The Impact of Threat on Behavioral and Neural Markers of Learning in Anxiety

Andrew D. Valdespino

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John A. Richey, Chair
Richard N. Aslin
Sheryl B. Ball
Pearl Chiu
Brooks King-Casas

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ABSTRACT

Anxiety is characterized by apprehensive expectation regarding the forecasted outcomes of choice. Decision science and in particular reinforcement learning models provide a quantitative framework to explain how the likelihood and value of such outcomes are estimated, thus allowing the measurement of parameters of decision-making that may differ between high- and low- anxiety groups. However, the role of anxiety in choice allocation is not sufficiently understood, particularly regarding the influence of transient threat on current decisions. The presence of threat appears to alter choice behavior and may differentially influence quantitatively derived parameters of learning among anxious individuals. Regarding the neurobiology of reinforcement learning, the dorsolateral prefrontal cortex (dlPFC) has been suggested to play a role in temporally integrating experienced outcomes, as well as in coordinating an overall choice action plan, both of which can be described computationally by learning rate and exploration, respectively. Accordingly, it was hypothesized that high trait anxiety would be associated with a lower reward learning rate, a higher loss learning rate, and diminished exploration of available options, and furthermore that threat would increase the magnitude of these parameters in the high anxiety group. We also hypothesized that the magnitude of neural activation (measured by functional near-infrared spectroscopy; FNIRS) across dissociable regions of the left and right dlPFC would be associated with model parameters, and that threat would further increase the magnitude of activation to model parameters. Finally, it was hypothesized that reward and loss

outcomes could be differentiated based on FNIRS channel activation, and that a distinct set of channels would differentiate outcomes in high relative to low anxiety groups. To test these hypotheses, a temporal difference learning model was applied to a decision-making (bandit) task to establish differences in learning parameter magnitudes among individuals high (N=26) and low (N=20) in trait anxiety, as well as the impact of threat on learning parameters. Results indicated a positive association between anxiety and both the reward and loss learning rate parameters. However, threat was not found to impact model parameters. Imaging results indicated a positive association between exploration and the left dlPFC. Reward and loss outcomes were successfully differentiated in the high, but not low anxiety group. Results add to a growing literature suggesting anxiety is characterized by differential sensitivity to both losses and rewards in reinforcement learning contexts, and further suggests that the dlPFC plays a role in modulating exploration-based choice strategies.

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GENERAL AUDIENCE ABSTRACT

Anxiety is characterized by worry about possible future negative outcomes. Mathematical models in the area of learning theory allow the representation and measurement of individual differences in decision-making tendencies that contribute to negative future apprehension. Currently, the role of anxiety in the allocation of choices, and particularly the influence of threat on decision-making is poorly understood. Threat may influence learning and alter choice-behavior, collectively causing negative future apprehension. With regards to how related decision-making is computed in the brain, the dorsolateral prefrontal cortex (dlPFC) has been suggested to play a role tracking and integrating current and past experienced outcomes, in order to coordinate an overall action plan. Outcome tracking and action plan coordination can be represented mathematically within a learning theory framework by learning rate and exploration parameters, respectively. It was hypothesized that high anxiety would be associated with a lower reward learning rate, a higher loss learning rate, and diminished exploration, and furthermore that threat would increase the magnitude of these tendencies in anxious individuals. We also hypothesized that brain activation in the dlPFC would be associated with these tendencies, and that threat would further increase activation in these brain areas. It was also hypothesized that reward and loss outcomes could be differentiated based on brain activation in the dlPFC. To test these hypotheses, a mathematical model was applied to establish differences in learning within high and low anxiety individuals, as well as to test the impact of threat on these learning

tendencies. Results indicated a positive association between anxiety and the rate of learning to reward and loss outcomes. Threat was not found to impact these learning rates. A positive association was found between activation in the dlPFC and the tendency to explore. Reward and loss outcomes were successfully differentiated based on brain activation in high, but not low anxiety individuals. Results add to a growing literature suggesting that anxiety is characterized by differential sensitivity to both losses and rewards, and further adds to our understanding of how the brain computes exploration-based choice strategies.

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Chapter 1 – Introduction

It has been appreciated for some time that reinforcement learning dispositions are relevant to the development and maintenance of anxiety and its disorders (Britton, Lissek, Grillon, Norcross, & Pine, 2011). Regarding the genesis of anxiety, exaggerated unconditioned responses, heightened orienting responses, and reduced response inhibition to safety cues during conditioning tasks have been previously established as risk factors for subsequent disorder development (Craske et al., 2008; Waters, Henry, & Neumann, 2009). Along similar lines, the maintenance of anxiety appears to be linked to avoidance of conditioned aversive stimuli (Grillon, Baas, Lissek, Smith, & Milstein, 2004). Avoidance, in turn, is linked to impaired extinction learning (Cornwell, Overstreet, Krimsky, & Grillon, 2013) thus highlighting the role of reinforcement learning principles in this condition. To date, research at the intersection of anxiety and reinforcement learning has focused primarily on behavioral response profiles associated with anxiety in reinforcement learning contexts and less on the neurobiological systems that subserve these processes. For example, impaired discrimination between safety and threat cues (Lissek et al., 2009), decreased choice accuracy (Verma & Nijhawan, 1976), and slower rates of extinction learning (Craske et al., 2008), have all been observed in various anxiety disorders. On the other hand, comparatively little research has focused on the systematic differences in neurobiological mechanisms underlying reinforcement learning in anxiety conditions. In light of the role of learning mechanisms in anxiety development and maintenance, research into such mechanisms will be critical for the development of new clinical interventions (Britton et al., 2011; Mineka & Oehlberg, 2008).

A related gap in knowledge regards the extent to which the presence of external threat modulates cognitive mechanisms of reinforcement learning in anxious individuals. Theoretical

accounts of anxiety etiology strongly suggest that heightened attention to threat disrupts learning by interfering with mechanisms of reinforcement. In particular, during transient periods of threat-induced stress, attention is diverted away from reward and towards loss, which exacerbates behavioral avoidance (Craske et al., 2009; Krypotos, Effting, Kindt, Beckers, & Bergstrom, 2015). Consistent with this idea, a significant empirical base suggests that anxiety is associated with biases to threat across multiple levels including visual attention, orienting, and learning (Britton et al., 2011; Koster, Crombez, Verschuere, Van Damme, & Wiersema, 2006; Mathews & MacLeod, 1985). Threat has also been found to increase avoidance in anxious individuals during a reinforcement learning task (Mkrtchian, Aylward, Dayan, Roiser, & Robinson, 2017). A specific gap in knowledge is the specific decision-making elements (e.g., reward and loss learning rates, or level of exploration) that are modified by threat in anxious individuals.

N, 2 To accomplish this, temporal difference model parameters were correlated with neural activation (FNIRS), and multi-channel pattern analysis (MCPA) was conducted on reward and loss outcomes, to identify the most informative set of channels that could differentiate between reward and loss outcomes.

1.1 - Trait Anxiety

Differences in patterns of reinforcement learning, including impaired outcome discrimination, as well as hyper- and hypo-responsiveness to threat and reward respectively, has been observed across anxiety disorders (Duits et al., 2015; LaFreniere & Newman, 2018; Lissek et al., 2009). This suggests that, in studying the clinical relevance of reinforcement learning, there is utility in choosing a psychological construct that spans multiple psychiatric disorders, and that has established relevance to reinforcement learning. Trait anxiety is observed across various psychiatric diagnoses, mood disorders, and obsessive-compulsive and related disorders,

and is also associated with biases in reinforcement learning (Corr, Pickering, & Gray, 1995; Kennedy, Schwab, Morris, & Beldia, 2001). Trait anxiety is a stable individual-difference variable denoting a general disposition to respond to a variety of stimuli with worry, fear, and nervousness (Spielberger, 1985). Given the dispositional and generally long-term nature of trait anxiety, this construct is conceptually and temporally distinct from state anxiety, which instead refers to brief and phasic fluctuations in experienced anxiety at a given point in time (Endler & Kocovski, 2001). However, trait and state anxiety are nevertheless interrelated, to the extent that individuals high in trait anxiety tend to report more intense levels of state anxiety in response to stressful events (Spielberger, Gorsuch, & Lushene, 1970). Overall, trait anxiety was the target psychological symptom in the current study, given its transdiagnostic presentation, combined with its empirically established role in moderating reinforcement learning tendencies.

1.2 - Anxiety, Reinforcement Learning, and Threat

While a large number of studies suggest that anxiety is associated increased sensitivity to punishment across multiple domains, including orienting to future punishment (Mueller, Nguyen, Ray, & Borkovec, 2010), avoidance of punishment (Mkrtchian et al., 2017), enhanced punishment sensitivity (Torrubia, Ávila, Moltó, & Caseras, 2001), recent empirical work also suggests that high anxiety individuals may also be differentially sensitive rewards in reinforcement learning contexts. Specifically, during a reward and punishment learning task, individuals high in anxiety made significantly more errors during both punishment and reward learning conditions (DeVido et al., 2009). Consistent with this finding, LaFreniere and Newman (2018) assessed learning accuracy across positive and negative reinforcement conditions in individuals with generalized anxiety disorder (GAD). It was found that GAD was associated with decreased learning accuracy during conditions of positive reinforcement, not during conditions

of negative reinforcement. Behavioral findings are also consistent with neuroimaging work, which suggests that anxiety is associated with disrupted processing of reward, both during the anticipation and experience of rewards (Forbes et al., 2006), as well as reduced differentiation of reward and loss outcomes at neural level (Kessel, Kujawa, Hajcak Proudfit, & Klein, 2015).

While a number of studies suggest anxiety is associated with a sensitivity to threat, heightened attention to threat, as well as impaired attentional disengagement from threat (Koster et al., 2006; MacLeod, 1986) there has been a dearth of empirical work that has sought to determine how threat impacts reinforcement learning in anxious individuals within a quantitative modelling framework. Mkrtchian and colleagues (2017) leveraged a quantitative learning model to assess for avoidance biases in anxiety under the presence of threat (i.e., electric shock). The findings indicate that anxious individuals were characterized by a pre-potent tendency to avoid, and further that the threat of electric shock exacerbated avoidance tendencies. In addition to providing insight into parameters of learning that are modulated by threat in anxious individuals, the study highlights the utility and plausibility of leveraging computational learning methodologies to probe for highly specific learning biases that characterize anxiety, in addition to the effect of threat on in exacerbating biases.

1.3 Temporal Difference Models of Learning

From the perspective of construct validity, temporal difference models of learning describe conceptual processes that materially link to clinical features of anxiety. Specifically, anxiety is conceptualized as a pathology of biased prediction, in that anxiety is associated with apprehensive expectation about future negative outcomes as well as negative biases regarding the probability of negative future events (Miranda & Mennin, 2007). A second feature is that anxiety is associated with reduced tolerance of uncertainty (Grupe & Nitschke, 2013). Regarding the

clinical feature of pessimistic predictions about the future, temporal difference models aim to explain how an organism predicts the magnitude and valence of future events. More specifically, a central claim motivating the model, is that the mere co-occurrence of a prospective (CS) and unconditioned stimulus (US) is insufficient for conditioning to occur (Rescorla, 1972). Rather, conditioning requires that an organism estimate the value of a CS by predicting the magnitude and valence, of a potential subsequent US. Subsequently, when the CS occurs, its value-assignment is updated depending on the deviation between the actual and expected outcome (US). With regards to uncertainty, temporal difference learning models occur within a probabilistic learning framework, such that choices are made within an inherently uncertain environment, where the probabilities associated choice-contingent outcomes are unknown.

Multi-arm bandit task paradigms are a widely used model to fit participants' choice-behavior to temporal difference learning models, in order to establish the set of learning parameters (i.e., learning rates and tendencies to explore) and dissociable neural correlates that are modulated by both anxiety and threat (Daw, O'Doherty, Dayan, Seymour, & Dolan, 2006). These tasks have been used in clinical (Dombrovski et al., 2010) and non-clinical contexts (Burke, Tobler, Baddeley, & Schultz, 2010; Daw, Gershman, Seymour, Dayan, & Dolan, 2011). Fitting temporal difference models to participants' choice behavioral allows for the establishment reward and loss learning rate parameters, as well as a parameter of exploration, which are central to the aims of the current study. A learning rate denotes the weight an agent applies to an unexpected outcome that was tied to a specific action, for purposes of updating the future expected-value of that action. An inverse-temperature parameter can be estimated as a computational operationalization of exploration. Specifically, this parameter represents the extent to which an agent engages in the choice-strategy of sticking with a stable rewarding set of

choices, or rather behaves more stochastically for purposes of exploring the environment (Lee & Seo, 2007).

1.4 - Dorsolateral Prefrontal Cortex and Reinforcement Learning

The dorsolateral prefrontal cortex (dlPFC) has been implicated in a variety of reinforcement learning functions in human and non-human primates, and has also been associated with pathological decision-making in the context of anxiety (Bishop, Duncan, Brett, & Lawrence, 2004; Lee & Seo, 2007). Barraclough, and colleagues (2004) recorded activity in the dlPFC of rhesus monkeys that played a modified matching pennies game. Leveraging a reinforcement learning algorithm, the dlPFC tracked the value of past decisions and payoffs, which in turn affected behavior in the game. The authors conclude that the dlPFC may guide decisions by taking reinforcement history into account. The dlPFC has also been found to compute an action value during learning, in that dlPFC activation tracked the probability that a self-initiated action would yield reward (Morris, Dezfouli, Griffiths, & Balleine, 2014). These findings are consistent with finds of Lee and Seo (2007), who found that the dlPFC may integrate information garnered from current and past choices to update the value of choices, for purposes of developing a future action plan (Lee & Seo, 2007). To date, while the temporal integration of experienced outcomes is functionally consistent with both learning rate and exploration computational parameters, the role of the dlPFC in these functions is not yet established. Specifically.

1.5 - Aims and Hypotheses

Overall, while it has been appreciated for some time that reinforcement-learning tendencies are relevant to the etiology of anxiety, little is known about the focal aspects of reinforcement learning that are associated with the manifestation of anxiety. Furthermore, while

it is understood that anxiety contributes to exaggerated threat appraisals, the impact of threat on reinforcement learning parameters is understudied in this population. Finally, non-clinical research suggests that the dlPFC plays a role in value-based decision-making. This suggests that this region may be a mechanism through which reinforcement learning is impacted in anxious individuals. To date, the degree to which the dlPFC contributes to probabilistic learning styles in anxious individuals, is also unknown.

Accordingly, the current study seeks to leverage a temporal difference reinforcement learning model in the context of a stress inducing, threat induction task, to assess the impact of both trait anxiety and threat on behavioral and neural decision-making parameters. In light of prior work illustrating increased sensitivity to loss and punishment, hyposensitivity to reward, and reduced diminished exploration, I specifically hypothesized (1) a positive association between trait anxiety and the loss learning rate parameter, as well as a negative association between trait anxiety and both the reward learning rate and exploration parameter. Given findings of impaired attentional disengagement from threat in anxiety, it was hypothesized (2) that for the threat versus safe condition, trait anxiety would be associated with a higher loss learning rate, lower reward learning rate, and decreased exploration. I further hypothesized (3) that the right dlPFC would be positively associated with the loss learning rate, and that the left dlPFC would be positively associated with both reward learning rate and exploration. Finally, I hypothesized (4) that in high relative to low anxiety participants, the loss learning rate would be positively associated with activity in within the right dlPFC, and that reward learning rate and exploration would be associated with decreased activation in the left dlPFC. Laterality-specific hypotheses stem from previous findings suggesting the left prefrontal cortex is involved in

positively-valenced functions (i.e., approach/reward), whereas the right prefrontal cortex has been associated with negatively-valenced functions (i.e., avoidance/loss; Spielberg et al., 2011).

As an exploratory analysis, a multi-channel pattern analysis (MCPA) was conducted on reward and loss outcomes, to identify the most informative set of channels that could differentiate between reward and loss outcomes. I hypothesized that a dissociable set of channels would distinguish reward from loss outcomes in high and low anxiety groups.

