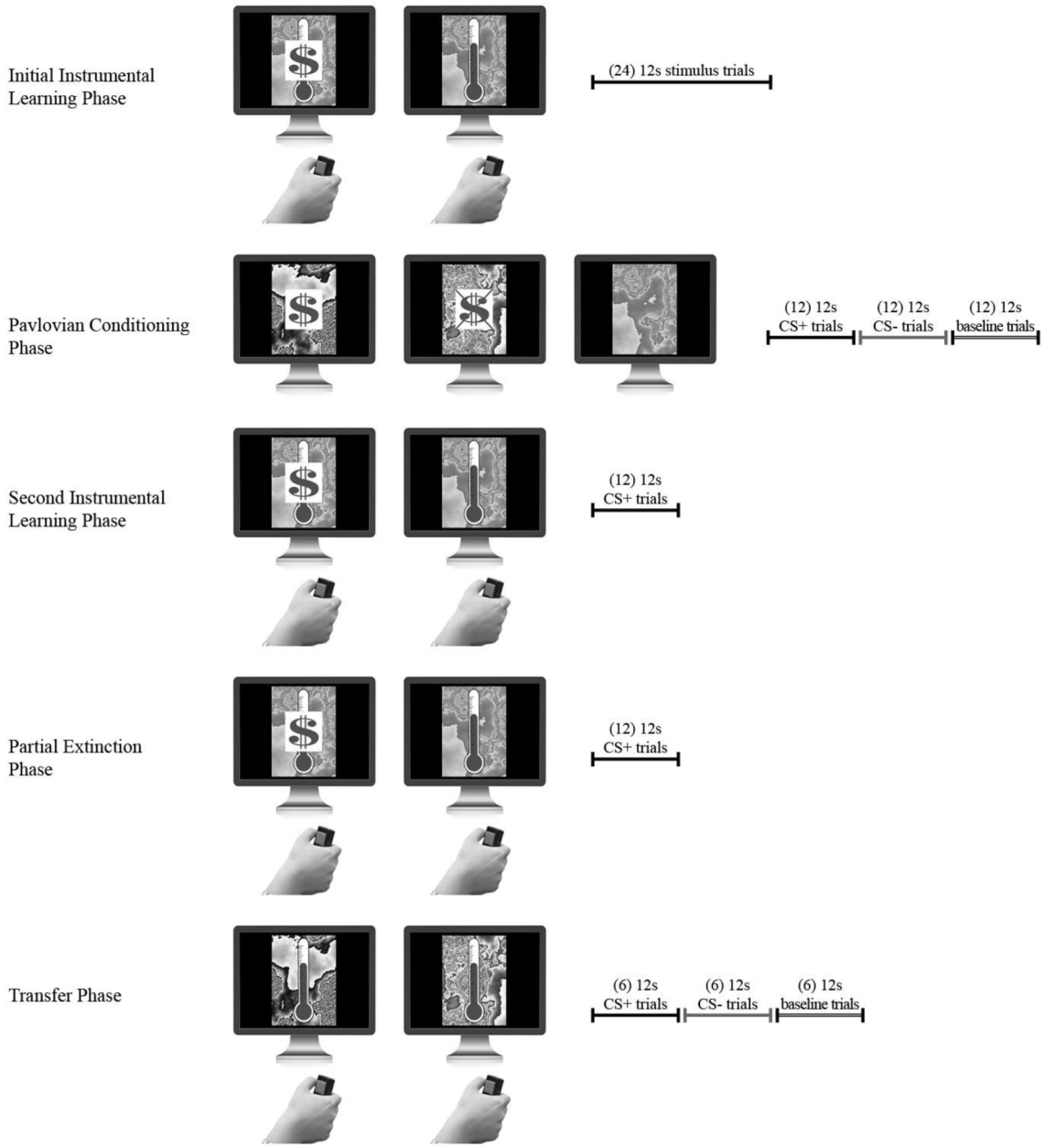
For the *Pavlovian phase*, participants were presented with 36 12-s trials, during which either the CS + or the CS- was presented, with the CS + paired with a reward symbol and the CS- presented with a "no reward" symbol. The reinforcement rate during Pavlovian conditioning was 100%. A baseline stimulus was presented during ITIs, during which neither the "reward" nor the "no reward" symbol was presented. CS +, CS- and baseline stimuli appeared in one of four randomly selected orders of stimuli, which were counterbalanced. Participants did not use the handgrip during this phase.

Over each CS, a gray "patch" image obscured the outcome (i.e., reward or no reward) and disappeared to reveal whether the reward was obtained during the Pavlovian phase. Participants were asked to press as quickly as possible the "1" key with their non-dominant index finger to reveal the outcome, however they were informed that this response simply monitored their attention to the task and had no bearing on the outcome. The patch was removed automatically to reveal the outcome regardless of participants' pressing. There were three equal monetary rewards for each CS + trial which were presented at random times equally distributed throughout the stimulus presentation. After each trial came a 4-s ITI, during which the baseline stimulus was presented. At the end of this phase, valence and arousal ratings of each fractal image were collected to assess evaluative learning.

Following the Pavlovian phase, participants completed *forced choice ratings* on preference for the CS +, CS-, and baseline stimuli. Participants were presented with each possible combination of two stimuli at a time (six trials total) in one of two randomly selected orders. The two stimuli were centered on the left and the right side of the screen. Participants selected a stimulus by pressing the right or left arrow key on the keyboard to indicate their preferred stimulus (i.e., CS +, CS-, or baseline fractal image). Each trial was followed by a 1-s ITI with a fixation cross. Choice scores per stimulus were computed as the number of times each stimulus was preferred.

Prior to the PIT test phase, each participant completed a *second instrumental phase with partial extinction* which was identical to the first instrumental phase followed by 12 partial extinction trials. Participants were instructed to use their intuition to decide when to grip as before. Each instrumental trial included three reward windows, while each partial extinction trial included one reward window. Partial extinction was included to increase the potential transfer effect (Dickinson et al., 2000).