Chapter 2 – Method

2.1 - Participants

Participants comprised members of the surrounding community as well as students enrolled at Virginia Tech. Participants were recruited using online advertisements and flyers posted on public billboards. A total of 46 participants were recruited. Participants were right handed with normal or corrected-to-normal vision, between the ages of 18 and 55. The following exclusion criteria were applied: history of neurological injury, uncontrolled epilepsy (seizure within 6 months prior to consent), current or past auditory pathology, current or past cardiac illness, current use of psychotropic medications (past 3 months). Inclusion and exclusion criteria were assessed via a phone screen initiated prior to the in-person visit. All participants provided written informed consent as approved by the Virginia Tech Institutional Review Board (IRB).

2.2 - Measures

Demographic Questionnaire. The demographic questionnaire included items to obtain information on gender, age, ethnicity, employment status, and income.

Beck Depression Inventory – BDI-II. The Beck Depression Inventory (BDI-II) is a 21-item self-report measure assessing the frequency of a variety of depressive symptoms (Beck et al., 1996). Items are rated on a 4-point scale, from “not at all” to “always.” The measure demonstrates high internal consistency, Cronbach’s $\alpha = 0.92$ (Smarr & Keefer, 2011).

State-Trait Anxiety Inventory – STAI. The state-trait anxiety inventory (STAI) is a 40-item self-report assessing anxiety symptomatology (Speilberger et al., 1970). The measure is comprised of separate trait anxiety and state anxiety subscales, each with 20-items, measuring how anxious the subject feels generally (i.e., trait anxiety) and how anxious the subject feels in the moment (i.e., state anxiety). Items are rated on a 4-point scale ranging from “almost never” to

"almost always." Internal consistency has been measured to be in the good to excellent range, with trait anxiety Cronbach's α (trait) = 0.87, state anxiety Cronbach's α = 0.93 (Knight, Waal-Manning, & Spears, 1983).

2.3 - fNIRS Recording and Software

Imaging was conducted using a 42-channel NIRScout fNIRS system (NIRx Medical Technologies). A 23-channel array of optodes was be used (9 sources, and 13 detectors), over the dlPFC (Figure 2). The dlPFC was localized with the 10-20 International System following previously established recommendations (Fitzgerald, Maller, Hoy, Thomson, & Daskalakis, 2009). Specifically, the FNIRS channel between F3 and AF3, and between F4 and AF4, correspond to the left and right dlPFC respectively (Figure 2). Two reference channels were placed in the bilateral occipital lobes. The source wave lengths 760 nm and 850 nm were used. Signal calibration and data recording was conducted using the NIRStar 13 software (NIRx Medical Technologies). NIRS data was preprocessed and analyzed using HOMER 2 (v2.2; http://homer-fnirs.org/). NIRS analyses were conducted using NIRS toolbox (https://bitbucket.org/huppertt/nirs-toolbox/wiki/Home).

2.4 - Procedures

Upon arrival to the laboratory, and after completing written informed consent, participants completed self-report measures. Specifically, state and trait anxiety were established using the State-Trait Anxiety Inventory (Speilberger et al., 1970). Participants also completed the Beck Depression Inventory (BDI – II; Beck et al., 1996) to control for depressive symptomatology. The rationale for including a control for depression is that depression co-occurs with anxiety (Fava et al., 2000), and depressive symptomatology systematically relates to the current learning parameters of interest (Dombrovski et al., 2010).

Aversive Noise. The aversive noise heard by participants during the threat run was the sound of a fork scraping against slate (Neumann & Waters, 2006). The noise used was provided by Neumann and colleagues (2008), and was identical to the recorded sound that was previously empirically validated as an aversive unconditioned stimulus, with adequate unpleasantness and arousal ratings in comparison to shock and loud noise (Neumann, Waters, & Westbury, 2008).

The peak intensity of the aversive noise was set at 85 dBA. This peak intensity was chosen to ensure a comparable peak intensity to the validation by Neumann and colleagues (2008). Sound intensity measurements were conducted using a KEMAR acoustic sound measurement manakin with artificial ears and ear canals (www.kemar.us). Following recommendations by the National Institute for Occupational Safety and Health, the peak intensity of the sound was computed using an A-weighted slow time constant across frequency bands (NIOSH, 1998). Participants rated their subjective response to the aversive noise from 0 (very unpleasant) to 8 (very pleasant).

Participants were told (during the noise run) that they would randomly hear the noise during the anticipation phase, on 10% of trials. In reality, participants each heard the noise exactly five times during the threat run, to control for habituation. The rationale for including the noise during the anticipatory phase of the task was as follows. Including the noise during the outcome phase of the task would make modeling the value of a choice problematic, due to methodological difficulties in non-arbitrarily assigning an explicit quantitative value to the magnitude of discomfort incurred by the noise. By including the noise during the anticipation phase of the task, the methodological function of the manipulation remains (i.e., to induce an aversive internal physiological state), while still allowing for the establishment of the model

parameters. The distribution of the noise onset (i.e., the specific trials the noise occurred on) was randomized across participants.

Four-arm bandit task. Participants completed a four-arm bandit task while undergoing fNIRS (Figure 1). Participants read written instructions explaining the nature of the task. After reading the instructions, they completed a 5-item multiple-choice quiz, to ensure that all instructions are fully understood. If a question was not answered correctly, study staff explained why the answer is incorrect, and the participant then asked to repeat that item on the quiz until a correct answer was given.

Participants completed 2 runs, with 60 trials in each run. One run was a 'safe' run, while the other was a 'threat' run. Each of these runs proceed identically, with the exception that for the noise run, the participant completed the trials under risk of hearing the aversive noise. For the safe run, participants competed the trials without the risk of aversive noise. For the noise run, participants are told that the risk of aversive noise was fixed at 10%.

On a single trial the participant chose between four gambles. The four gamble options were high win (60% chance win $5), low win (40% chance win $5), high loss (60% lose $5), or low loss (40% lose $5). The gambles were represented as four shapes. The probabilities and outcomes associated with each shape were unknown to participants. After the participant chose a gamble option, the choice was highlighted. Subsequently a blank screen was shown. During the blank screen there was either the possibility (noise trials) or no possibility (safe trials) of aversive noise. Subsequently, the outcome was revealed, and the trial was over. Participants started with a $20 endowment at the beginning of the task. One outcome during each run was randomly chosen and added or subtracted to the endowment. Participants were compensated based on the resulting modified endowment amount.

Each trial in a given run consisted of the following: (1) A fixation cross was centered on the screen (1000ms). (2) Text was displayed on the screen, reading "You are at risk of aversive noise" for noise trials, and "You are safe from aversive noise" for safe trials (4000ms). (3) The four gamble options were then shown, and participants had an open-ended amount of time to make a choice (decision phase). (4) The participant's choice was the highlighted (1000ms). (5) A blank screen was then shown, during which there was the possibility of noise, or no possibility of noise, depending on the condition (3000ms). (6) The monetary outcome (i.e., either +$5, $0, or -$5) was then displayed as text centered on the screen (4000ms).

The position of each shape on the screen, as well as the assigned association between a shape and outcome, was randomized across participants for each run. Participants saw a unique set of shapes for noise and safe runs, such that any single type of shape was only used for a single run. This functioned to prevent shape association learning effects from occurring across runs. The order or runs (i.e., safe and noise) were counterbalanced across participants. The total length of the four-arm bandit task, for noise and safe runs combined, was approximately 30 minutes. Participants rated their subjective response to the aversive noise pre-and post-task, to assess for habituation effects.

2.5 - Quantitative Model

A temporal difference reinforcement model of learning was used to establish the parameters of interest (i.e., learning rate for rewards, learning rate for punishments, and inverse temperature). Given that the study hypotheses pertain to the specific learning rate valence, learning rates for rewards and losses were both established.

Model explanation. A participant was assumed to assign an expected value to a possible action, denoted by EV_t. This value assignment was made by performing an action, and then

updating the expected value of that action based on the outcome. Specifically, once a participant experienced an outcome (V_t), the participant compared that outcome to the expected value of that choice. If the outcome was better (i.e., positive prediction error) or worse (i.e., negative prediction error) than expected, the participant experienced a prediction error (δ). Upon experiencing the prediction error, the participant learned from that error at a rate, denoted by the learning rate (α). This rate was established separately for rewards and losses (reward learning rate = α_{reward}; loss learning rate = α_{loss}). This yields the following temporal difference model:

$$EV_t = EV_{t-1} + \alpha * (\delta)$$

Prediction errors are computed as:

$$\delta = V_t - EV_t$$

In order to establish individual differences in the tendency to explore during learning, an inverse temperature parameter (ε) was calculated. This parameter indicates the probability of choosing a stimulus (P_t), modelled as a function of the reinforcement history of that choice, as well as the tendency to either fully take into account (i.e., not explore) or not take into account at all (i.e., explore) the reinforcement history of that choice. A higher inverse temperature value suggests an agent is less inclined to explore, and rather chooses to stick with a discovered high value option. Conversely, a low inverse temperature suggests a lower tendency to choose the higher valued option, but rather to explore the choices. Specifically, the probability of choosing a stimulus based on its expected value was:

$$P_t = sigmoid([\varepsilon] * EV_t)$$

To find the parameters that reflect individual choice patterns, the likelihood function $l(parameters|y)$ was maximized for each participant, where y was the participant's set of

choices. Solving this likelihood function yielded subject parameter estimations for reward and loss learning rates and inverse temperature.

$$l(parameters|y) = \prod_t choice_t|parameters)$$

2.6 - Hypotheses

Hypothesis 1: Trait anxiety would be positively associated with loss learning rate, negatively associated with reward learning rate, and negatively associated with exploration. A set of three multiple regressions were computed for each parameter (i.e., reward learning rate, loss learning rate, and inverse temperature) separately as dependent variables. This set of regressions was conducted for the threat and safe conditions combined (Combined Regressions), as well as for the threat (Threat Regressions) and safe (Safe Regressions) conditions separately (see Table 5 for regression coefficients and p-values for trait anxiety as an independent variable, for all regression sets). This yielded a total of 9 regressions (i.e., 3 separate regressions, with each parameter as a dependent variable, repeated for Combined, Threat, and Safe regression sets). For all regressions, the trait anxiety subscale of the STAI was entered as an independent variable. The BDI-II total score was added as an independent variable to control for co-occurring depressive symptoms. Due to the positive association between trait and state anxiety (Endler & Kocovski, 2001), and given the goal of isolating the effect of trait anxiety on model parameters, the state anxiety subscale of the STAI was also entered. Given the unequal gender distribution across high and low anxiety groups, gender was also entered as a predictor. Given that the high anxiety group rated the aversive noise as more aversive relative to low anxiety participants, the mean noise rating (across pre- and post-task measurements) was also entered as a predictor. Age was also entered as a covariate. Finally, for each regression, the two remaining model parameters were also entered as predictors (i.e., for a regression where the loss learning rate was a dependent

variable, the reward learning rate and exploration parameter were entered as covariates). This was done to control for potential associations between model parameters.

A positive association was predicted between the STAI total score and the loss learning rate. A negative association was expected with regards to the reward learning rate and exploration parameter. These parameter predictions are consistent with an expectation that when anxious individuals experience unexpected rewards and losses, they will more heavily (loss) and less heavily (reward) incorporate those outcomes into future choices, relative to low anxiety individuals.

Hypothesis 2: Higher trait anxiety would be associated with a higher loss learning rate, lower reward learning rate, and decreased exploration, for threat versus safe runs. A two-way mixed analysis of variance was conducted for Group (low/high anxiety) × Noise (safe/noise), separately for all parameters (i.e., loss learning rate reward learning rate, and exploration). In all cases, a main effect of Group was expected, such that high anxiety would be associated with a higher loss learning rate, lower reward learning rate, and higher inverse temperature, relative to low anxiety participants. An interaction between Group and Noise was also expected, such that threat of noise would only affect high anxiety participants, by further increasing loss learning rate, decreasing reward learning rate, and increasing inverse temperature.

Hypothesis 3: The right dlPFC would be positively associated with the loss learning rate. The left dlPFC cortex would be positively associated with reward learning rate, and negatively associated with inverse temperature. Blood-oxygen-level-dependent (BOLD) data was analyzed with an autoregressive general linear model (GLM) framework to correct for motion and serially correlated errors (Barker, Aarabi, & Huppert, 2013). The decision phase was entered as first-level regressor and convolved with a γ hemodynamic response function (O_2Hb

time series was used). At the higher level, a statistical model was constructed to compute the main effect of phase (decision phase) as well as the interaction between phase and model parameters (reward learning rate, loss learning rate, and inverse temperature). Specifically, the interaction between phase and each of the three parameters, were entered as three separate model predictors. This was done in order to derive the dissociable effect of each parameter on neural activity. The leveraged statistical model is indicated below, in Wilkinson-Rogers notation.

$$beta \sim -1 + Decision.Phase + Decision.Phase * Reward.Learning.Rate + Decision.Phase * Loss.Learning.Rate + Decision.Phase * Inverse.Temperature + (1|Subject)$$

At the group-level mixed-effects model stage, contrasts were specified. A student's t-test was used to compare contrasts. Specifically, to establish channel-regions that tracked a model parameter, the following contrasts were applied at the group-level. Reward learning rate is used as an example:

1 [*Decision Phase* × *Reward Learning Rate*]
0 [*Decision Phase* × *Loss Learning Rate*]
0 [*Decision Phase* × *Inverse Temperature*]
0 [*Decision Phase*]

Hypothesis 4: Loss learning rate would be associated with increased activation in high relative to low anxiety participants, within the right dlPFC. Reward learning rate would be associated with decreased activation in the left dlPFC in high relative to low anxiety participants. Inverse temperature will be associated with increased activation in the left dlPFC in high relative to low anxiety participants. BOLD data was analyzed with an

autoregressive general linear model (GLM) framework to correct for motion and serially correlated errors (Barker et al., 2013). The decision phase was entered as first-level regressor and convolved with a γ hemodynamic response function (O_2Hb time series was used). At the higher level, a statistical model was constructed to compute the main effect of phase (decision phase) as well as the interaction between phase, group (high/low anxiety), and model parameters (reward learning rate, loss learning rate, and inverse temperature). Specifically, the interaction between phase, group, and each of the three parameters, were entered separately as three model predictors. This was done in order to derive the dissociable effect of each parameter on neural activity, while also being able to test for between group differences in neural activity that are associated with model parameters. The leveraged statistical model is indicated below, in Wilkinson-Rogers notation.

$$beta \sim -1 + Decision.Phase + Decision.Phase * Reward.Learning.Rate * Group + Decision.Phase * Loss.Learning.Rate * Group + Decision.Phase * Inverse.Temperature * Group + (1|Subject)$$

At the group-level mixed-effects model stage, contrasts were specified. A student's t-test was used to compare contrasts. Specifically, to establish channel-regions that tracked between-group differences in neural activity associated with a model parameter, the following contrasts were applied at the group level. Reward learning rate is used as an example:

1 [*Decision Phase* × *Reward Learning Rate* × *High Anxiety*]
- 1 [*Decision* Phase × *Reward Learning Rate* × *Low Anxiety*]
0 [*Decision Phase* × *Loss Learning Rate* × *High Anxiety*]
0 [*Decision Phase* × *Loss Learning Rate* × *Low Anxiety*]

0 [*Decision Phase* × *Inverse Temperature* × *High Anxiety*]
0 [*Decision Phase* × *Inverse Temperature* × *Low Anxiety*]
0 [*Decision Phase*]

Hypothesis 5: Reward and loss outcome conditions would be successfully differentiated based on a channel activation. A Multichannel Pattern Analysis (MCPA) was conducted on reward and loss outcomes to establish the set of three channels that most successfully differentiated between reward and loss outcome events (Emberson, Zinszer, Raizada, and Aslin, 2016). Oxygenated hemoglobin (HbO) was averaged across a 4000ms time window, starting at the outcome phase onset, separately for reward and loss outcomes. This averaging was first done for a single channel (*chan*), for a single outcome instance:

$$x_{chan=}\frac{1}{t}\sum_{i=1}^{t} HbO_{chan,i}$$

The average HbO response was computed identically, separately for each channel. Channel averages (x_{chan}) were combined into a single vector. All channel averages were ascertained:

$$\vec{x} = [x_1, x_2, \dots x_n]$$

The multichannel pattern was then averaged across all outcomes trials (*out*), for each channel, for a single participant. This averaging was completed separately from reward and loss trials. This yielded the participant-level multichannel pattern for reward and loss outcomes. This resulted in two vectors (one for reward, and one for loss):

$$\vec{x}_{Participant,outcome} = \frac{1}{out}\sum_{i=1}^{r} \vec{x}_{Participant,outcome,Trial,i}$$

The participant-level multichannel patterns were then averaged together. This yielded a group-level model for reward and loss outcomes. Group models were calculated separately for

high anxiety and low anxiety groups, for reward and loss. Separate group models were calculated for safe and threat runs .