During the *PIT test phase*, participants underwent 18 full-extinction trials (six trials per cue) during which instead of the instrumental fractal image, the three



Note. During the initial *instrumental/earning phase,* participants squeezed a handgrip to work for reward. During the *Pavlovian conditioning phase,* participants used a non-dominant index finger to press the "1" key to remove a gray patch on a screen to reveal a reward($) over a fractal image (CS+), no reward($ with X superimposed) over a fractal image (CS-), or just the fractal image (baseline). During the second *instrumental learning phase,* participants squeezed a handgrip to work for reward with the same reinforcement rate as the initial instrumental phase. During *the partial extinction phase,* participants continued to squeeze the handgrip for reward with a lower reinforcement rate. During *the transfer phase,* participants squeezed the handgrip under full extinction with the thermometer overlayed over the Pavlovian cue.

Fig. 1 Depiction of Pavlovian, instrumental and transfer phases during PIT task

Pavlovian stimuli were presented with the thermometer to assess the Pavlovian-Instrumental interaction. Participants viewed one of four randomly selected orders of stimuli, which were counterbalanced. Participants responded by squeezing the handgrip during these trials. The PIT test trials were 12 s in duration and were followed by 4–12 s (mean of 8 s) ITIs. The durations of ITIs were randomized across the phase.

Data Analyses

Two indices—force and frequency—were calculated across task phases to index performance. Force was operationalized as mean force per trial. Frequency was calculated by counting the number of squeezes that surpassed a threshold of 50% of the participant's maximum grip per task phase (Talmi et al., 2008). To calculate the strength of the PIT effect, we subtracted the average performance index across trials associated with the CS- from those of the CS+. Therefore, the larger the positive difference, the larger the PIT effect. An exploratory baseline-reward PIT indicator was calculated by subtracting the average performance index across trials associated with the baseline cue (non-signal) from those of the CS+ (reward signal). While the CS- signaled inhibition of reward delivery, the baseline cue signaled reward non-delivery.

A series of multivariate analysis of variance (MANOVA) were conducted to examine the behavioral experiment data given the violation of the sphericity assumption across all portions of the task. Initial instrumental, second instrumental, and partial extinction phase data were analyzed using a one-way repeated-measures MANOVA looking at effect of trial. Data from all trials were examined for each task phase with the exception of instrumental learning. Given previous work demonstrating number and force of grips stabilizing after the first two blocks (Talmi et al., 2008), instrumental learning analysis focused on blocks 2–24. Response rate and linear trend analyses were used to examine instrumental response in line with previous PIT studies (Talmi et al., 2008; Vogel et al., 2020).

Valence and arousal ratings during the Pavlovian phase was analyzed using a one-way repeated-measures MANOVA examining effect of cue. Forced choice during the Pavlovian phase was analyzed using specified contrasts within a repeated-measures MANOVA. A paired samples *t*-test was used to examine differences in average response time to CS+ versus CS- cues across trials. To test the PIT effect, both PIT effect metrics were entered into a series of 3 (cue: CS+, CS-, baseline) × 6 (blocks) repeated measures MANOVA. Planned contrasts were used to compare the magnitude of response to each cue type. We chose to examine general distress and fears, in addition to anhedonia, to explore whether there was any indication of specificity of the relationship between PIT effect strength and anhedonia or whether the relationship was generalized across depression and anxiety symptoms. Partial correlations between summary scores of the PIT effect and tri-level factors were calculated. Multiple regression analyses were calculated to predict the PIT effect (performed separately for each metric) based general distress, anhedonia, and fears. Time between tri-level symptom questionnaires and PIT task completion was controlled for in correlation and regression analyses.

All analyses were conducted using SPSS, Version 26 (IBM Corp). The level of statistical significance in all inferential analyses was $p < 0.05$. Planned contrasts were Bonferroni corrected. 27.69% of the Pavlovian reaction time data were coded as non-response. As response time was not recorded in the case of non-response, and analyses with more than 10% missingness result in bias (Madley-Dowd et al., 2019), imputation was completed. Specifically, a non-response (participant failed to respond within the response window during the Pavlovian phase) was counted as 1000 ms (maximum response time) following procedures used in previous associative learning studies (e.g., Craddock et al., 2012). Individual responses were visually inspected for outliers but there were no extreme datapoints that indicated removal.

Results

Instrumental and Pavlovian Learning Phases

Participants responded to 100% of the instrumental trials. As demonstrated in Fig. 2, participants continued to squeeze for reward during each trial representing the instrumental cue throughout the task phase, demonstrating the expected pattern of a random interval reinforcement schedule (Perez & Dickinson, 2020; Perez, 2021). There was no significant effect of trial according to the frequency metric ($F(22, 18) = 1.063$, $p = 0.453$; linear trend: $t(39) = -1.060$, $p = 0.296$, 95% CI [-3.898, 1.217]. The effect of trial was also nonsignificant for the mean force metric ($F(22, 18) = 1.292$, $p = 0.293$). However, a significant linear trend was observed with mean force ($t(39) = -3.899$, $p = 0.003$, 95% CI [-25.146, -7.967]), indicating strength of participant squeezes declined across trials. Therefore, participants maintained the squeeze frequency during the instrumental phase albeit with reduced force across trials, indicative of instrumental learning.

Pavlovian phase data are displayed in Fig. 3. The effect of CS+ vs. CS- on reaction times was significant,