Multichannel patterns were conducted comparing the Group and the left-out participant, using Spearman correlations (Equation 4). Successful coding occurs if the sum of the correlations for correct labels, is greater than the sum of correlations for incorrect labels:

$$corr\left(\vec{x}_{Group,Cond,reward,Trial}, \vec{x}_{Test,Unl1}\right) + corr\left(\vec{x}_{Group,Cond,loss,Trial}, \vec{x}_{Test,Unl2}\right)$$

$$corr\left(\vec{x}_{Group,Cond,reward,Trial}, \vec{x}_{Test,Unl2}\right) + corr\left(\vec{x}_{Group,Cond,loss,Trial}, \vec{x}_{Test,Unl1}\right)$$

Subsequently, the top 3 most informative channels were established for the low and high anxiety groups, separately for threat and safe conditions. Specifically, classifications were conducted within four group by epoch instances (i.e., high anxiety/safe, high anxiety/noise, low anxiety/safe, low anxiety/noise). The top 3 (most informative) channels were established across all instances. While including the top 3 most informative channels has yielded reliable decoding in prior research, restricting to the most informative channels does not necessarily yield superior decoding accuracy relative to including all channels (Emberson et al., 2016). Therefore, decoding accuracy was also computed leveraging all channels. Statistical significance thresholds were established based on running computer simulations, for all combinations of channels, to assess the expected decoding accuracy of channels that would occur by chance. From these simulations, a binomial distribution was constructed that allowed for the establishment of statistical testing thresholds. We hypothesized that partially dissociable channel locations would characterize the two groups within noise and safe conditions.

Chapter 3 – Results

3.1 - Descriptive Statistics

Low and high anxiety groups did not differ in age, $t(44) = 1.48$, $p = .147$ (low anxiety: *Mage* = 25.20, *SD* = 10.30; high anxiety: *Mage* = 21.96, *SD* = 3.88). The low anxiety group (*N*=20; 6 females) and high anxiety group (*N*=26; 17 females) differed on gender, $\chi^2(1) = 5.66$, $p < .05$). A group comparison of scores for self-report measures are presented in Table 2.

3.2 - Subjective Rating of Aversive Noise

Subjective noise ratings were measured before (pre-task) and after (post-task) the imaging task to assess for habituation and group interaction effects. A two-way mixed analysis of variance (ANOVA) was conducted for Group (low anxiety/high anxiety) × Noise Epoch (pre-task/post-task) on the self-reported subjective noise rating. There was a significant main effect of Group [$F(1,85) = 8.54$, p = .004] and Noise Epoch [$F(1,85) = 13.84$, $p = .013$]. The interaction between Group and Noise Epoch was not significant [$F(1,85) = 0.95$, $p = .333$]. Regarding the effect of group, post-hoc comparisons indicate that high anxiety participants rated the noise as more aversive than low anxiety participants [$t(43) = 2.91$, $p = .006$]. Regarding the main effect of epoch, participants rated the noise as more aversive post-task relative to pre-task [$t(89) = 2.26$, $p = .026$]. Overall, both low and high anxiety participants rated the noise as unpleasant in valence (low anxiety: $M_{rating} = 3.21$, *SD* = 1.75; high anxiety: $M_{rating} = 2.63$, SD = 1.55).

3.3 - Decision Phase Reaction Times

The time taken to make a choice during the decision phase of the multi-arm bandit task was compared across high and low anxiety groups. Specifically, a relatively higher or lower reaction time may be indicative of impulsive or perseverative responding respectively, which may affect model parameters (Edman, Schalling, & Levander, 1983; Fischer et al., 2005). A two-

way mixed analysis of variance (ANOVA) was conducted for Group (low anxiety/high anxiety) × Noise (safe/noise) on participants' choice reaction time during the decision phase of multi-arm bandit task. The main effect of Group [$F(1,86) = 1.138$, $p = .289$] nor the main effect of Noise [$F(1,86) = 0.01$, $p = .923$] were significant. The interaction between Group and Noise was also not significant [$F(1,86) = 0.00$, $p = .996$].

3.4 - Behavioral and Neuroimaging Hypotheses Data Inclusion Procedure

Behavioral hypotheses data inclusion (Hypothesis 1 and Hypothesis 2). To preserve the accurate representation of model parameters for purposes of behavioral analyses (i.e., regression and ANOVA estimations), all participants were included in the maximum likelihood estimations. Subsequently, for reward and loss learning rates, model parameters were removed from behavioral analyses if a corresponding event was not experienced by a participant. For example, if a participant did not experience a loss event, the establishment of a loss learning rate was not possible. Therefore, the loss learning rate estimate for such a participant was not included in behavioral analyses. Subsequently, all model parameters (i.e., reward learning rate, loss learning rate, and inverse temperature), were inspected for plausibility. Parameters that converged on an implausibly extreme estimate were discarded. Specifically, if a reward or loss learning rate estimation was equal to 1, or 0, that learning rate estimate was discarded. Inverse temperature estimates that exceeded an extreme value (i.e., a cutoff of >100 was applied) were discarded. The resulting number of observations for each parameter, presented for each group (i.e., low and high anxiety) and condition (i.e., safe and threat) are included in Table 3.

Regarding the reward learning rate regressions and ANOVAs, 11 observations were discarded from the safe condition (0 discarded due to not experiencing a reward event; 11 discarded due to an extreme parameter estimate). A total of 13 observations were discarded from

the threat condition (0 discarded due to not experiencing a reward event; 13 discarded due to an extreme parameter estimate).

Regarding the loss learning rate regressions and ANOVAs, 26 observations were discarded from the safe condition (2 discarded due to not experiencing a loss event; 24 discarded due to an extreme parameter estimate). A total of 24 observations were discarded (2 discarded due to not experiencing a loss event; 22 discarded due to an extreme parameter estimate).

Regarding the inverse temperature parameter regressions and ANOVAs, 7 observations were discarded from the safe condition due to an extreme parameter estimate. A total of 7 observations were discarded during the threat condition due to an extreme parameter estimate.

General linear model neuroimaging hypotheses data inclusion (Hypothesis 3 and Hypothesis 4). Following the behavioral data inclusion procedure, if it was possible to obtain a parameter for only one of the experimental conditions, that parameter was included as representative for that participant. If parameters for both experimental conditions cold be retained, parameter values were averaged for that participant. This data cleaning process yielded a sample of 25 participants that were passed to general linear model FNIRS imaging analyses. See Table 4 for the sample of participants, and associated parameter values, that were passed to all subsequent analyses.

Multi-channel pattern analysis hypotheses (MCPA) data inclusion (Hypothesis 5). To preserve an adequate number of reward and loss outcomes to perform the MCPA procedure, only participants who experienced at least 2 reward outcomes, and 2 loss outcomes, in both the safe and threat conditions, were included. This yielded a total MCPA sample of 32 participants (see Table 6).

3.5 - Results for Hypotheses

Hypothesis 1: Trait anxiety would be positively associated with loss learning rate, negatively associated with reward learning rate, and negatively associated with exploration. A set of multiple regressions were computed for each parameter separately as dependent variables. This set of regressions was conducted for the threat and safe conditions combined (Combined Regressions), as well as for the noise (Noise Regressions) and safe (Safe Regressions) conditions separately (see Table 4 for regression coefficients and p-values for trait anxiety as an independent variable, for all regression sets). Regarding Combined Regressions, trait anxiety was positively associated with the reward learning rate [R^2=.16, F(7,17)=1.633, p=.193; Trait Anxiety (β=.77, p=.042)]. Trait anxiety was not associated with loss learning rate or inverse temperature. Regarding Noise Regressions trait anxiety was positively associated with the reward learning rate [R^2=.33, F(7,11)=2.283, p=.107; Trait Anxiety (β=1.31, p=.016). Trait anxiety was not associated with loss learning rate or inverse temperature. Regarding Safe Regressions trait anxiety was positively associated with the reward learning rate [R^2=.80, F(7,7)=8.794, p=.005; Trait Anxiety (β=0.89, p=.025). Trait anxiety was also positively associated with the loss learning rate [R^2=.86, F(7,7)=13.21, p=.001; Trait Anxiety (β=0.79, p=.006). Trait anxiety was not associated with inverse temperature during the Safe condition. State anxiety was not the focus of study hypotheses. However, given the clinical focus of the study on anxiety study, regression coefficients indicating the association between state anxiety and model parameters are also included in Table 5.

Hypothesis 2: High trait anxiety will be associated with a relatively higher loss learning rate, reward learning rate, and exploration, for noise versus safe runs. Two-way mixed analyses of variance conducted for Group (low/high anxiety) × Noise (safe/noise), separately for all parameters suggested no main effect of Group or Noise, nor a significant

interaction. Specifically regarding the reward learning there was no significant Group × Noise interaction [$F(1, 62) = 0.10$, p=.755], nor was there a main effect of Group [$F(1,62)=0.01$, p=.934] or Noise [$F(1,62)=0.10$, p =.753]. Regarding the loss learning rate there was no significant Group × Noise interaction [$F(1, 62) = 0.10$, p=.758, or main effect of Group [$F(1, 62) = 1.19$, p=.282], or Noise [$F(1, 62)=0.84$, p=.366]. Finally, regarding the inverse temperature, there was no significant Group × Noise interaction [$F(1, 62) = 0.70$, p=.407] or main effect of Group [$F(1, 62)=1.00$, p=.320], or Noise [$F(1, 62) =0.80$, p=.373].

Hypothesis 3: Association between model parameters and dlPFC activity. Measurement channels that were significantly associated with model parameters are depicted in Figure 3. In all cases, channel activations were False Discovery Rate (FDR) corrected at $p < 0.05$ (Benjamini, Hochberg, & Benjamini, Yoav, 1995). Hypotheses were partially supported. Specifically, while the dlPFC was not associated with the reward or loss learning rate, the left dlPFC activation magnitude was negatively correlated with inverse temperature. It is noted that this finding is consistent with a positive association between the left dlPFC and exploration (i.e., a lower inverse temperature indicates increased stochastic choice, and hence increased exploration). Region of interest analyses are listed in Table 7, for all channels surviving a corrected FDR threshold of $p < 0.05$.

Hypothesis 4: Between-group comparisons of dlPFC-modulated activation. Hypotheses were not supported. Specifically, while between group differences in model-parameter-driven neural activation were observed in areas of the prefrontal cortex, findings were not indicated for the dlPFC region specifically (Figure 4). Region of interest analyses are listed in Table 8, for all channels surviving a corrected FDR threshold of $p < 0.05$.

Hypothesis 5: Multi-channel pattern analyses of reward and loss outcomes. Hypotheses were partially supported. Regarding decoding accuracy using the top 3 most informative channels, all outcome couplet combinations (including reward and loss couplets) were successfully classified within the safe condition (Figure 5; Table 6) for high anxiety participants. No-win relative to loss outcomes were successfully classified in the high anxiety group, within the noise condition. For the low anxiety group, the no-win and win outcome conditions were successfully classified within the safe condition. Regarding our hypothesis that a differential set of channels would classify outcomes in low and anxiety participants, differentiation of no-win and win outcomes was classified by distinct channel triplets across anxiety groups. Decoding using the top 3 channels was superior to decoding using all channels. Specifically, of the 12 decoding instances (i.e., decoding for all event couplets, for each group, across safe and threat conditions) there was only one instance for which decoding accuracy leveraging all channels was superior to decoding accuracy leveraging the top 3 channels (Table 6).

Chapter 4 – Discussion

This study assessed the decision-making parameters and underlying neural correlates that are associated with anxiety during reinforcement learning. The study also investigated the extent to which threat modifies the magnitude of these parameters. The study adds to a growing literature suggesting anxiety is characterized by differential sensitivity to both rewards and losses in reinforcement learning contexts. Further, it suggests that the dlPFC plays a role in modulating exploration-based choice strategies.

Behavioral results suggested a positive association between trait anxiety and the learning rate for rewards and losses. Reaction times during the decision-making phase of the task did not differ between anxiety groups, suggesting that constructs measured by reaction time, such as perseveration and impulsivity, did not contribute to the effect of anxiety on model parameters. Inverse temperature was not associated with trait anxiety. Finally, threat did not modulate any decision-making parameters in either the high or low anxiety groups. To date, while learning rates have not been measured in anxious individuals, increased sensitivity to punishment, as well as selective attention towards losses have been observed (Matthews, Panganiban, & Hudlicka, 2011; Torrubia et al., 2001). Therefore, we expected a positive association between trait anxiety and the loss learning rate. Specifically, an increased loss learning rate would be consistent with increased weight given to an unexpected outcome in the context of loss, when estimating the future expected value of that choice. Regarding the reward learning rate, given that individuals with GAD have been found to underestimate the probability of positive reinforcement, we expected a negative association between trait anxiety and the reward learning rate (LaFreniere & Newman, 2018). A decreased reward learning rate is consistent with placing less weight on an unexpected reward outcome when estimating the future expected value of that choice.

Hypotheses were partially supported. Specifically, a positive association between the loss learning rate and anxiety was observed. However, this association was restricted to the safe condition. Contrary to hypotheses, the association between reward learning rate and trait anxiety was positive. Inverse temperature was not associated with trait anxiety in safe nor threat conditions.

Together, these findings suggest a generally increased learning rate in anxious individuals, for both rewards and losses. Interpreting this finding requires consideration of the computational function fulfilled by the learning rate parameter within temporal difference learning models. A high learning rate does not necessarily equate to optimal learning. Specifically, an agent with an extremely high learning rate (e.g., a learning rate of '1') would incorporate the full magnitude of a prediction error into future expected value estimations of a choice. Therefore, in the case of a very high loss learning rate, a single anomalous loss outcome may prevent that agent from repeating that choice, even if the choice had exhibited a robust history of positive returns. Conversely, an agent with an extremely high reward learning rate is more likely to repeat a choice that garners a reward, even in cases where that choice has exhibited a history of negative returns. While a learning rate of '1' is an extreme hypothetical example, the purpose is to highlight how an increased learning impacts reinforcement learning. Overall, the current results suggest that regardless of outcome type (i.e., reward or loss), anxiety is associated with a tendency to more heavily weight a recent unexpected outcome, when updating the expected value of a choice.

To date, one previous study assessed probabilistic reinforcement learning patterns in GAD (LaFreniere & Newman, 2018). While participants in the current study did not comprise a GAD sample, the trait anxiety measure used to characterize the sample encapsulates the

diagnostic features of GAD (Stanley, Beck, & Zebb, 1996). Therefore, a comparison of findings is potentially informative. Findings of LaFreniere and Newman (2018) suggest decreased reinforcement learning accuracy in individuals with GAD, across both positive and negative reinforcement conditions. Findings of decreased accuracy during the positive reinforcement condition, combined with current findings of an increased learning reward learning rate in trait anxiety, is consistent with an emerging literature suggesting that pathology of reinforcement learning in anxiety may extend beyond loss learning to the reward-related learning differences (Forbes et al., 2006).

The finding of an increased learning rate for rewards and losses yields useful clinical implications. Specifically, within temporal difference models, the learning rate is computationally distinct from other outcome-centric parameters, such as reward or loss *sensitivity*. Specifically, whereas a learning rate weights against a prediction error, reward or loss sensitivity parameters (which were not measured in the current study) weight against the actual outcome. From the standpoint of the clinical presentation of anxiety, this is a subtle yet important distinction. That is, the current learning rate finding suggests that high anxiety individuals more readily update their choice-outcome forecasts when the outcome experienced is either a reward *or* loss, *and* when that outcome garners a prediction error. Regarding the clinical presentation of anxiety, this suggests that anxious individuals may perceive a relatively unstable outcome-landscape, due to sub-optimal cognitive computations that overemphasize predictions errors when making future outcome estimations.

While prior work has found increased sensitivity to threat, impaired disengagement to threat, and increased avoidance due to threat in anxious individuals (Koster et al., 2006; MacLeod, 1986; Mkrtchian et al., 2017), the null results of the study demonstrate that the effect

of threat does not extend to exploration strategies (at least measured by an inverse temperature parameter), nor reward and loss learning rates.

Consistent with neuroimaging hypotheses, the left dlPFC was positively associated with exploration (i.e., as indicated by a *negative* association with the inverse temperature parameter). Furthermore, multi-channel pattern analyses (MCPA) indicated that in both high and low anxiety groups, activation channels outside of, yet just peripheral to the dlPFC, decoded reward and loss outcomes in anxious individuals. The exploration parameter finding, combined with MCPA findings, are consistent with, and extend prior findings, which suggest that the dlPFC is involved in action value learning (Morris et al., 2014). Additionally, the results suggest that the dlPFC integrates information garnered from current and past choices, and in computing action-value comparisons (Lee & Seo, 2007; Morris et al., 2014). Specifically, consistent with the computational function of past action-outcome tracking, the inverse temperature parameter is a metric of exploration that necessarily integrates prior action-values. That is, exploration tracks the degree to which an agent chooses to depart from prior choices that garnered reward. In this sense, the dlPFC can be thought to integrate action-values, by modulating exploration, while simultaneously tracking the values of prior rewarding actions. Furthermore, MCPA findings are consistent with action-value comparison, in that neuroimaging channels just adjacent to the dlPFC were found (in combination) to decode reward and loss outcomes. Together, this suggests that the dlPFC, and regions adjacent to it, can differentiate and compare between action-values, for purposes of computing an exploratory choice-strategy.

4.1 - Limitations

Results of the study should be evaluated in light of the following limitations. There was a low number of loss outcomes experienced by participants. This suggests that participants tended

to converge on an efficient strategy relatively quickly. Consequently, the establishment of the loss learning parameter was relatively more difficult than the reward learning parameter, which in turn yielded a reduction in the overall participant sample available for computational behavioral and neuroimaging analyses. The present sample assessed anxiety on a dimensional scale, measuring both state and trait anxiety. Therefore, while these findings have utility in informing how a transdiagnostic symptom dimension affects reinforcement learning, this may limit generalization to diagnostic samples.

4.2 - Conclusions

To our knowledge, this study is the first to assess both behavioral and neural markers of probabilistic learning in anxious individuals, and the associated impact of threat, within a computational framework. By leveraging quantitative (i.e., temporal difference learning) and classification approaches (i.e., multi-channel pattern analyses), this study builds on related neuroimaging literature, by further clarifying the role of the dlPFC in reinforcement learning. Specifically, the current study highlights a specific cognitive mechanism that may be hypersensitive in anxious individuals (i.e., the updating of future outcomes expectations based on unexpected events). Future research in this area may seek to assess whether anxiety is characterized by similar, yet computationally distinct perturbations, such as reward or loss sensitivity, outside of the context of a prediction error. Given findings of the association between state anxiety and both the reward and loss learning rate in the current study, further research may seek to highlight the differential impact of state and trait anxiety on reinforcement learning strategies, by including multiple measurements of state anxiety during critical epochs of the experiment (e.g., during safe and threatening portions of the behavioral task). Neuroimaging

results extend the understanding of dlPFC functioning, by highlighting the role of this region in guiding explorative learning strategies in reinforcement learning contexts.

References

Barker, J. W., Aarabi, A., & Huppert, T. J. (2013). Autoregressive model based algorithm for correcting motion and serially correlated errors in fNIRS. *Biomedical Optics Express*, *4*(8), 1366. https://doi.org/10.1364/boe.4.001366

Barraclough, D. J., Conroy, M. L., & Lee, D. (2004). Prefrontal cortex and decision making in a mixed-strategy game. *Nature Neuroscience*, *7*(4), 404–410. https://doi.org/10.1038/nn1209

Benjamini, Y., Hochberg, Y., & Benjamini, Yoav, H. Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society. Series B (Methodological)*. https://doi.org/10.2307/2346101

Bishop, S., Duncan, J., Brett, M., & Lawrence, A. D. (2004). Prefrontal cortical function and anxiety: controlling attention to threat-related stimuli. *Nature Neuroscience*, *7*(2), 184–188. https://doi.org/10.1038/nn1173

Britton, J. C., Lissek, S., Grillon, C., Norcross, M. A., & Pine, D. S. (2011). Development of anxiety: The role of threat appraisal and fear learning. *Depression and Anxiety*. https://doi.org/10.1002/da.20733

Burke, C. J., Tobler, P. N., Baddeley, M., & Schultz, W. (2010). Neural mechanisms of observational learning. *Proceedings of the National Academy of Sciences of the United States of America*, *107*(32), 14431–14436. https://doi.org/10.1073/pnas.1003111107

Cornwell, B. R., Overstreet, C., Krimsky, M., & Grillon, C. (2013). Passive avoidance is linked to impaired fear extinction in humans. *Learning & Memory (Cold Spring Harbor, N.Y.)*, *20*(3), 164–169. https://doi.org/10.1101/lm.028902.112

Corr, P. J., Pickering, A. D., & Gray, J. A. (1995). Personality and reinforcement in associative and instrumental learning. *Personality and Individual Differences*, *19*(1), 47–71.

https://doi.org/10.1016/0191-8869(95)00013-V

Craske, M. G., Rauch, S. L., Ursano, R., Prenoveau, J., Pine, D. S., & Zinbarg, R. E. (2009). What is an anxiety disorder? *Depression and Anxiety*, *26*(12), 1066–1085. https://doi.org/10.1002/da.20633

Craske, M. G., Waters, A. M., Lindsey Bergman, R., Naliboff, B., Lipp, O. V., Negoro, H., & Ornitz, E. M. (2008). Is aversive learning a marker of risk for anxiety disorders in children? *Behaviour Research and Therapy*, *46*(8), 954–967. https://doi.org/10.1016/j.brat.2008.04.011

Daw, N. D., Gershman, S. J., Seymour, B., Dayan, P., & Dolan, R. J. (2011). Model-based influences on humans' choices and striatal prediction errors. *Neuron*, *69*(6), 1204–1215. https://doi.org/10.1016/j.neuron.2011.02.027

Daw, N. D., O'Doherty, J. P., Dayan, P., Seymour, B., & Dolan, R. J. (2006). Cortical substrates for exploratory decisions in humans. *Nature*, *441*(7095), 876–879. https://doi.org/10.1038/nature04766

DeVido, J., Jones, M., Geraci, M., Hollon, N., Blair, R. J. R., Pine, D. S., & Blair, K. (2009). Stimulus-reinforcement-based decision making and anxiety: Impairment in generalized anxiety disorder (GAD) but not in generalized social phobia (GSP). *Psychological Medicine*, *39*(7), 1153–1161. https://doi.org/10.1017/S003329170800487X

Dombrovski, A. Y., Clark, L., Siegle, G. J., Butters, M. a., Ichikawa, N., Sahakian, B. J., & Szanto, K. (2010). Reward/punishment reversal learning in older suicide attempters. *American Journal of Psychiatry*, *167*(6), 699–707. https://doi.org/10.1176/appi.ajp.2009.09030407

Duits, P., Cath, D. C., Lissek, S., Hox, J. J., Hamm, A. O., Engelhard, I. M., … Baas, J. M. P.

(2015). Updated meta-analysis of classical fear conditioning in the anxiety disorders. *Depression and Anxiety*, *32*(4), 239–253. https://doi.org/10.1002/da.22353

Edman, G., Schalling, D., & Levander, S. (1983). Impulsivity and speed and errors in a reaction time task: A contribution to the construct validity of the concept of impulsivity. *Acta Psychologica*, *53*(1), 1–8. https://doi.org/10.1016/0001-6918(83)90012-4

Emberson, L. L., Zinszer, B. D., Raizada, R. D. S., & Aslin, R. N. (2016). Decoding the infant mind: Multichannel Pattern Analysis (MCPA) using fNIRS. *BioRxiv Preprint*, 1–29.

Endler, N. S., & Kocovski, N. L. (2001). State and trait anxiety revisited. *Journal of Anxiety Disorders*, *15*(3), 231–245. https://doi.org/10.1016/S0887-6185(01)00060-3

Fava, M., Rankin, M. R., Wright, E. C., Alpert, J. E., Nierenberg, A. a, Pava, J., & Rosenbaum, J. F. (2000). Anxiety disorders in Major Depression. *Comprehensive Psychiatry*, *41*(2), 97–102. https://doi.org/0010-440X/00/4102-0013$10.00/0

Fischer, M., Barkley, R. A., Smallish, L., Fletcher, K., Fischer, M., Barkley, R. A., … Barkley, R. A. (2005). Executive Functioning in Hyperactive Children as Young Adults : Attention , Inhibition , Response Perseveration , and the Impact of Comorbidity Executive Functioning in Hyperactive Children as Young Adults : Attention , Inhibition , Response Perseveration, *5641*(October), 107–133. https://doi.org/10.1207/s15326942dn2701

Fitzgerald, P. B., Maller, J. J., Hoy, K. E., Thomson, R., & Daskalakis, Z. J. (2009). Exploring the optimal site for the localization of dorsolateral prefrontal cortex in brain stimulation experiments. *Brain Stimulation*, *2*(4), 234–237. https://doi.org/10.1016/j.brs.2009.03.002

Forbes, E. E., Christopher May, J., Siegle, G. J., Ladouceur, C. D., Ryan, N. D., Carter, C. S., … Dahl, R. E. (2006). Reward-related decision-making in pediatric major depressive disorder: An fMRI study. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *47*(10),

1031–1040. https://doi.org/10.1111/j.1469-7610.2006.01673.x

Grillon, C., Baas, J. P., Lissek, S., Smith, K., & Milstein, J. (2004). Anxious responses to predictable and unpredictable aversive events. *Behavioral Neuroscience*, *118*(5), 916–924. https://doi.org/10.1037/0735-7044.118.5.916

Grupe, D. W., & Nitschke, J. B. (2013). Uncertainty and anticipation in anxiety: an integrated neurobiological and psychological perspective. *Nature Reviews*, *14*(July), 488–501. https://doi.org/10.1038/nrn3524

Kennedy, B. L., Schwab, J. J., Morris, R. L., & Beldia, G. (2001). Assessment of state and trait anxiety in subjects with anxiety and depressive disorders. *Psychiatric Quarterly*, *72*(3), 263–276. https://doi.org/10.1023/A:1010305200087

Kessel, E. M., Kujawa, A., Hajcak Proudfit, G., & Klein, D. N. (2015). Neural reactivity to monetary rewards and losses differentiates social from generalized anxiety in children. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *56*(7), 792–800. https://doi.org/10.1111/jcpp.12355

Knight, R. G., Waal-Manning, H. J., & Spears, G. F. (1983). Some norms and reliability data for the State-Trait Anxiety Inventory and the Zung Self-Rating Depression scale. *British Journal of Clinical Psychology*, *22*, 245–249. https://doi.org/10.1111/j.2044-8260.1983.tb00610.x

Koster, E. H. W., Crombez, G., Verschuere, B., Van Damme, S., & Wiersema, J. R. (2006). Components of attentional bias to threat in high trait anxiety: Facilitated engagement, impaired disengagement, and attentional avoidance. *Behaviour Research and Therapy*, *44*(12), 1757–1771. https://doi.org/10.1016/j.brat.2005.12.011

Krypotos, A., Effting, M., Kindt, M., Beckers, T., & Bergstrom, H. C. (2015). Avoidance

learning : a review of theoretical models and recent developments, *9*(July). https://doi.org/10.3389/fnbeh.2015.00189

LaFreniere, L. S., & Newman, M. G. (2018). Probabilistic Learning by Positive and Negative Reinforcement in Generalized Anxiety Disorder. *Clinical Psychological Science*, 216770261880936. https://doi.org/10.1177/2167702618809366

Lee, D., & Seo, H. (2007). Mechanisms of reinforcement learning and decision making in the primate dorsolateral prefrontal cortex. *Annals of the New York Academy of Sciences*, *1104*, 108–122. https://doi.org/10.1196/annals.1390.007

Lissek, S., Rabin, S. J., McDowell, D. J., Dvir, S., Bradford, D. E., Geraci, M., … Grillon, C. (2009). Impaired discriminative fear-conditioning resulting from elevated fear responding to learned safety cues among individuals with panic disorder. *Behaviour Research and Therapy*, *47*(2), 111–118. https://doi.org/10.1016/j.brat.2008.10.017

MacLeod, C. (1986). Anxiety and the allocation of attention to threat. *The Quarterly Journal of Experimental Psychology*, *40*(4), 653–670.

Mathews, A., & MacLeod, C. (1985). Selective Cues Processing in Anxiety of Threat. *Behaviour Research and Therapy*, *23*(5), 563–569. https://doi.org/10.1016/0005-7967(90)90160-K

Matthews, G., Panganiban, A. R., & Hudlicka, E. (2011). Anxiety and selective attention to threat in tactical decision-making. *Personality and Individual Differences*, *50*(7), 949–954. https://doi.org/10.1016/j.paid.2010.09.005

Mineka, S., & Oehlberg, K. (2008). The relevance of recent developments in classical conditioning to understanding the etiology and maintenance of anxiety disorders. *Acta Psychologica*, *127*(3), 567–580. https://doi.org/10.1016/j.actpsy.2007.11.007

Miranda, R., & Mennin, D. S. (2007). Depression, generalized anxiety disorder, and certainty in

pessimistic predictions about the future. *Cognitive Therapy and Research*, *31*(1), 71–82. https://doi.org/10.1007/s10608-006-9063-4

Mkrtchian, A., Aylward, J., Dayan, P., Roiser, J. P., & Robinson, O. J. (2017). Modelling avoidance in mood and anxiety disorders using reinforcement-learning. *Biological Psychiatry*, 1–8. https://doi.org/10.1016/j.biopsych.2017.01.017

Morris, R. W., Dezfouli, A., Griffiths, K. R., & Balleine, B. W. (2014). Action-value comparisons in the dorsolateral prefrontal cortex control choice between goal-directed actions. *Nat Commun*, *5*, 4390. https://doi.org/10.1038/ncomms5390

Mueller, E. M., Nguyen, J., Ray, W. J., & Borkovec, T. D. (2010). Future-oriented decision-making in Generalized Anxiety Disorder is evident across different versions of the Iowa Gambling Task. *Journal of Behavior Therapy and Experimental Psychiatry*, *41*(2), 165–171. https://doi.org/10.1016/j.jbtep.2009.12.002

Neumann, D. L., & Waters, A. M. (2006). The use of an unpleasant sound as an unconditional stimulus in a human aversive Pavlovian conditioning procedure. *Biological Psychology*, *73*(2), 175–185. https://doi.org/10.1016/j.biopsycho.2006.03.004

Neumann, D. L., Waters, A. M., & Westbury, H. R. (2008). The use of an unpleasant sound as the unconditional stimulus in aversive Pavlovian conditioning experiments that involve children and adolescent participants. *Behavior Research Methods*, *40*(2), 622–625. https://doi.org/10.3758/BRM.40.2.622

Rescorla, R. A., & Haven, N. E. W. (1969). in Pavlovian Conditioning, 147–152.

Smarr, K. L., & Keefer, A. L. (2011). Measures of depression and depressive symptoms: Beck Depression Inventory-II (BDI-II), Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale

(HADS), and Patient Health Questionna. *Arthritis Care and Research*, *63*(SUPPL. 11), 454–466. https://doi.org/10.1002/acr.20556

Spielberg, J. M., Miller, G. A., Engels, A. S., Herrington, J. D., Sutton, B. P., Banich, M. T., & Heller, W. (2011). Trait approach and avoidance motivation: Lateralized neural activity associated with executive function. *NeuroImage*, *54*(1), 661–670. https://doi.org/10.1016/j.neuroimage.2010.08.037

Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). State-Trait Anxiety Inventory for adults (Form X).