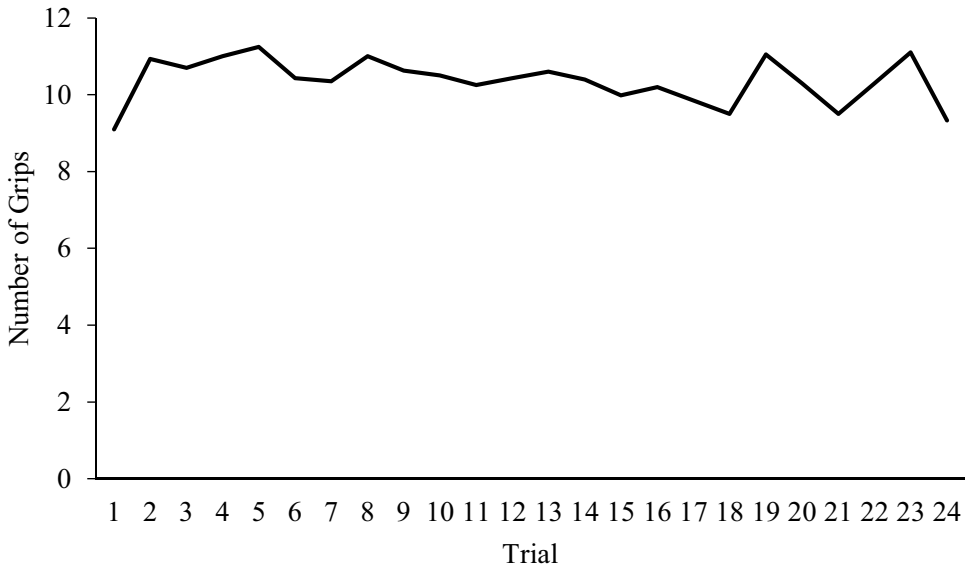


Fig. 2 Frequency of response for instrumental cue through task phase

$t(39) = -2.034$, $p = 0.049$, indicating that the CS + induced a faster reaction time than the CS-. Of note, the same trend was observed when this analysis was performed with non-response data treated as missing (handled via list-wise deletion) instead of imputed.[2]

Valence and Arousal

The instrumental cue was rated as pleasant ($M = 4.950$, $SD = 1.197$) and arousing ($M = 4.325$, $SD = 1.559$). As displayed in Fig. 3, the effect of Pavlovian cue (CS +, CS-, baseline) was significant for valence ($F(2, 38) = 65.898$, $p < 0.001$) and arousal ($F(2, 38) = 38.509$, $p < 0.001$) ratings. Planned contrasts of valence ratings per Pavlovian cue indicated that CS + was rated higher on valence ($M = 5.900$, $SD = 1.008$) than both CS- ($M = 3.875$, $SD = 1.224$; $t(39) = 9.411$, $p < 0.001$; 95% CI [2.120, 3.280]) and baseline cues ($M = 3.875$, SD = 0.791; $t(39) = 10.415$, $p < 0.001$; 95% CI [1.632, 2.418]). CS- and baseline cues were also significantly different on valence ratings, $t(39) = 2.580$, $p = 0.014$; 95% CI [0.146, 1.204]). Similarly, planned contrasts of arousal ratings indicated that CS + ($M = 4.550$, $SD = 1.300$) was rated higher on arousal than both CS- ($M = 2.850$, $SD = 1.167$; $t(39) = 5.549$, $p < 0.001$; 95% CI [1.080, 2.320] and baseline ($M = 2.950$, $SD = 1.467$; $t(39) = 8.186$, $p < 0.001$; 95% CI [1.205, 1.995]). CS- and baseline cues did not significantly differ on arousal ratings, $t(39) = 0.317$, $p = 0.753$, 95% CI [-0.539, 0.739].

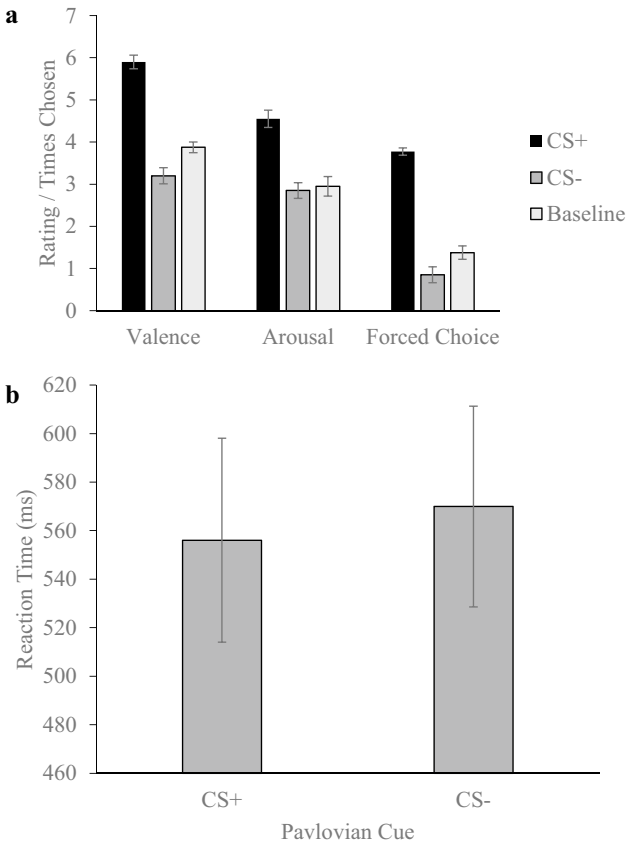


Fig. 3 Pavlovian conditioning. *Note.* Figure 3a depict forced choice preferences, valence ratings of each of the stimuli and arousal ratings of each of the stimuli. Figure 3b depicts latency to respond to the cue that preceded the CS + or CS-. See results section for inferential statistics. Error bars represent standard errors

[2] In the analyses in which we treated non-response to reward windows as missing (missing data handled with list-wise deletion), we observed a longer response time to CS- ($M = 404.213$ ms) compared to CS + ($M = 393.632$ ms). However, this difference did not reach statistical significance level ($t(27) = -2.012$, $p = .054$), likely as a result of decreased power.