Stanley, M. A., Beck, J. G., & Zebb, B. J. (1996). Psychometric properties of four anxiety measures in older adults. *Behav. Res. Ther*, *34*(10), 827–838.

Torrubia, R., Ávila, C., Moltó, J., & Caseras, X. (2001). The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) as a measure of Gray's anxiety and impulsivity dimensions. *Personality and Individual Differences*, *31*(6), 837–862. https://doi.org/10.1016/S0191-8869(00)00183-5

Verma, P., & Nijhawan, H. K. (1976). The effect of anxiety, reinforcement, and intelligence on the learning of a difficult task. *Journal of Experimental Child Psychology*, *22*(2), 302–308. https://doi.org/10.1016/0022-0965(76)90010-2

Waters, A. M., Henry, J., & Neumann, D. L. (2009). Aversive Pavlovian Conditioning in Childhood Anxiety Disorders: Impaired Response Inhibition and Resistance to Extinction. *Journal of Abnormal Psychology*, *118*(2), 311–321. https://doi.org/10.1037/a0015635

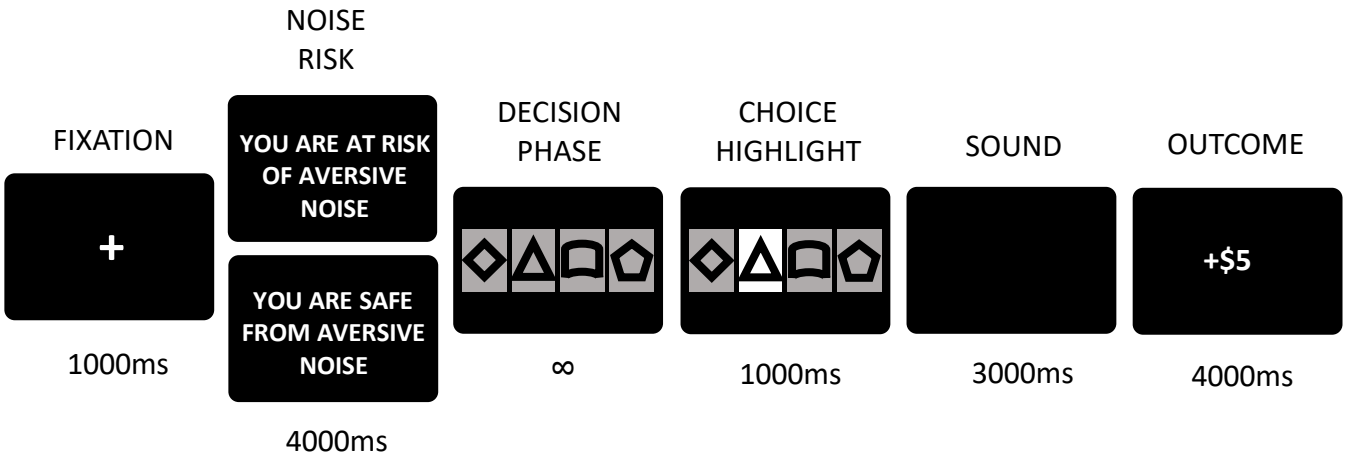


Figure 1. Behavioral Task Depiction.
Participants alternated between Noise Risk and No Noise Risk runs, as denoted by an instructional screen at the beginning of each trial. Participants had an open-ended period of time to choose a shape. The participant's choice was then highlighted. Subsequently, the noise was played during a blank screen (Noise Risk run), or a blank screen was shown, without the occurrence of noise (No Noise Risk run). Finally, the outcome was shown.

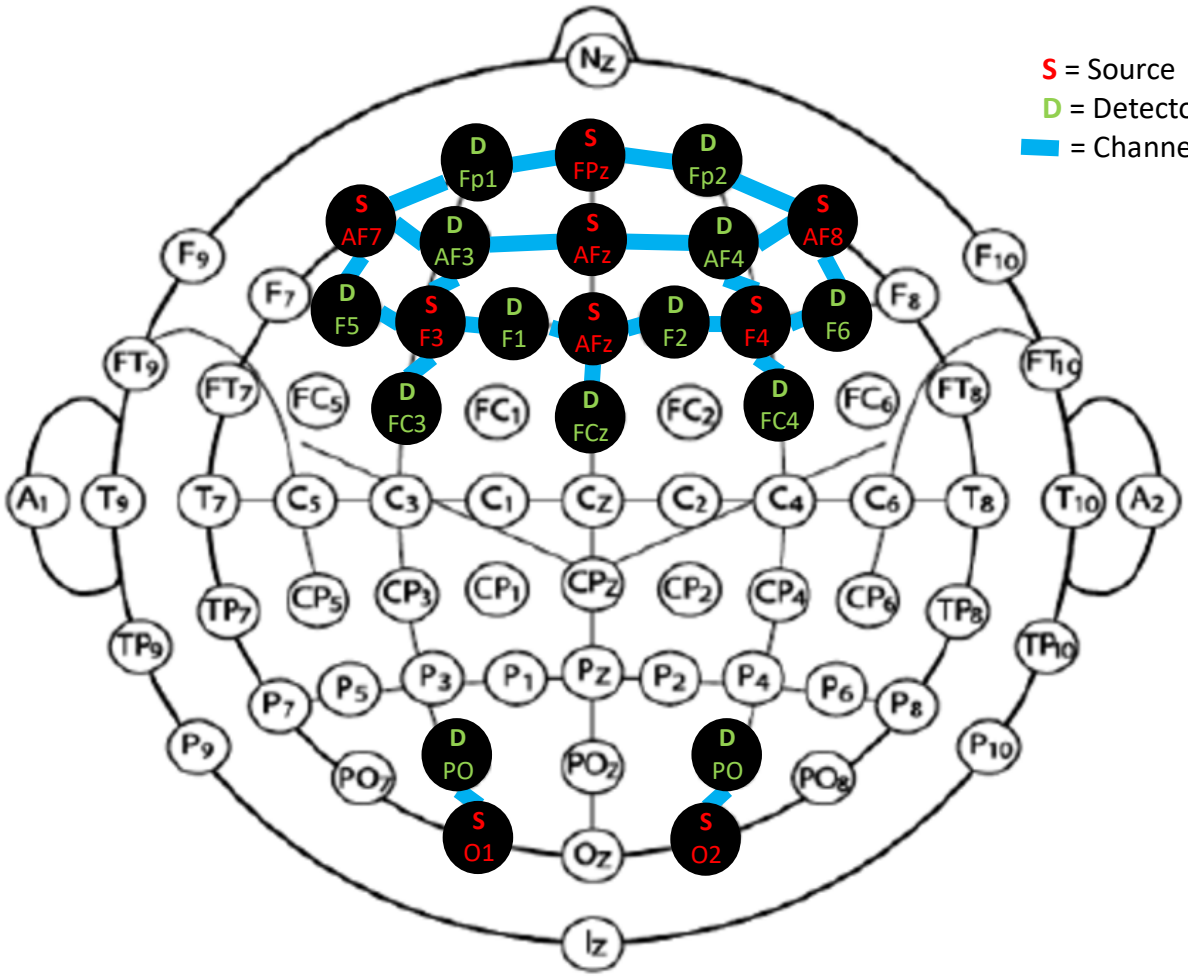


Figure 2. FNIRS Channel Configuration.
Source and detector locations are denoted by the labels ‘S’, and ‘D’, respectively. Measurement channels are indicated by blue lines. A 23-channel array was used (9 sources, and 13 detectors), spanning bilateral surfaces of the dorsolateral prefrontal cortex (DLPFC). Reference channels were included in the bilateral occipital lobes. Optode locations are displayed using the International 10-20 system.

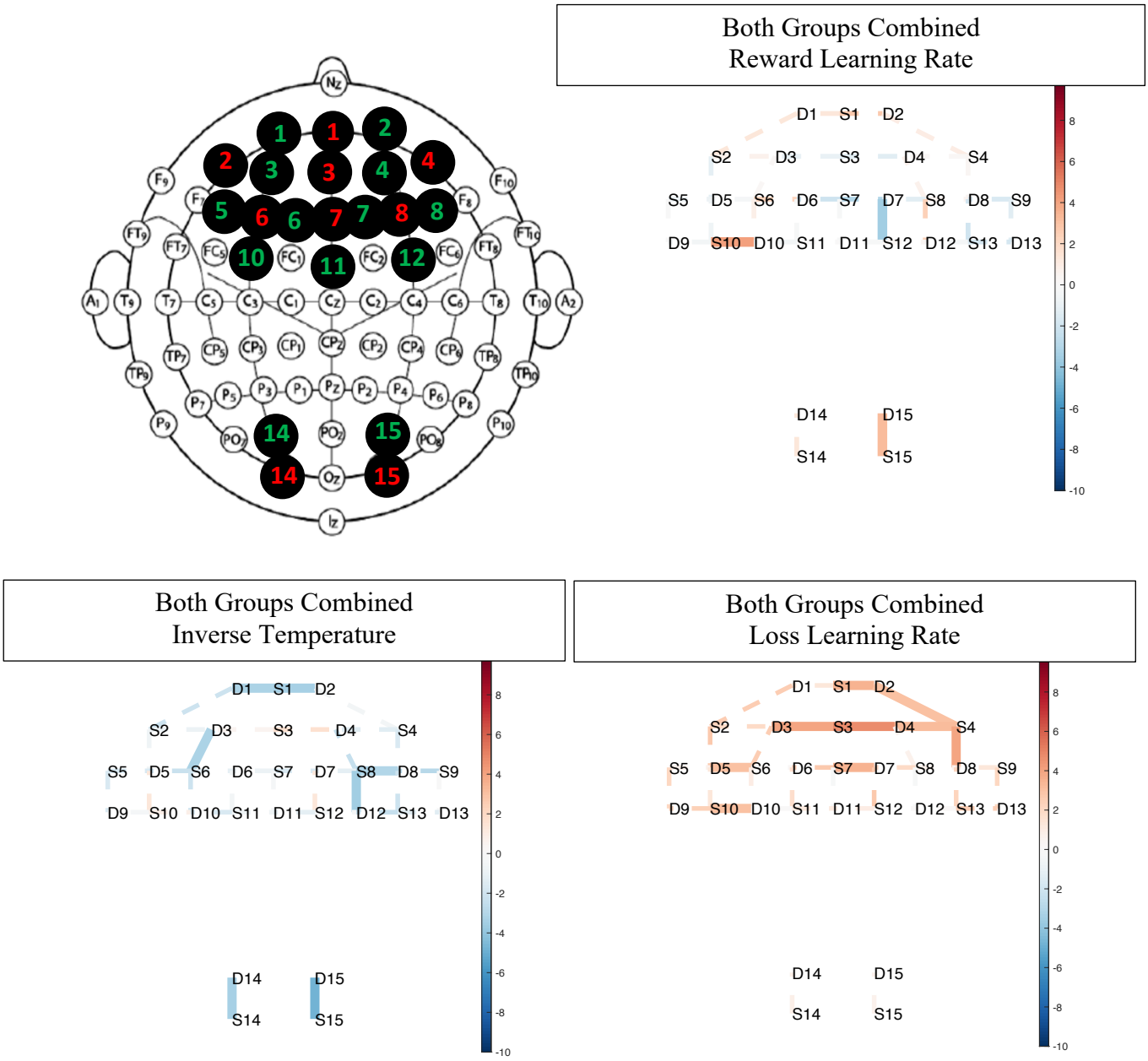


Figure 3. Combined-Group FNIRS Model Parameter Results.
FNIRS channels that were modulated by model parameters for both groups combined. A thick line indicates channel activation was significant at FDR < 0.05. Colored bars indicate the t-statistic size. Source and detector numbers are denoted by 'S' and 'D' respectively. A source-detector map superimposed onto EEG 10-20 space is pictured in the top left for reference (sources indicated in red, detectors indicated in green).

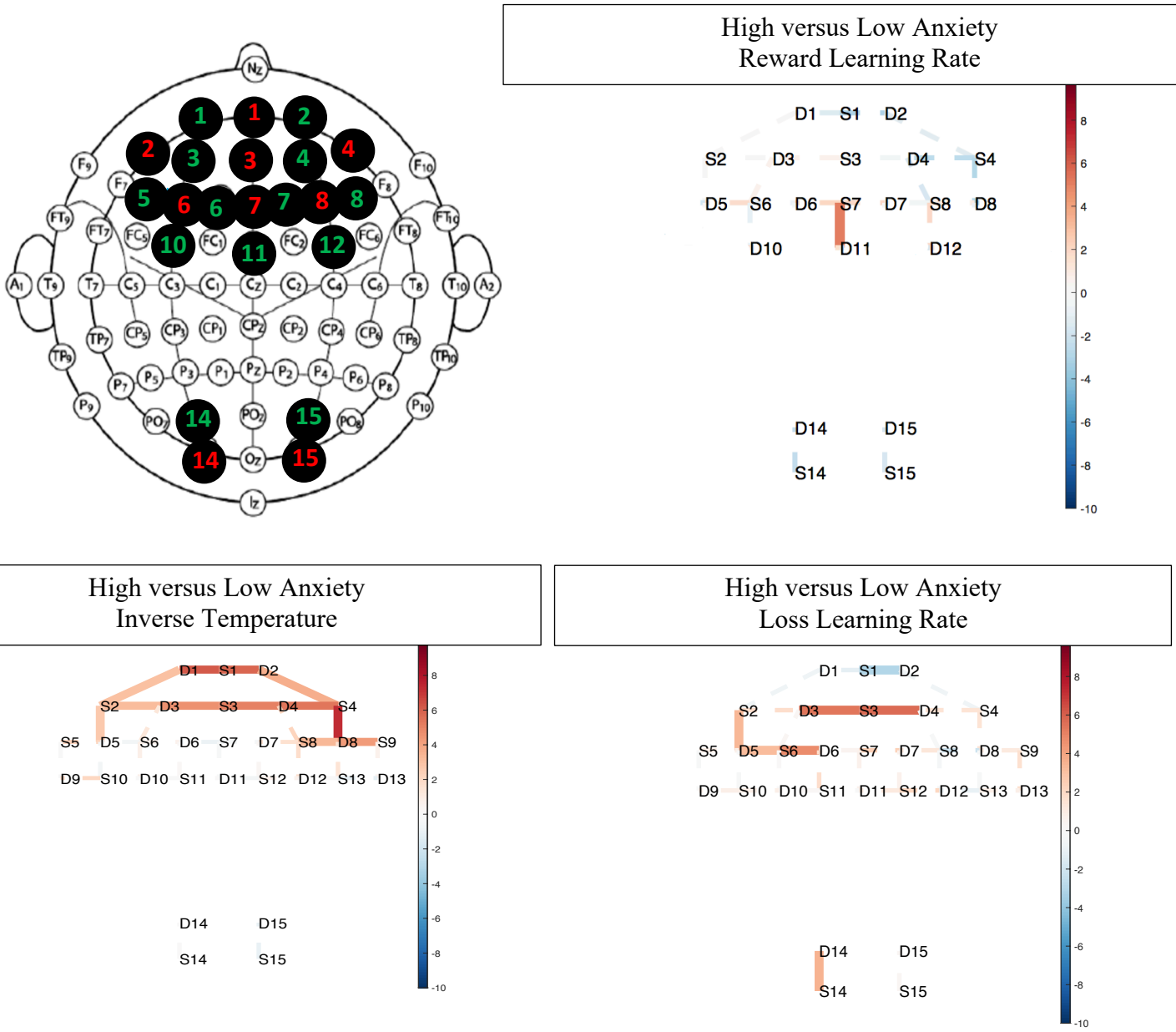


Figure 4. Between-Group FNIRS Model Parameter Results.
FNIRS channels that were differentially modulated by group. A thick line indicates channel activation was significant at FDR < 0.05. Colored bars indicate the t-statistic size. Source and detector numbers are denoted by 'S' and 'D' respectively. A source-detector map superimposed onto EEG 10-20 space is pictured in the top left for reference (sources indicated in red, detectors indicated in green).