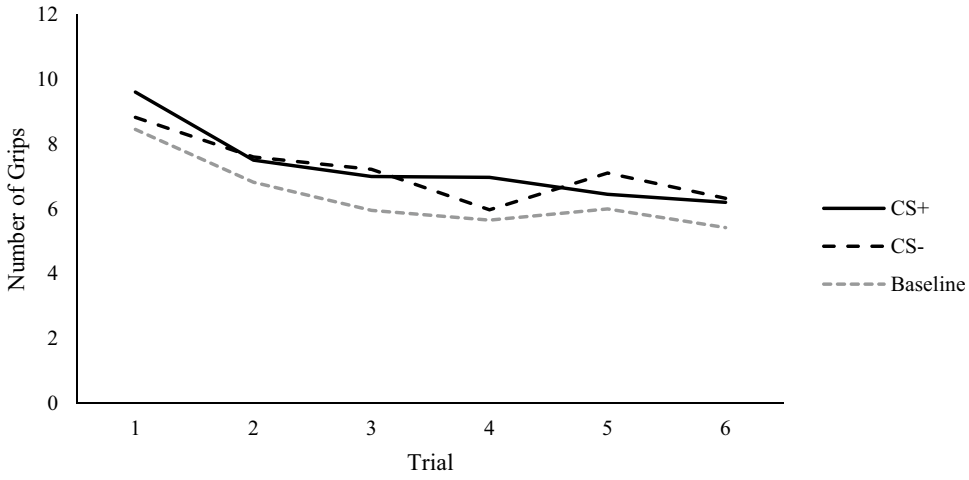


Fig. 4 Frequency of response per cue type during PIT test

Forced Choice

As portrayed in Fig. 3, the effect of cue (CS + , CS-, baseline) was significant for forced choice ($F(2, 38) = 238.090$, $p < 0.001$). Planned contrasts indicated that participants chose the CS + ($M = 3.775$, $SD = 0.530$) significantly more often than the CS- ($M = 0.850$, $SD = 1.189$; $t(39) = 11.994$, $p < 0.001$, 95% CI [2.431, 3.418]) and the baseline cue ($M = 1.375$, $SD = 1.005$; $t(39) = 14.037$, $p < 0.001$, 95% CI [2.054, 2.746]). The number of times participants chose the baseline cue compared to CS- was not significantly different ($t(39) = 1.554$, $p = 0.128$; 95% CI [-0.158, 1.208]). Preference for the CS + was therefore apparent in forced choice scores following Pavlovian conditioning.

Table 2 MANOVA results for Pavlovian-instrumental task phases

	F	*df*	Error *df*	*p-value*
Initial Instrumental Phase				
Mean force	1.292	22	18	.293
Frequency	1.063	22	18	.453
PIT Test: Block				
Mean force	5.350	5	35	.001*
Frequency	4.617	5	35	.002*
PIT Test: Cue				
Mean force	2.183	2	38	.127
Frequency	5.084	2	38	.011*
PIT Test: Block x Cue				
Mean force	.603	10	30	.799
Frequency	.648	10	30	.762

* $p < .05$

PIT Test

Figure 4 displays squeeze frequency in response to each cue type during the PIT test and Table 2 displays the MANOVA results of the PIT test. The effect of cue was significant ($F(2, 38) = 5.084$, $p = 0.011$). Extinction was apparent in the significant effect of blocks, $F(5, 35) = 4.617$, $p = 0.002$, although blocks and cue type did not interact significantly, $F(10, 30) = 0.648$, $p = 0.762$. Planned contrasts (Table 3) indicated a significant difference between CS + and baseline cues ($t(39) = 2.718$, $p = 0.010$). Of note, the difference between CS + and baseline cues approached significance according to the Bonferroni corrected alpha using the mean force metric ($t(39) = 2.029$, $p = 0.049$). CS + and CS- cues were not significantly different, $t(39) = 0.236$, $p = 0.815$. CS- cue response was also elevated compared to the baseline cue and approached significance according to the Bonferonni corrected alpha, $t(39) = 2.059$, $p = 0.046$. Therefore, participants responded more in the presence of CS + compared to the baseline cue, but not in comparison to CS-. This

Table 3 Planned contrast results for cues during Pavlovian-instrumental transfer phase

	t	*df*	Error *df*	*p-value*
Mean Force				
CS + vs. Baseline	2.029	1	39	.049
CS + vs. CS-	.557	1	39	.581
CS- vs. Baseline	1.247	1	39	.220
Frequency				
CS + vs. Baseline	2.718	1	39	.010*
CS + vs. CS-	.236	1	39	.815
CS- vs. Baseline	2.059	1	39	.046

* $p < .017$ (Bonferonni-corrected alpha)

Table 4 Descriptive statistics for tri-level factors and partial correlations with PIT effect metrics

Descriptive Statistics		
	M (range)	*SD*
Anhedonia	0.335 (-1.294–1.957)	0.748
Fears	0.045 (-1.543–1.831)	0.860
General Distress	0.149 (-1.054–1.633)	0.859
PIT Effect (Frequency)	0.113 (-9.000–6.500)	3.020
PIT Effect (Mean Force)	0.902 (-20.478–26.531)	10.243
Baseline-Reward PIT Effect (Frequency)	0.904 (-1.667–7.500)	2.104
Baseline-Reward PIT Effect (Mean Force)	2.723 (-22.074–23.993)	8.487

Correlations						
	Anhedonia		**Fears**		**General Distress**	
	r	***p-value***	***r***	***p-value***	***r***	***p-value***
Anhedonia	–	–				
Fears	.07	.68	–	–		
General Distress	.15	.35	.34	.04*	–	–
Mean Force (PIT)	-.07	.69	-.15	.36	-.01	.98
Frequency (PIT)	.02	.91	-.15	.37	.02	.92
Mean Force (Baseline-Reward PIT)	.03	.86	-.16	.33	-.07	.68
Frequency (Baseline-Reward PIT)	.15	.36	-.30	.07	-.11	.51

Correlations among tri-level factor score are bivariate correlations. Correlations among trilevel factors and PIT effect metrics are partial correlations, controlling for time between tri-level symptom measures and task completion

* $p < .05$

indicates a preference for the CS + compared to baseline cue. Together, PIT results indicate disruption in responding to reward and non-reward cues.

Tri-level Factors and Associations with PIT

Table 4 displays descriptive statistics for the tri-level factors for this sample and partial correlations with PIT effect indices. No correlations between PIT effect metrics and tri-level factors reached our significance threshold ($ps \geq 0.344$). Multiple regression analysis results are displayed in Table 5. Results indicate that tri-level factors do not predict the PIT effect according to either metric (mean force: $F(3, 36) = 0.456$, $p = 0.714$, $R^2 = 0.037$; frequency: $F(3, 36) = 0.355$, $p = 0.786$, $R^2 = 0.029$). As shown in Table 5, no individual tri-level factors significantly predicted any PIT level metrics. These analyses indicate no evidence for a relationship between the PIT effect and the tri-level factors in this sample.

We also ran correlation and regression analyses to explore potential significant relations with the exploratory baseline-reward PIT effect observed. No correlations between baseline-reward PIT effect metrics and tri-level factors reached our significance threshold ($ps \geq .066$; See Table 4). Similarly, no significant predictive relationships were found in multiple regression analyses (See Table 5).

Table 5 Summary of regression analyses for tri-level factors predicting PIT effect metrics

	Mean Force (PIT)			Frequency (PIT)			Mean Force (Baseline-Reward PIT)			Frequency (Baseline-Reward PIT)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*β*
General Distress	.739	2.139	.061	.253	.628	.071	-.230	1.782	-.023	-.092	.424	-.037
Anhedonia	-.925	2.137	-.068	.074	.696	.018	.489	1.974	.043	.509	.470	.181
Fears	-1.973	2.080	-.166	-.597	.611	-.170	-1.524	1.733	-.154	-.719	.412	-.294
R^2	.053			.060			.042			.119		
F	.489			.561			.387			1.178		

No results reached the $p < .05$ significance level. Time between completion of self-report questionnaires and PIT task was included as a covariate in these analyses

Discussion

Our study demonstrates that Pavlovian cues influence instrumental responding in a young adult sample ranging in scores across dimensions of depression and anxiety symptoms. Following successful instrumental and Pavlovian learning, participants increased the vigor with which they responded (both handgrip frequency and mean force) in the presence of the cue paired with reward (CS +) compared to a baseline cue under extinction, indicating the presence of a baseline-reward PIT effect. Participants also exhibited elevated response to the CS- cue, indicating overall disruption in response toward reward and non-reward. We found no evidence of associations between the strength of the appetitive PIT effect and the tri-level factors of anhedonia, fears, and general distress.

Our findings contribute to the literature by demonstrating a baseline-reward PIT effect of the CS + compared to the baseline stimulus in young adults ranging in scores across dimensions of depression and anxiety symptoms. This study utilized a PIT paradigm previously used in Talmi et al. (2008) that makes use of handgrip squeezes, as opposed to the more commonly used button presses. Handgrip squeezes are a more sensitive effort response (i.e., squeezing hard for a reward) compared to simply pressing a button, which would not record the magnitude of vigorous effort involved. This paradigm also allowed for investigation of both force exerted as well as frequency of response in our analyses. On the one hand, we observed stronger responding to CS + than the baseline cue, whereas responding to the CS- did not differ significantly from the baseline cue, which together is suggestive of a transfer of Pavlovian to instrumental conditioning. On the other hand, responding to the CS + did not differ significantly from responding to the CS- in the transfer phase. Thus, we failed to find evidence for differentiation between the CS + and CS- cues suggesting unexpected elevations in responding to the CS- cue in our sample.

Our study failed to find evidence for the CS + and CS- differentiation whereas a previous study using the same paradigm in a small sample of healthy adults found differentiation between these cues (Talmi et al., 2008. Our failure to find evidence for the CS + and CS- differentiation may be a result of the nature of our sample. 30% of our sample met criteria for current depressive or anxiety disorders diagnoses and possible diagnoses. Previous work has demonstrated that behaviors in depressed individuals are influenced by mood-congruent biases such that there is an under-responsiveness to positive stimuli and an over-responsiveness to negative stimuli (Nord et al., 2018). Individuals with elevated anxiety have also previously been found to respond more to non-rewarding cues (Quail et al., 2017). It is possible that participants in our study were influenced by mood congruent biases such that the elevated responding to negative stimuli, and potentially reduced response to positive stimuli compared to a healthy sample, led to a lack of differentiation between response to the CS + and CS- cues. However, given that we do not have mood data from the day of task completion, this explanation should be considered speculative. Another explanation may be that participants responded to both cues that were related to reward delivery (CS + and CS-). Participants may have responded to any cue that could signal reward to optimize their chances of receiving reward. Together, our results provide evidence for disrupted responding in this paradigm. More research is needed to determine whether this may be due to an influence of mood states or other factors.

Other factors that may have mitigated the PIT effect include insufficient training, since amount of training has been shown to relate to the degree of the transfer effect (Holmes et al., 2010). Moreover, the inhibition of reward may not have been as aversive as the reward was small. Future research could include a debrief procedure to ask participants whether they found monetary rewards to be rewarding in this paradigm to rule-out whether this contributed to their response patterns. Lastly, whereas CS- and baseline cues were evaluated differently in terms of pleasantness (valence), these cues were not found to be significantly different in autonomic activation (arousal; Russell, 1980). This suggests that the loss of reward was no more activating than the absence of reward for participants. The central feature of Pavlovian learning models is an error-correction mechanism such that associative change occurs when there is a discrepancy between what was predicted and what actually occurs (Rescorla & Wagner, 1972). This finding therefore suggests that associative learning between these cues did not occur and therefore a potential reason for a weaker association during PIT. However, given that depression is characterized by diminished ability to use reward information to guide behavior (Treadway et al., 2012) and blunted responding (Huys et al., 2013), more research is needed to clarify whether lack of arousal differentiation led to a disrupted display of PIT.

The second aim of our study was to explore whether the PIT effect related to anhedonia and other transdiagnostic features of depression and anxiety, including general distress and fears. We hypothesized a negative correlation between the PIT effect and anhedonia based on the link between decreased motivation for monetary reward (Treadway et al., 2009, 2012) and overall influences of depression and anxiety symptoms on reward processes (Schwabe & Wolf, 2009; Huys et al., 2013). Correlations between anhedonia, general distress, and fears and PIT effect metrics were not statistically significant. Regression analyses failed to support a predictive

relationship between the tri-level symptom structure of depression and anxiety and PIT effect metrics. This could be due to the nature of our sample, which consisted of 30% of individuals with depression and/or anxiety diagnoses. The effects of anhedonia may be more robust in a patient sample with more marked anhedonia given documented behavioral reward responses (e.g., Huys et al., 2013, 2015; Treadway et al., 2012). A mood induction procedure could also be employed in future research to strengthen the ability to find an association between mood and PIT effect strength. Further, although we restricted the sample to those who completed tri-level symptom questionnaires within 30 days of the PIT task and controlled for time elapsed in analyses, the lack of synchronous assessments may have limited our ability to detect an association. It is possible that symptoms could differ at the time of questionnaire completion compared to at the time of task completion.