Outcome	Classification Accuracy	Top Channels
Low Anxiety (*n* = 14)		
Safe -$5, +$5	57%	1 4 13
Threat -$5, +$5	36%	2 20 21
High Anxiety (n = 18)		
Safe -$5, +$5	89%*	**7 17 23**
Threat -$5, +$5	56%	4 15 23

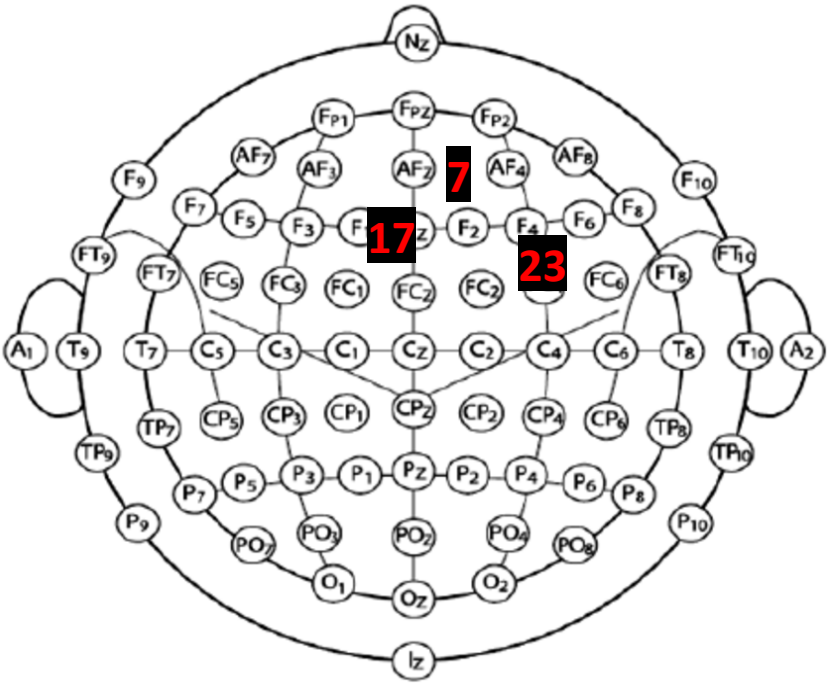


Figure 5. Multi-Channel Pattern Analysis Classification Results.
Successful MCPA classification for high anxiety participants, within the safe condition. Channel locations of successful decoding channels are depicted. Significant decoding at p<.05 indicated by '*'.

Table 1

Participant Characteristics (n = 46)

	M	SD	Minimum	Maximum
Age (years)	23.40	7.47	18	55
			n	% sample
Gender				
Male			23	50.0
Female			23	50.0
Race/Ethnicity				
Black/African American			1	2.2
Asian			4	8.7
White Caucasian			37	80.4
Other			4	8.7

Table 2

Group Descriptive Statistics
(n = 46)

Self-Report Measures	Low Anxiety (n = 20)			High Anxiety (n = 26)			Group Comparison
	M	SD	Range	M	SD	Range	Low Anxiety vs. High Anxiety
BDI-II	3.35	2.94	0-10	13.62	9.01	3-47	<.001
STAI							
State	25.65	5.57	20-37	37.27	9.12	23-59	<.001
Trait	26.95	4.14	21-34	50.27	8.92	34-72	<.001

Table 3

Behavioral Data Inclusion Sample Sizes

	Group Low Anxiety		
	Reward Learning Rate	Loss Learning Rate	Inverse Temperature
Condition			
Safe	*n = 15*	n = 8	n = 16
Threat	n = 14	n = 11	n = 16
	Group High Anxiety		
Condition			
Safe	n = 20	n = 12	n = 23
Threat	n = 19	n = 11	n = 19
Total Safe	***n = 35***	***n = 20***	***n = 39***
Total Threat	***n = 33***	***n = 22***	***n = 35***

Table 4

Model Parameters for Participants (n = 25)

Participant	Reward Learning Rate	Loss Learning Rate	Inverse Temperature
1	0.80	0.84	7.14
2	0.40	0.77	4.05
3	0.49	0.23	0.46
4	0.23	0.87	4.23
6	0.82	0.77	3.29
7	0.86	0.49	14.06
8	0.77	0.79	6.13
9	0.60	0.71	3.38
10	0.88	0.01	3.74
12	0.97	0.28	11.01
13	0.79	0.36	12.73
14	0.84	0.80	3.75
15	0.55	0.28	0.92
16	0.72	0.01	6.18
17	0.46	0.06	19.66
18	0.72	0.87	5.89
21	0.86	0.86	3.78
27	0.30	0.98	8.65
29	0.28	0.62	3.29
32	0.61	0.51	10.86
33	0.19	0.34	3.62
35	0.88	0.84	21.88
40	0.12	0.73	0.28
41	0.81	0.42	6.61
45	0.79	0.02	5.51

Table 5

Beta coefficients (β) and p-values (p) for All Regressions (Trait and State Anxiety Listed)

		Trait Anxiety		State Anxiety	
Condition	Dependent Variable	β	*p*	β	*p*
Combined	Reward Learning Rate	**0.77**	**0.042***	**-0.83**	**0.049***
	Loss Learning Rate	0.29	0.498	-0.45	0.336
	Inverse Temperature	-0.33	0.201	0.24	0.416
Noise	Reward Learning Rate	**1.31**	**0.016***	-0.72	0.079
	Loss Learning Rate	0.42	0.586	-0.29	0.596
	Inverse Temperature	-0.66	0.096	0.41	0.150
No Noise	Reward Learning Rate	**0.89**	**0.025***	-1.16	0.084
	Loss Learning Rate	**0.79**	**0.006***	**-1.13**	**0.018***
	Inverse Temperature	-0.57	0.131	0.53	0.400

Note: State anxiety was ascertained at one timepoint, at the same time all other self-report measures were administered. (i.e., just prior to beginning the behavioral task). Significant regression coefficients ($p<.05$) are denoted by '*'

Table 6

Multi-Channel Pattern Analysis Classification Results

Low Anxiety (n = 14)			
Outcome	Classification Accuracy Top 3 Channels	Top 3 Channels	Classification Accuracy All Channels
No Noise			
-$5, +$5	57%	1, 4, 13	14%
$0, +$5	71%*	6, 14, 22	36%
$0, -$5	78%	2, 21, 38	50%
Noise			
-$5, +$5	36%	2, 20, 21	50%
$0, +$5	57%	10, 18, 19	50%
$0, -$5	50%	10, 19, 20	50%

High Anxiety (n = 18)			
Outcome	Classification Accuracy Top 3 Channels	Top 3 Channels	Classification Accuracy All Channels
No Noise			
-$5, +$5	89%*	7, 17, 23	67%
$0, +$5	83%*	7, 19, 21	56%
$0, -$5	67%*	10, 17, 19	50%
Noise			
-$5, +$5	56%	4, 15, 23	50%
$0, +$5	61%	4, 14, 19	39%
$0, -$5	67%*	8, 19, 23	28%

Note: Significant decoding at $p<.05$ was computed for the top 3 channel combinations. Significant decoding is denoted by '*'. Classification accuracy results using all channels combined are included as a comparative reference.

Table 7

Region of Interest Analyses for Parameter-Modulated Channels (All Participants Combined)

Source	Detector	Parameter	Beta Estimate	Standard Error	t-statistic	FDR
1	2	Inverse Temperature	-44.47	9.22	-4.82	0.001
15	15	Inverse Temperature	-42.05	10.86	-3.87	0.009
4	8	Inverse Temperature	-24.57	7.12	-3.45	0.024
4	2	Inverse Temperature	-13.94	4.58	-3.05	0.050
3	4	Loss Learning Rate	50.53	9.90	5.11	0.000
3	3	Loss Learning Rate	52.00	12.70	4.10	0.004
7	7	Loss Learning Rate	67.14	16.11	4.17	0.004
4	8	Loss Learning Rate	40.09	12.52	3.20	0.039
2	5	Loss Learning Rate	39.23	13.51	2.90	0.049
6	5	Loss Learning Rate	39.54	13.29	2.97	0.049
7	6	Loss Learning Rate	49.96	17.00	2.94	0.049
7	7	Reward Learning Rate	-65.99	17.39	-3.79	0.017
3	4	Reward Learning Rate	-37.83	11.70	-3.23	0.044

Table 8

Region of Interest Analyses for Parameter Modulated Channels (High versus Low Anxiety)

Source	Detector	Parameter	Beta Estimate	Standard Error	t-statistic	FDR
15	15	Inverse Temperature	-4.15	0.88	-4.74	0.002
1	1	Inverse Temperature	-3.08	0.96	-3.23	0.030
1	2	Inverse Temperature	-2.54	0.76	-3.34	0.030
6	3	Inverse Temperature	-2.70	0.83	-3.24	0.030
8	12	Inverse Temperature	-3.12	0.87	-3.58	0.030
14	14	Inverse Temperature	-2.80	0.81	-3.46	0.030
8	8	Inverse Temperature	-1.74	0.57	-3.05	0.042
3	4	Loss Learning Rate	43.27	9.15	4.73	0.002
3	3	Loss Learning Rate	45.60	11.26	4.05	0.006
4	8	Loss Learning Rate	42.18	10.49	4.02	0.006
1	2	Loss Learning Rate	50.50	14.09	3.58	0.015
7	7	Loss Learning Rate	44.05	12.51	3.52	0.015
4	4	Loss Learning Rate	30.32	9.39	3.23	0.030
4	2	Loss Learning Rate	20.53	6.57	3.13	0.030
6	5	Loss Learning Rate	36.21	11.75	3.08	0.030
15	15	Reward Learning Rate	63.15	19.12	3.30	0.036

Appendices

Appendix A

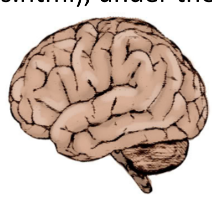
Community Study Advertisement

Volunteers needed for study on reward and loss financial decision-making

Are you between 18 – 55 years of age?
You may be eligible to participate in our research study!

The study involves completing an online questionnaire, for which you will be entered into a raffle to receive a $50 Amazon gift card.

You might then be contacted to complete an optional second part of the study, which will be conducted on the Virginia Tech campus, during which brain activity measurements will be taken while you make financial decisions. Compensation for this second optional study is between $10 and $30 dollars. Brain activity will be measured using FNIRS (functional near-infrared spectroscopy). FNIRS leverages optical processes to enable the measurement of real-time neural activity. The study be found on our lab website (http://www.scanlab.org/projects.html), under the section ***Study on Reward and Loss Learning***.



Social Clinical Affective Neuroscience Lab, Virginia Tech
vt.scanlab@gmail.com, (540) 315-2406

Signup for the study at:
http://www.scanlab.org/projects.html
under the section titled:
STUDY ON REWARD AND LOSS LEARNING

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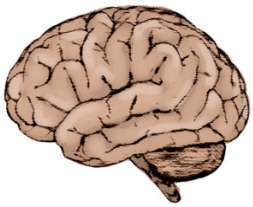
Appendix B

Student Study Advertisement

Volunteers needed for study on reward and loss financial decision-making

Are you a Virginia Tech student between 18 – 55 years of age? You may be eligible to participate in our research study!

The study involves completing an online questionnaire, for which you will receive extra-credit (0.5 units). You might then be contacted to complete an optional second part of the study, during which brain activity measurements will be taken while you make financial decisions. For the second part of the study, extra credit (2 units), and financial compensation ($10 - $30), will be offered. Brain activity will be measured using FNIRS (functional near-infrared spectroscopy). FNIRS leverages optical processes to enable the measurement of real-time neural activity. The study can be found on SONA (https://vt-psyc.sona-systems.com/). Alternatively, if you are not completing the study via SONA, but you are still eligible to receive extra credit in your psychology course, please sign up at our lab website (http://www.scanlab.org/projects.html), under the section called ***Reward and Loss Learning Study***.



Social Clinical Affective Neuroscience Lab, Virginia Tech

vt.scanlab@gmail.com, (540) 315-2406

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Appendix C

Online Study Advertisement

Volunteers needed for study on reward and loss financial decision-making

Are you between 18 – 55 years of age?

You may be eligible to participate in our research study!

The study involves completing an online questionnaire, for which you will be entered into a raffle to receive a $50 Amazon gift card.

You might then be contacted to complete an optional second part of the study, which will be conducted on the Virginia Tech campus, during which brain activity measurements will be taken while you make financial decisions. Compensation for this second optional study is between $10 and $30 dollars. Brain activity will be measured using FNIRS (functional near-infrared spectroscopy). FNIRS leverages optical processes to enable the measurement of real-time neural activity. The link to complete the study (i.e., the online questionnaire) can be found on our lab website (http://www.scanlab.org/projects.html), under the section Reward and Loss Learning Study.

Social Clinical Affective Neuroscience Laboratory, Virginia Tech

vt.scanlab@gmail.com

(540) 315-2406

Appendix D

SONA Description (Study Part 1)

Study Name	Reward and Loss Learning (part 1)
Abstract	The current study segment is part of a larger study assessing how decisions are affected by experiencing financial rewards and losses, in threatening and non-threatening contexts. For the current study segment, subjects complete a series of online questionnaires about their current and past mood.
Description	The goal of the current study segment is to ascertain individual differences in subjects' current and past mood. Subjects will complete an online questionnaire lasting approximately 20 minutes. A **subset** of subjects will then be contacted for an **optional** brain imaging study (FNIRS; functional near-infrared spectroscopy). FNIRS leverages optical processes to enable the measurement of real-time neural activity. All subjects are awarded full credit for the online questionnaires regardless of whether they decide to complete the FNIRS study.
Eligibility Requirements	Participants must be 18 or older to participate.
Duration	20 minutes
Credits	0.5 Credit
Researcher	Andrew Valdespino Email: **andrewdv@vt.edu**
Participant Sign-Up Deadline	n/a: This is an online study
Participant Cancellation Deadline	n/a: This is an online study

Appendix E

SONA description (Study Part 2)

Study Name	Reward and Loss Learning (part 2)
Abstract	The current study segment is part of a larger study assessing how decisions are affected by experiencing financial rewards and losses, in threatening and non-threatening contexts. For the current study segment, subjects complete an aversive loud noise task while undergoing functional near-infrared spectroscopy (FNIRS).
Description	Participants will complete an in-lab monetary choice task while undergoing FNIRS. FNIRS leverages optical processes to enable the measurement of real-time neural activity. The task will be completed both with, and without the periodic occurrence of aversive loud noise. In addition to extra credit, participants will also receive between $10 and $30 dollars, depending their task choices and the task outcome.
Eligibility Requirements	Participants must be 18 or older to participate. Participants must first have completed the SONA study titled "Reward and Loss Learning (part 1)." A subset of individuals who completed part 1 of the study will be contacted and offered the possibility to participate in the current study part of the study (i.e. part 2). Participants eligible to complete part 2 will receive an invitation code that will allow them to sign up.
Duration	90 minutes
Credits	2.0 Credits
Researcher	Andrew Valdespino Email: **andrewdv@vt.edu**
Participant Sign-Up Deadline	n/a: an invitation code will be sent.
Participant Cancellation Deadline	24 hours prior to study.

Appendix F

Phone Screen

Phone Screening Script Assessment
Date _____

Subject # _____

Lab initiated call:

Hello, my name is _____ and I am calling about the FNIRS research study you were interested in.

Participant initiated call:

Thank you for your interest in our study. My name is _____.

Introduction to study:
You had participated in the first part of our research study, which is being conducted by the Social Clinical Affective Neuroscience Lab in the Psychology department at Virginia Tech. The first part of this study involved completing an online questionnaire. This study was titled "Reward and Loss Learning in Anxiety (Part 1)." You are being contacted because you had expressed interest in participating in the subsequent brain-imaging portion of our study. What I would like to do is first tell you about our research study, and then later ask some questions to help us determine if you qualify to participate. These questions will involve some basic information about your medical history. Answering these questions is voluntary. You are under no obligation to answer them. However, not answering the questions means that you will not be able to participate in this research study. You are also free to stop answering questions at any time.

The phone call today will take about 10-15 minutes. Is this ok?

Dr. John Richey is the principle investigator of this study. We are interested in learning more about how the brain processes reward and loss learning. If you are interested in this study after our phone call and eligible to participate, you will complete an FNIRS aversive loud noise task (FNIRS stands for functional near-infrared spectroscopy), as well as a series of paper and pencil measures asking about your current and past mood and demographics. FNIRS is a safe, non-invasive method enabling the measurement of neural activity. It uses optical emitters and detectors to detect regional blood flow in the brain, which can be used as a proxy for neuronal activity. FNIRS does not use x-rays or other radiation. Expect the total study time to last approximately 90 minutes.

Here is some information about the confidentiality of the information I collect today. If you do not qualify for the study or decide not to participate, we will not keep the information we collect today. If you do qualify for the study and decide to participate, we will ask you to sign a consent form at your first appointment. The personal information you give me today will become part of your research record and will be reviewed by Dr. Richey and the research staff. Your name will not appear on this screening information. We will assign a code number and the key to the code will be kept on our secure laboratory server. If you change your mind at any time and decide that you

do not want to participate, you can call us and we will immediately destroy the private information that we collect today.

Now I will give you additional information about the details of the study. In this study, FNIRS images will be taken while you complete an aversive loud noise monetary choice gambling task. You will sit comfortably in a chair, and the FNIRS technician, matched to your gender, will place the FNIRS cap on your head. The FNIRS cap is made of an elastic fabric, and covers the area of your scalp. This cap functions to hold optodes, which are small devices used to provide measurements of brain activity. The study staff will place the optodes in the cap while you are sitting comfortably in the chair. The study staff may apply a gel-like substance to certain areas of your scalp to allow the optodes to function correctly. We have a variety of cap sizes, and the study staff will work with you to ensure the cap is properly sized.

During this study, you will also receive shorts bursts of aversive loud noise. These aversive loud noises will be 3-second, 85 decibel aversive noise events (i.e., the sound of metal scraping slate), delivered by headphones, that is comparable in intensity to the following real-world sounds: a diesel truck, a kitchen blender, or a snow blower. There is a possibility that anticipation of noise bursts might cause anxiety, but such anxiety is minimal in relation to the normal stress experienced in daily life. In addition, these noise bursts are loud and might therefore elicit some physical discomfort, but this stimulation is not damaging or harmful on a long-term basis. Specifically, to ensure the stimulation is not damaging, we follow recommendations outlined by the National Institute for Occupational Safety and Health (Occupational Noise Exposure Guide – revised edition, 1998). This requirement dictates that individuals not exceed exposure to an 85 dbA sound (which is the noise level of the stimulus you will hear) for longer than a duration of 8 hours. In this task, you will hear approximately 8 spaced out noise epochs of 3 seconds. Therefore, total exposure to this sound during the experiment is 24 seconds.

The compensation for this study is as follows. This task you will complete is a gambling task. Given the nature of the task, you could either win, or lose money. You will start with an endowment that we will give you of $20. The monetary outcomes of this task depend on your choices during the task. Specifically, depending on your choices during the task, you could then lose some of your endowment, or win more money. The total compensation will be between $10 and $30 dollars. You will also receive 2 units of extra credit for participation if you are completing the study for extra credit.

Would you like to continue to the pre-screening questions?

If yes: Continue
If no: Ask participant if they would like to reschedule the Phone Screen, or if participant declines, thank participant for his/her time, indicate that if they change their mind they are free to re-contact us and politely hang up.

Screening Questions:

To see if you may be eligible for this study, I would like to ask you some prescreening questions. If you are not eligible or decide not to participate, all the information collected today will be destroyed immediately. If you qualify for the study and decide to participate, we will ask you to sign a consent form when you come in for your appointment. The personal information you give me today will become part of your research record and will be reviewed by our research staff. Your name will not appear on this screening information. We will assign a code number and the code will be kept on our laboratory server. If you change your mind at any time and decide that

you do not want to participate, you can call us and we will immediately destroy the health information that we collect today. If at any time during this prescreening you would like to stop and not participate or if you have any questions, just let me know.

Would you like to continue now with the prescreening questions?"

If yes: Continue
If no: Ask participant if they would like to reschedule the Phone Screen, or if participant declines, thank participant for his/her time, indicate that if they change their mind they are free to re-contact us and politely hang up.

If the participant has not yet indicated how they heard about the study:
May I also ask how you heard about our study? _____

Where do you live currently? _____

Phone: [Do not record here]
Email: [Do not record here]

What is the best way to contact you? _____

What's your name? [Do not record here] Age? [Do not record here]
☐ If not between 18-55 years old, say "We are currently only recruiting individuals 18-55 years old, so you are not eligible to participate in this study."

Are you right or left handed? _____
☐ If not right handed, say "We are currently only recruiting right handed individuals, so you are not eligible to participate in this study."

Individuals currently taking certain medications will not be eligible to participate in this study.

Over the past 3 months, have you taken any mood stabilizers, such as Lithium or Depakote?
- ❑ No
- ❑ Yes

Ove the past 3 months, have you taken any benzodiazepines, such as Xanax or valium?
- ❑ No
- ❑ Yes

Over the past 3 months, have you taken any anti-psychotics, like Haldol, Clozaril, or Abilify?
- ❑ No
- ❑ Yes

Over the past 3 months, have you taken any stimulants, like Adderall, or Vyvanse?
- ❑ No
- ❑ Yes

Over the past 3 months, have you taken any anti-anxiety agents, like Clonezepam, or Alprazolam?

- ❑ No
- ❑ Yes

Over the past 3 months, have you taken any other psychotropic medications?

- ❑ No
- ❑ Yes

(If not qualified) Unfortunately, you did not meet criteria for participation in this study.

(If qualified, continue.)

Do you have a history of epilepsy?

- ❑ No
- ❑ Yes

If yes, please describe:_____

Do you have a history of stroke, seizures, brain tumor, head trauma, or other neurological disorder?

- ❑ No
- ❑ Yes

If yes, please describe:_____

Do you have any current or past cardiac illness?

- ❑ No
- ❑ Yes

If yes, please specify prescription (if known):_____

Do you have any current or past auditory pathology (including but not limited to hearing loss/damage, or tinnitus)?

- ❑ No
- ❑ Yes

Do you currently have a fever or other acute illness?

- ❑ No
- ❑ Yes

    - ❑ No (to all questions - continue)
    - ❑ Yes (to any questions) – I will need to check and see if that's allowed and get back to you.

Those are all the questions I have for you now. What questions do you have for me?

IF QUALIFIED:

You qualify for the experimental session I described earlier. As a reminder, that appointment lasts approximately 1.5 hours. What days and times are convenient for you? [schedule

appointment]. When you come in for the study, you will review a Consent document with further details of the study, which, if you decide to participate, you will sign. For your convenience, we will email you the Consent document so you can review it prior to coming to our lab.

IF NOT QUALIFIED:

Thank you for providing this information. Based on this information, I find that you don't qualify to participate in this study. All the information I collected for this prescreening will be erased. Thank you for your time.

Appendix G

Consent Document

Virginia Tech

Consent document

Research study titled "Reward and Loss Learning in Anxiety."

You are being asked to participate in a research study. Research studies include only people who choose to take part. This research study is being conducted by the psychology laboratory of Dr. John Richey at Virginia Tech. Participation is voluntary. Please read this consent form carefully. As the staff member discusses this Consent document with you, please ask him/her to explain any words or information that you do not clearly understand.

You will be given a copy of this consent form for your records.

Throughout this document, the acronym FNIRS will be used. FNIRS stands for *functional near-infrared spectroscopy*. FNIRS is a safe, non-invasive method enabling the measurement of real-time hemodynamic data, including total hemoglobin volume as well as blood oxygenation. FNIRS leverages these measurements to provide a measure of brain activity. FNIRS does not use x-rays or other radiation.

Overview of the study
You will undergo *Study Segments* 1) and 2) listed below. Total study time is approximately 1.5 hours. A description of each segment is outlined in this document.

Study Segments:

1) *Paper and pencil measures*
2) *FNIRS aversive loud noise task*

Purpose of the study
This study is being conducted in order to better understand learning mechanisms that are associated with anxiety.

How Many People Will Take Part In This Study?
Approximately 60 subjects will take part in this portion of the study.

Study Inclusion and Exclusion Criteria:

Inclusion Criteria
1. Male or female of any race or ethnicity.
2. Age at consent of 18-55 years.
3. Ambulatory status (outpatient) at time of consent.
4. Normal or corrected to normal vision.

Exclusion Criteria
1. Age less than 18 years or greater than 55 years, at time of consent.
2. Left handed-subjects excluded.
3. Inability to communicate satisfactorily and directly (without a translator) in English.
4. History of neurological injury.

5. Uncontrolled epilepsy.
6. Current use of psychotropic medication (past 3 months). Medications excluded are mood stabilizers, benzodiazepines, antipsychotics, stimulants, anti-depressants, and anti-anxiety agents.
7. Any cardiac illness.
8. Any auditory pathology.
9. Current fever or other acute illness.

How Long Will This Study Take?
Total study time is approximately 1.5 hours.

Description of Equipment, and Associated Risks
Throughout the task, you will undergo both FNIRS and an aversive loud noise procedure. Before describing the experimental procedures, we now describe both the FNIRS and aversive loud noise procedure, as well as the associated risks.

FNIRS risks
There are no known risks from FNIRS. However, it is not assured that harmful effects will not be recognized in the future.

Current scientific literature has not identified any risks to the developing fetus in pregnant women undergoing FNIRS. However, the researchers would strongly urge that women who are pregnant, or who may become pregnant prior to participating in the study, consult with their personal physician to determine whether the physician would or would not recommend their participation in the study.

You may feel uncomfortable or confined once the FNIRS cap is on your head. This feeling usually passes within a few minutes as the study staff talks with you and the study begins. However, if this feeling persists, you can tell the investigators and the cap will be removed immediately.

Loud noise risks
The aversive loud noise will be a series of 3-second, 85 decibel aversive noise blasts, delivered by headphones. This intensity of noise is comparable to the following: a passing diesel truck, a snow blower, or a food blender in the immediate vicinity. The specific aversive loud noise that will be used is the sound of metal scraping on slate. There is a possibility that the anticipation of aversive noise bursts might cause anxiety or irritation. In addition, these noise bursts are loud and might therefore elicit some physical discomfort, but this stimulation is not damaging or harmful on a long-term basis. Specifically, to ensure the stimulation intensity is not damaging, we follow recommendations outlined by the National Institute for Occupational Safety and Health (Occupational Noise Exposure Guide – revised edition, 1998). This requirement dictates that individuals not exceed exposure to an 85 decibel sound (which is the noise level of the stimulus you will hear) for longer than a duration of 8 hours. In this task, you will hear approximately 8 spaced out noise epochs of 3 seconds. Therefore, total exposure to this sound during the experiment is approximately 24 seconds. Neither the PI nor Virginia Tech have funds set aside for clinical treatment should it be necessary after the aversive noise exposure, and those costs would be incurred by the research subject.

Description of Procedures

During this study, you will complete a series of paper and pencil measures asking about your current and past mood. You will then complete an FNIRS aversive loud noise session. Each of these procedures is explained in more detail below.

Paper and pencil measures: You may be asked to fill out the following questionnaires: Demographic Questionnaire, Beck Depression Inventory (BDI-II), the State-Trait Anxiety Inventory (STAI), the Behavioral Inhibition and Activation Scales (BIS/BAS), and the Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ).

FNIRS and aversive loud noise sessions: In this portion of the study, FNIRS images will be taken while you complete a monetary choice task. FNIRS will provide information about the areas of the brain made active by particular kinds of stimuli and cognitive processes. You will complete a monetary choice task, during which you can choose to make various kinds of monetary gambles. The study staff will tell you exactly what stimuli you will receive during this study.

You will sit comfortably in a chair and the FNIRS technician, matched to your gender, will place the FNIRS cap on your head. The FNIRS cap is made of an elastic fabric, and covers the area of your scalp. This cap functions to hold optodes, which are small devices used to provide measurements of brain activity. The study staff will place the optodes in the cap while you are sitting comfortably in the chair. The study staff may apply a gel-like substance to certain areas of your scalp to allow the optodes to function correctly. We have a variety of cap sizes, and the study staff will work with you to ensure the cap is properly sized. While reviewing the Consent document in our laboratory, you will also be provided with an information sheet that lists the procedures indicating how the FNIRS device will be setup, and fitted to your head. At the end of the experiment, the gel can be completely washed from your hair, by washing your hair in the same way that you would remove shampoo (i.e., washing it out with water). Prior to completely washing your hair, wiping your hair with a paper towel will remove some (but not all) of the gel. You will be provided with paper towels.

During this FNIRS task, you will receive shorts bursts of aversive loud noise. Specifically, during some points in the task, you will be able to gamble without any possibility of receiving an aversive loud noise. For other trials, gambles will be accompanied with the possibility of receiving an aversive loud noise. You will be told when gamble choices might yield the possibility of loud noise. In addition to hearing the aversive loud noise during the FNIRS task, you will also hear the noise once before, and once after, the FNIRS task. The function of this is for you to provide a subjective rating of the experience of the noise.

Below is an overview of the study procedures:

1) You will complete a series of paper and pencil measures asking about your demographics, and current and past mood (25 minutes).

2) You will read instructions about the nature of the experimental tasks. You will also complete a 5-item multiple-choice quiz after reading the instructions, to ensure that all instructions are fully understood (10 minutes).

3) You will complete a "set up" that involves setting up both the FNIRS and aversive loud noise equipment (20 minutes).

4) Finally, you will complete the FNIRS/loud noise monetary choice task (30 minutes).

5) Before and after the FNIRS task, you will listen to the aversive loud noise, and rate your associated level of subjective aversion (5 minutes).

Other risks

One potential risk is that there is a loss of confidentiality. Every effort will be made to protect your confidential information, but this cannot be guaranteed. Your name will not be associated (i.e., written on) any of the data you provide. A numeric ID linking your name to your data will be kept on a secure laboratory server.

During the study you may answer questions about your current and/or past psychological history. One potential risk is that these questions may be difficult to think about.

Research Related Injuries
Neither the researchers nor Virginia Tech have money set aside to pay for medical care should you be injured during this research project, and any medical or psychological care that you seek during or after your participation will be at your own expense.

Incidental Findings
It must be emphasized that scans acquired during the study will not be evaluated by a medical professional. It should also be emphasized that the FNIRS staff and the principal investigators involved in this study, while qualified to administer FNIRS scans, are not medical doctors, and thus it is possible that abnormalities may go undetected by them.

Benefits
This research study is not a diagnostic medical test and will be of no direct benefit to you. Medical specialists will not examine the brain information gathered by FNIRS. If you believe that you require a diagnostic brain scan, you should discuss your concerns with your doctor. This study will be of no direct benefit to you but will improve our knowledge about the function of the human brain. There will be no charge to you for the research procedure.

Compensation
The compensation for this study is as follows. The task you will complete is a gambling task. Given the nature of the task, you could either win, or lose money. You will start with an endowment that we will give you of $20. The monetary outcomes of this task depend on your choices during the task. Specifically, depending on your choices during the task, you could then lose some of your endowment, or win more money. The total compensation will be between $10 and $30 dollars. In addition to this, if you are completing the study via SONA, or if you are enrolled in a psychology class that allows extra credit for completing studies, you will be offered 2 units of extra credit for participating in the study. You are free to choose not to participate. If you do participate, you are free to withdraw from this study at any time without loss of compensation to which you would have otherwise been entitled.

Data Storage and Confidentiality

Study records that identify you will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of Virginia Tech. Upon arrival in the lab, you may be asked questions to discern whether you have intentions to harm yourself or another. If you disclose information regarding child abuse, elder abuse, threat to harm self or others, or if a judge subpoenas identifying information regarding the data, the researchers are required by state law to break confidentiality and report that information to the appropriate local authorities.