Previous work found that significant associations with anxiety was dependent on the PIT type examined: specific versus general (Quail et al., 2017). The current paradigm is unable to distinguish between general and specific PIT effects, which may have further mitigated relationships with symptoms. However, the combination of specific and general PIT is thought to be more powerful approach (Talmi et al., 2008) and has yet to be explored in relation to depression and anxiety. Additionally, depression and anxiety symptoms may alter the balance between the approach and withdrawal behaviors displayed by individuals as opposed to the strength of the PIT effect (Huys et al., 2016). However, our PIT paradigm prevented exploration of action specificity.

Our results suggest that there is disrupted responding in a reward paradigm in young adults ranging in scores across dimensions of depression and anxiety symptoms. Further, there is no detectable differential effect when considering transdiagnostic symptoms of depression and anxiety on PIT in this sample. As such, this PIT paradigm may not be ideal to detect reward system differences in non-clinical samples given its nonspecific nature. It is also possible that the PIT paradigm is better suited to detect an effect in a larger sample, given that we did not have the power to detect a small effect. The effect of predictive cues on instrumental actions is an important phenomenon to understand as cues can promote or deter both adaptive and maladaptive actions. If individuals display reduced reflexive approach responses, they may in turn display reduced attention to and motivation for reward. Clinically, this could hinder positive coping strategies and further negative responses in individuals with depression and anxiety. Whereas there was no evidence for associations between behavioral metrics and symptom dimensions in the present study, how individual characteristics could affect performance in the PIT paradigm should continue to be a topic of research to target these clinically-relevant processes.

Author contributions The first draft of the manuscript was written by Allison Metts and all authors provided critical revisions. Data extraction and analysis was performed by Allison Metts and Inna Arnoudova. Material preparation and data collection were performed by Inna Arnoudova, Lindsay Staples-Bradley, and Michael Sun. Michelle Craske, Richard Zinbarg and Robin Nusslock developed the study concept and contributed to the study design. All authors read and approved the final manuscript.

Funding This work was supported by National Institute of Mental Health (NIMH R01 MH100117-01).

Data and code availability Data is available upon email request to the corresponding author. Additionally, data has been submitted to open science framework and is publicly available: https://doi.org/10.17605/OSF.IO/RZ9YQ.

Declarations

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Institutional Review Board at the University of California–Los Angeles (protocol #13–001606).

Consent to participate Informed consent was obtained from all individual participants included in the study.

Conflicts of interest The authors have no conflicts of interest to declare that are relevant to the content of this article.

Experiment Participants The present study was approved by the IRB at University of California, Los Angeles. This study was performed in line with the principles of the Declaration of Helsinki.

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Author.

Brown, T. A., Chorpita, B. F., & Barlow, D. H. (1998). Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *Journal of Abnormal Psychology, 107*(2), 179–192. https://doi.org/10.1037/0021-843x.107.2.179

Cartoni, E., Balleine, B., & Baldassarre, G. (2016). Appetitive Pavlovian-instrumental transfer: A review. *Neuroscience & Biobehavioral Reviews, 71*, 829–848. https://doi.org/10.1016/j.neubiorev.2016.09.020

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS scales. *Journal of Personality and Social Psychology, 67*(2), 319–333. https://doi.org/10.1037/0022-3514.67.2.319

Chung, Y. S., & Barch, D. (2015). Anhedonia is associated with reduced incentive cue related activation in the basal ganglia. *Cognitive, Affective & Behavioral Neuroscience, 15*(4), 749–767. https://doi.org/10.3758/s13415-015-0366-3

Clark, L. A., & Watson, D. (1991). Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications.

Journal of Abnormal Psychology, 100, 316–336. https://doi.org/10.1037/0021-843X.100.3.316

Corr, P. J. (2004). Reinforcement sensitivity theory and personality. *Neuroscience & Biobehavioral Reviews, 28*(3), 317–332. https://doi.org/10.1016/j.neubiorev.2004.01.005

Craddock, P., Molet, M., & Miller, R. R. (2012). Reaction time as a measure of human associative learning. *Behavioural Processes, 90*(2), 189–197. https://doi.org/10.1016/j.beproc.2012.01.006

Craske, M. G., Meuret, A. E., Ritz, T., Treanor, M., & Dour, H. J. (2016). Treatment for anhedonia: A neuroscience driven approach. *Depression and Anxiety, 33*(10), 927–938. https://doi.org/10.1002/da.22490

Di Nardo, P. A., & Barlow, D. H. (1988). *Anxiety disorders interview schedule--revised (ADIS-R)*. Phobia and Anxiety Disorders Clinic, Center for Stress and Anxiety Disorders, State University of New York at Albany.

Dickinson, A., Smith, J., & Mirenowicz, J. (2000). Dissociation of Pavlovian and instrumental incentive learning under dopamine antagonists. *Behavioral Neuroscience, 114*(3), 468–483. https://doi.org/10.1037/0735-7044.114.3.468

Epstein, J., Pan, H., Kocsis, J. H., Yang, Y., Butler, T., Chusid, J., Hochberg, H., Murrough, J., Strohmayer, E., Stern, E., & Silbersweig, D. A. (2006). Lack of ventral striatal response to positive stimuli in depressed versus normal subjects. *The American Journal of Psychiatry, 163*(10), 1784–1790. https://doi.org/10.1176/ajp.2006.163.10.1784

Eshel, N., & Roiser, J. P. (2010). Reward and punishment processing in depression. *Biological Psychiatry, 68*, 118–124. https://doi.org/10.1016/j.biopsych.2010.01.027

Eysenck, H. J., & Eysenck, S. B. G. (1975). *Manual of the Eysenck Personality Questionnaire (junior and adult)*. London, England: Hodder and Stoughton.

First, M. B., Williams, J. B., Karg, R. S., & Spitzer, R. L. (2016). *SCID-5-CV: Structured clinical interview for DSM-5 disorders: Clinician version*. American Psychiatric Association Publishing Washington.

Foa, E. B., Huppert, J. D., Leiberg, S., Langner, R., Kichic, R., Hajcak, G., & Salkovskis, P. M. (2002). The Obsessive-Compulsive Inventory: Development and validation of a short version. *Psychological Assessment, 14*(4), 485–496. https://doi.org/10.1037/1040-3590.14.4.485

Geer, J. H. (1965). The development of a scale to measure fear. *Behaviour Research and Therapy, 3*(1), 45–53. https://doi.org/10.1016/0005-7967(65)90040-9

Greenberg, T., Chase, H. W., Almeida, J. R., Stiffler, R., Zevallos, C. R., Aslam, H. A., Deckersbach, T., Weyandt, S., Cooper, C., Toups, M., Carmody, T., Kurian, B., Peltier, S., Adams, P., McInnis, M. G., Oquendo, M. A., McGrath, P. J., Fava, M., Weissman, M., ... & Phillips, M. L. (2015). Moderation of the Relationship Between Reward Expectancy and Prediction Error-Related Ventral Striatal Reactivity by Anhedonia in Unmedicated Major Depressive Disorder: Findings From the EMBARC Study. *The American Journal of Psychiatry, 172*(9), 881–891. https://doi.org/10.1176/appi.ajp.2015.14050594

Holmes, N. M., Marchand, A. R., & Coutureau, E. (2010). Pavlovian to instrumental transfer: A neurobehavioural perspective. *Neuroscience & Biobehavioral Reviews, 34*(8), 1277–1295. https://doi.org/10.1016/j.neubiorev.2010.03.007

Huys, Q. J., Daw, N. D., & Dayan, P. (2015). Depression: A decision-theoretic analysis. *Annual Review of Neuroscience, 38*(1), 1–23. https://doi.org/10.1146/annurev-neuro-071714-033928

Huys, Q. J., Gölzer, M., Friedel, E., Heinz, A., Cools, R., Dayan, P., & Dolan, R. J. (2016). The specificity of Pavlovian regulation is associated with recovery from depression. *Psychological Medicine, 46*(5), 1027–1035. https://doi.org/10.1017/s0033291715002597

Huys, Q. J., Pizzagalli, D. A., Bogdan, R., & Dayan, P. (2013). Mapping anhedonia onto reinforcement learning: A behavioural meta-analysis. *Biology of Mood & Anxiety Disorders, 3*(1), 1–16. https://doi.org/10.1186/2045-5380-3-12

Kashdan, T. B. (2007). Social anxiety spectrum and diminished positive experiences: Theoretical synthesis and meta-analysis. *Clinical Psychology Review, 27*(3), 348–365. https://doi.org/10.1016/j.cpr.2006.12.003

Kashdan, T. B., Weeks, J. W., & Savostyanova, A. A. (2011). Whether, how, and when social anxiety shapes positive experiences and events: A self-regulatory framework and treatment implications. *Clinical Psychology Review, 31*(5), 786–799. https://doi.org/10.1016/j.cpr.2011.03.012

Khazanov, G. K., & Ruscio, A. M. (2016). Is low positive emotionality a specific risk factor for depression? A meta-analysis of longitudinal studies. *Psychological Bulletin, 142*(9), 991–1015. https://doi.org/10.1037/bul0000059

Kotov, R., Gamez, W., Schmidt, F., & Watson, D. (2010). Linking "big" personality traits to anxiety, depressive, and substance use disorders: A meta-analysis. *Psychological Bulletin*, *136*(5), 768–821. https://doi.org/10.1037/a0020327

Kramer, A. M., Kelley, N. J., Chat, I. K., Young, K. S., Nusslock, R., Craske, M. G., & Zinbarg, R. E. (2019). Replication of a tri-level model of anxiety and depression in a sample of young adults. *PsyArXiv*. https://doi.org/10.31234/osf.io/8mpd2

Krypotos, A. M., & Engelhard, I. M. (2020). Pavlovian-to-instrumental transfer in subclinical obsessive–compulsive disorder. *Journal of Experimental Psychopathology, 11*(3), 1–11. https://doi.org/10.1177/2043808720925244

Madley-Dowd, P., Hughes, R., Tilling, K., & Heron, J. (2019). The proportion of missing data should not be used to guide decisions on multiple imputation. *Journal of Clinical Epidemiology, 110*, 63–73. https://doi.org/10.1016/j.jclinepi.2019.02.016

Manglani, H. R., Lewis, A. H., Wilson, S. J., & Delgado, M. R. (2017). Pavlovian-to-instrumental transfer of nicotine and food cues in deprived cigarette smokers. *Nicotine & Tobacco Research, 19*(6), 670–676. https://doi.org/10.1093/ntr/ntx007

Mattick, R. P., & Clarke, J. C. (1998). Development and validation of measures of social phobia scrutiny fear and social interaction anxiety. *Behaviour Research and Therapy, 36*, 455–470. https://doi.org/10.1016/s0005-7967(97)10031-6

Meyer, T. J., Miller, M. L., Metzger, R. L., & Borkovec, T. D. (1990). Development and validation of the Penn State Worry Questionnaire. *Behaviour Research and Therapy, 28*(6), 487–495. https://doi.org/10.1016/0005-7967(90)90135-6

Naragon-Gainey, K., Prenoveau, J. M., Brown, T. A., & Zinbarg, R. E. (2016). A comparison and integration of structural models of depression and anxiety in a clinical sample: Support for and validation of the tri-level model. *Journal of Abnormal Psychology, 125*(7), 853–867. https://doi.org/10.1037/abn0000197

Nord, C. L., Lawson, R. P., Huys, Q. J., Pilling, S., & Roiser, J. P. (2018). Depression is associated with enhanced aversive Pavlovian control over instrumental behaviour. *Scientific Reports, 8*(1), 1–10. https://doi.org/10.1038/s41598-018-30828-5

Perez, O. D. (2021). Instrumental behavior in humans is sensitive to the correlation between response rate and reward rate. *Psychonomic Bulletin & Review, 28*(2), 649–656. https://doi.org/10.31234/osf.io/g8fxe

Perez, O. D., & Dickinson, A. (2020). A theory of actions and habits: The interaction of rate correlation and contiguity systems in free-operant behavior. *Psychological Review, 127*(6), 945. https://doi.org/10.1101/807800

Prenoveau, J. M., Zinbarg, R. E., Craske, M. G., Mineka, S., Griffith, J. W., & Epstein, A. M. (2010). Testing a hierarchical model of anxiety and depression in adolescents: A tri-level model. *Journal*

of Anxiety Disorders, 24(3), 334–344. https://doi.org/10.1016/j.janxdis.2010.01.006

Quail, S. L., Morris, R. W., & Balleine, B. W. (2017). Stress associated changes in Pavlovian-instrumental transfer in humans. *The Quarterly Journal of Experimental Psychology, 70*(4), 675–685. https://doi.org/10.1080/17470218.2016.1149198

Rapee, R. M., Craske, M. G., & Barlow, D. H. (1994). Assessment instrument for panic disorder that includes fear of sensation-producing activities: The Albany Panic and Phobia Questionnaire. *Anxiety, 1*, 114–122. https://doi.org/10.1002/anxi.3070010303

Rescorla, R.A., and Wagner, A.R. (1972). In Classical Conditioning II: Current Theory and Research, A.H. Black and W.F. Prokasy, eds. (New York: Appleton Century Crofts), pp. 65–99.

Russell, J. A. (1980). A circumplex model of affect. *Journal of Personality and Social Psychology, 39*(6), 1161–1178. https://doi.org/10.1037/h0077714

Schwabe, L., & Wolf, O. T. (2009). Stress prompts habit behavior in humans. *Journal of Neuroscience, 29*(22), 7191–7198. https://doi.org/10.1523/jneurosci.0979-09.2009

Snaith, R. P. (1993). Identifying depression: the significance of anhedonia. *Hospital Practice, 28,* 55–60. https://doi.org/10.1080/21548331.1993.11442922

Srivastava, S., Sharma, H. O., & Mandal, M. K. (2003). Mood induction with facial expressions of emotion in patients with generalized anxiety disorder. *Depression and Anxiety, 18*, 144–148. https://doi.org/10.1002/da.10128

Steele, J. D., Kumar, P., & Ebmeier, K. P. (2007). Blunted response to feedback information in depressive illness. *Brain, 130*(9), 2367–2374. https://doi.org/10.1093/brain/awm150

Stoy, M., Schlagenhauf, F., Sterzer, P., Bermpohl, F., Hägele, C., Suchotzki, K., Schmack, K., Wrase, J., Ricken, R., Knutson, B., Adli, M., Bauer, M., Heinz, A., & Ströhle, A. (2011). Hyporeactivity of ventral striatum towards incentive stimuli in unmedicated depressed patients normalizes after treatment with escitalopram. *Journal of Psychopharmacology., 26*(5), 677–688. https://doi.org/10.1016/s1053-8119(09)71680-5

Talmi, D., Seymour, B., Dayan, P., & Dolan, R. J. (2008). Human Pavlovian–instrumental transfer. *Journal of Neuroscience, 28*(2), 360–368. https://doi.org/10.1523/jneurosci.4028-07.2008

Treadway, M. T., Bossaller, N. A., Shelton, R. C., & Zald, D. H. (2012). Effort-based decision-making in major depressive disorder: A translational model of motivational anhedonia. *Journal of Abnormal Psychology., 121*, 553–558. https://doi.org/10.1037/a0028813

Treadway, M. T., Buckholtz, J. W., Schwartzman, A. N., Lambert, W. E., & Zald, D. H. (2009). Worth the 'EEfRT'? The effort expenditure for rewards task as an objective measure of motivation and anhedonia. *PLoS ONE, 4*(8), e6598. https://doi.org/10.1371/journal.pone.0006598

Ubl, B., Kuehner, C., Kirsch, P., Ruttorf, M., Diener, C., & Flor, H. (2015). Altered neural reward and loss processing and prediction error signaling in depression. *Social Cognitive and Affective Neuroscience, 10*(8), 1102–1112. https://doi.org/10.1093/scan/nsu158

Vogel, V., Dittrich, M., Horndasch, S., Kratz, O., Moll, G. H., Erim, Y., ... & Steins-Loeber, S. (2020). Pavlovian-to-instrumental transfer in Anorexia Nervosa: A pilot study on conditioned learning and instrumental responding to low-and high-calorie food stimuli. *European Journal of Neuroscience, 51*(8), 1794–1805. https://doi.org/10.1111/ejn.14592

Watson, D., Weber, K., Assenheimer, J. S., Clark, L. A., Strauss, M. E., & McCormick, R. A. (1995). Testing a tripartite model: I. Evaluating the convergent and discriminant validity of anxiety and depression symptom scales. *Journal of Abnormal Psychology*, *104*(1), 3–14. https://doi.org/10.1037/0021-843x.104.1.3

Yang, X. H., Huang, J., Zhu, C. Y., Wang, Y. F., Cheung, E. F., Chan, R. C., & Xie, G. R. (2014). Motivational deficits in effort-based decision making in individuals with subsyndromal depression, first-episode and remitted depression patients. *Psychiatry Research, 220*(3), 874–882. https://doi.org/10.1016/j.psychres.2014.08.056

Young, K. S., Hasratian, A. M., Parsons, C. E., Zinbarg, R. E., Nusslock, R., Bookheimer, S. Y., & Craske, M. G. (2020). Positive social feedback alters emotional ratings and reward valuation of neutral faces. *Quarterly Journal of Experimental Psychology, 73*(7), 1066–1081. https://doi.org/10.1177/1747021819890289

Zimmerman, M., Coryell, W., Corenthal, C., & Wilson, S. (1986). A self-report scale to diagnose major depressive disorder. *Archives of General Psychiatry, 43*, 1076–1081. https://doi.org/10.1001/archpsyc.1986.01800110062008

Zinbarg, R. E., & Barlow, D. H. (1996). Structure of anxiety and the anxiety disorders: A hierarchical model. *Journal of Abnormal Psychology, 105*, 181–193. https://doi.org/10.1037/0021-843x.105.2.181