For records disclosed outside of Virginia Tech, you will be assigned a unique code number. The key to the code will be kept on a secure server associated with our laboratory. Your study records will be identifiable to Dr. Richey and staff while stored in the lab at Virginia Tech. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Virginia Tech Institutional Review Board. If this group reviews your research record, they may also need to review the data that we gather as part of this study. Your name will not be associated with these audits.

Privacy regulations

The study results will be retained in your research record for at least six years after the study is completed. At that time either the research information not already in your record will be destroyed or information identifying you will be removed from such study results at Virginia Tech.

Right Not to Participate or to Withdraw

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled.

Who Do I Call If I Have Questions or Problems?

For questions about the study or a research-related injury, or if you have complaints, concerns or suggestions about the research, contact Dr. Richey at (540) 231-1453 during regular business hours. You may also email Dr. Richey at <richey@vt.edu>. You may also contact the Chair of the Human Subject's Committee, Dr. David Harrison (540) 231-4422.

Should you have any questions or concerns about the study's conduct or your rights as a research subject, or need to report a research-related injury or event, you may contact the Virginia Tech Institutional Review Board at irb@vt.edu or (540) 231-3732.

Statement of Consent:

"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask the questions that I have, and my questions have been answered to my satisfaction. I have been informed that I may contact Dr. Richey at (540-231-1453) to answer any questions I may have during the investigation and that I may contact the Virginia Tech Institutional Review Board (IRB) Office at (540) 231-3732 for any questions concerning my rights as a research participant or to discuss problems or concerns related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time."

Upon signing below, you are consenting to participate in study segments *1) Paper and pencil measures,* and *2) FNIRS aversive loud noise task*, described in this document.

1) *Paper and pencil measures*
2) *FNIRS aversive loud noise task*

_____	_____
Signature of Research Subject	Date
_____	_____
Signature of Person Obtaining Consent	Date

In addition to the study you will be completing today, it is possible that you may be eligible for other studies that our labs will be conducting in the future. If you are willing to be contacted, please indicate your willingness to be contacted by checking the "yes" box below.

If you do not wish to be contacted, do not fill out any of this information. If you do not wish to be contacted in the future this will have no bearing on your participation in the current study.

Yes, I wish to be contacted about future studies for which I may be eligible.

_____
Name

_____
Email

_____
Phone

_____

_____
Home Mailing Address

Preferred method of contact

EMAIL PHONE HOME ADDRESS (circle one)

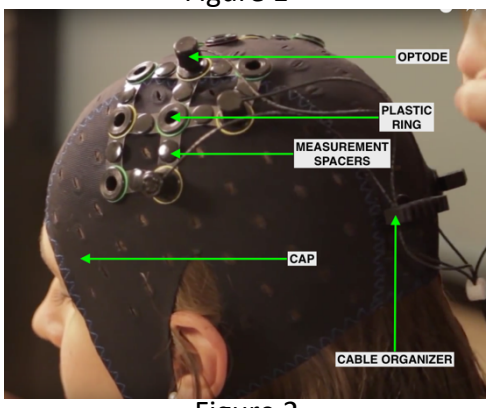
Appendix H

Participant FNIRS Capping Information Sheet

Information sheet: functional near-infrared spectroscopy (FNIRS) capping procedures

Study staff will place the FNIRS cap on your head. The cap holds the optodes. The optodes provide the ability to acquire the blood-oxygen-level dependent signal, which is the signal that represents neuronal activity. The measurement spacers will be placed on the cap, to ensure the optodes are appropriately spaced. The optodes will be placed into small plastic rings on the cap. These rings hold the optodes, and prevent the optodes from poking your head harshly (Figure 1).

Figure 1



To provide you with a cap that fits, a head measurement will be taken using a bendable plastic tape measure. After fitting the cap, the study staff will ask you whether the fitted size is comfortable. If the cap is too tight, the study staff will replace the cap with a larger cap size.

A wooden applicator will then be used to move the hair to the left and right, in the designated positions where the optodes will go (Figure 2). A small amount of optode gel may also be used (Figure 3). Moving the hair, and applying gel, functions to maximize the quality of the optode signal.

Figure 2

A cable organizer will be inserted into the back of the cap. This will organize the cables, and further, prevent movement of the optodes (Figure 1). Small clips may also be placed on the rear of your shirt, if additional stabilization if necessary.

Figure 3

An over-cap will then be placed over the optodes. This cap is made of a light fabric, and holds together via Velcro. The over-cap prevents light from interfering with the optode signal (Figure 4).

Figure 4

The ultrasonic gel can be completely washed from your hair, by washing your hair in the same way that you would remove shampoo (i.e., washing it out with water). Prior to washing your hair, while it is safe for the gel to be in contact with your skin, wiping your hair with a paper towel will remove some (but not all) of the gel. You will be provided with paper towels.

Appendix I

Demographic Data Form

DEMOGRAPHIC DATA FORM

1. Gender:

Male ____ Female ____ Other (please specify): ____

2. Age:

_____ years

3. Ethnicity/Race:

Are you of Hispanic or Latino heritage? YES NO

Please check the racial background or backgrounds that fit you best. If none of the categories are accurate for you, please write the correct information in on the last line.

____ American Indian/Alaska Native
____ Asian
____ Black/African American
____ Native Hawaiian or Other Pacific Islander
____ White/Caucasian
____ Other: _____

6. Current Employment Status:

____ Full-time
____ Part-time
____ Not employed

7. Student Status:

____ Full-time
____ Part-time
____ Not a student

8. Income Range: *(please check combined income if married)*

____ 0 - $10,000
____ $10,001 - $20,000
____ $20,001 - $40,000
____ $40,001 - $65,000
____ $65,001 - $100,000
____ more than $100,000

Appendix J

Beck Depression Inventory (BDI-II)

BDI-II

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. Sadness
- 0 I do not feel sad.
- 1 I feel sad much of the time.
- 2 I am sad all the time.
- 3 I am so sad or unhappy that I can't stand it.

2. Pessimism
- 0 I am not discouraged about my future.
- 1 I feel more discouraged about my future than I used to be.
- 2 I do not expect things to work out for me.
- 3 I feel my future is hopeless and will only get worse.

3. Past Failure
- 0 I do not feel like a failure.
- 1 I have failed more than I should have.
- 2 As I look back, I see a lot of failures.
- 3 I feel I am a total failure as a person.

4. Loss of Pleasure
- 0 I get as much pleasure as I ever did from the things I enjoy.
- 1 I don't enjoy things as much as I used to.
- 2 I get very little pleasure from the things I used to enjoy.
- 3 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings
- 0 I don't feel particularly guilty.
- 1 I feel guilty over many things I have done or should have done.
- 2 I feel quite guilty most of the time.
- 3 I feel guilty all of the time.

6. Punishment Feelings
- 0 I don't feel I am being punished.
- 1 I feel I may be punished.
- 2 I expect to be punished.
- 3 I feel I am being punished.

7. Self-Dislike
- 0 I feel the same about myself as ever.
- 1 I have lost confidence in myself.
- 2 I am disappointed in myself.
- 3 I dislike myself.

8. Self-Criticalness
- 0 I don't criticize or blame myself more than usual.
- 1 I am more critical of myself than I used to be.
- 2 I criticize myself for all of my faults.
- 3 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes
- 0 I don't have any thoughts of killing myself.
- 1 I have thoughts of killing myself, but I would not carry them out.
- 2 I would like to kill myself.
- 3 I would kill myself if I had the chance.

10. Crying
- 0 I don't cry anymore than I used to.
- 1 I cry more than I used to.
- 2 I cry over every little thing.
- 3 I feel like crying, but I can't.

_____ Subtotal Page 1

11. Agitation

0 I am no more restless or wound up than usual.
1 I feel more restless or wound up than usual.
2 I am so restless or agitated that it's hard to stay still.
3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of interest

0 I have not lost interest in other people or activities.
1 I am less interested in other people or things than before.
2 I have lost most of my interest in other people or things.
3 It's hard to get interested in anything.

13. Indecisiveness

0 I make decisions about as well as ever.
1 I find it more difficult to make decisions than usual.
2 I have much greater difficulty in making decisions than I used to.
3 I have trouble making any decisions.

14. Worthlessness

0 I do not feel I am worthless.
1 I don't consider myself as worthwhile and useful as I used to.
2 I feel more worthless as compared to other people.
3 I feel utterly worthless.

15. Loss of Energy

0 I have as much energy as ever.
1 I have less energy than I used to have.
2 I don't have enough energy to do very much.
3 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0 I have not experienced any change in my sleeping pattern.
1a I sleep somewhat more than usual.
1b I sleep somewhat less than usual.
2a I sleep a lot more than usual.
2b I sleep a lot less than usual.
3a I sleep most of the day.
3b I wake up 1-2 hours early and can't get back to sleep

17. Irritability

0 I am no more irritable than usual.
1 I am more irritable than usual.
2 I am much more irritable than usual.
3 I am irritable all the time.

18. Changes in Appetite

0 I have not experienced any change in my appetite.
1a My appetite is somewhat less than usual.
1b My appetite is somewhat greater than usual.
2a My appetite is much less than before.
2b My appetite is much greater than usual.
3a I have no appetite at all.
3b I crave food all the time.

19. Concentration Difficulty

0 I can concentrate as well as ever.
1 I can't concentrate as well as usual.
2 It's hard to keep my mind on anything for very long.
3 I find I can't concentrate on anything.

20. Tiredness or Fatigue

0 I am no more tired or fatigued than usual.
1 I get more tired or fatigued more easily than usual.
2 I am too tired or fatigued to do a lot of the things I used to do.
3 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

_____ Subtotal Page 2
_____ Subtotal Page 1

_____ **Total Score**

Appendix K

State-Trait Anxiety Inventory

SELF-EVALUATION QUESTIONNAIRE
STAI Y-1

DIRECTIONS: A number of statements which people used to describe themselves are given below. Read each statement and then blacken in the appropriate circle to the right of the statement to indicate how you feel RIGHT NOW, that is, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

		Not at all	Some-what so	Moder-ately	Very much so
1.	I feel calm	(1)	(2)	(3)	(4)
2.	I feel secure	(1)	(2)	(3)	(4)
3.	I feel tense	(1)	(2)	(3)	(4)
4.	I feel strained	(1)	(2)	(3)	(4)
5.	I feel at ease	(1)	(2)	(3)	(4)
6.	I feel upset	(1)	(2)	(3)	(4)
7.	I am presently worrying over possible misfortunes	(1)	(2)	(3)	(4)
8.	I feel satisfied	(1)	(2)	(3)	(4)
9.	I feel frightened	(1)	(2)	(3)	(4)
10.	I feel comfortable	(1)	(2)	(3)	(4)
11.	I feel self-confident	(1)	(2)	(3)	(4)
12.	I feel nervous	(1)	(2)	(3)	(4)
13.	I feel jittery	(1)	(2)	(3)	(4)
14.	I feel indecisive	(1)	(2)	(3)	(4)
15.	I feel relaxed	(1)	(2)	(3)	(4)
16.	I feel content	(1)	(2)	(3)	(4)
17.	I am worried	(1)	(2)	(3)	(4)
18.	I feel confused	(1)	(2)	(3)	(4)
19.	I feel steady	(1)	(2)	(3)	(4)
20.	I feel pleasant	(1)	(2)	(3)	(4)

SELF-EVALUATION QUESTIONNAIRE
STAI Y-2

DIRECTIONS: A number of statements which people used to describe themselves are given below. Read each statement and then blacken in the appropriate circle to the right of the statement to indicate how you GENERALLY feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

		Not at all	Some-what so	Moder-ately	Very much so
21.	I feel pleasant	(1)	(2)	(3)	(4)
22.	I feel nervous and restless	(1)	(2)	(3)	(4)
23.	I feel satisfied with myself	(1)	(2)	(3)	(4)
24.	I wish I could be as happy as others seem to be	(1)	(2)	(3)	(4)
25.	I feel like a failure	(1)	(2)	(3)	(4)
26.	I feel rested	(1)	(2)	(3)	(4)
27.	I am calm, cool, and collected	(1)	(2)	(3)	(4)
28.	I feel that difficulties are piling up so that I cannot overcome them	(1)	(2)	(3)	(4)
29.	I worry too much over something that really doesn't matter	(1)	(2)	(3)	(4)
30.	I am happy	(1)	(2)	(3)	(4)
31.	I have disturbing thoughts	(1)	(2)	(3)	(4)
32.	I lack self-confidence	(1)	(2)	(3)	(4)
33.	I feel secure	(1)	(2)	(3)	(4)
34.	I make decisions easily	(1)	(2)	(3)	(4)
35.	I feel inadequate	(1)	(2)	(3)	(4)
36.	I am content	(1)	(2)	(3)	(4)
37.	Some unimportant thought runs through my mind and bothers me	(1)	(2)	(3)	(4)
38.	I take disappointments so keenly that I can't put them out of my mind	(1)	(2)	(3)	(4)
39.	I am a steady person	(1)	(2)	(3)	(4)
40.	I get in a state of tension or turmoil as I think over my recent concerns and interests	(1)	(2)	(3)	(4)

Appendix L

Bandit Task Quiz

Task Quiz
(please circle True or False)

The position of a shape on the screen affects the outcome tied to that shape.
True
False

For the Aversive Noise rounds, every time you make a choice, there is a 10% chance that you will hear an aversive noise.
True
False

You will complete all Aversive Noise rounds together, and all Safe rounds together
That is, all Aversive Noise rounds will be blocked together, and all Safe rounds will be blocked together.
True
False

The outcomes tied to the shapes are completely random, and as such, some shapes are not better than others.
True
False

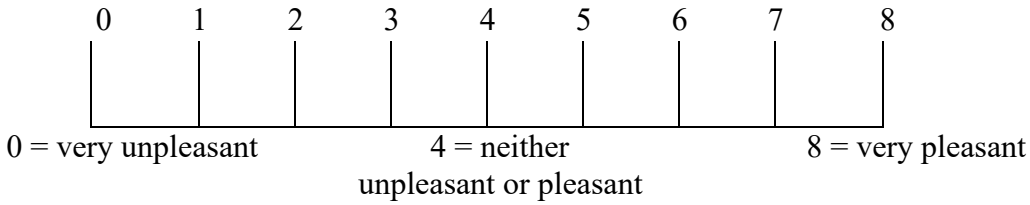
During Safe rounds, there is absolutely no possibility that you will hear an aversive noise.
True
False

Appendix M

Noise Subjective Rating Scale

Noise subjective rating scale

Please rate your subjective experience of the aversive loud noise on the following scale (please circle a number):



Appendix N

IRB Approval Document

VIRGINIA TECH

Division of Scholarly Integrity and Research Compliance
Institutional Review Board
North End Center, Suite 4120 (MC 0497)
300 Turner Street NW
Blacksburg, Virginia 24061
540/231-3732
irb@vt.edu
http://www.research.vt.edu/sirc/hrpp

MEMORANDUM

DATE: May 16, 2019

TO: John Anthony Richey, Maria Eddleman, Andrew D Valdespino, Benjamin Bradford DeVore, Jessica Tourville

FROM: Virginia Tech Institutional Review Board (FWA00000572, expires January 29, 2021)

PROTOCOL TITLE: Reward and Loss Learning in Anxiety

IRB NUMBER: **17-882**

Effective April 6, 2019, the Virginia Tech Institution Review Board (IRB) approved the Amendment request for the above-mentioned research protocol.

This approval provides permission to begin the human subject activities outlined in the IRB-approved protocol and supporting documents.

Plans to deviate from the approved protocol and/or supporting documents must be submitted to the IRB as an amendment request and approved by the IRB prior to the implementation of any changes, regardless of how minor, except where necessary to eliminate apparent immediate hazards to the subjects. Report within 5 business days to the IRB any injuries or other unanticipated or adverse events involving risks or harms to human research subjects or others.

All investigators (listed above) are required to comply with the researcher requirements outlined at:

https://secure.research.vt.edu/external/irb/responsibilities.htm

(Please review responsibilities before beginning your research.)

PROTOCOL INFORMATION:

Approved As:	**Full Review**
Protocol Approval Date:	**October 24, 2018**
Protocol Expiration Date:	**October 23, 2019**
Continuing Review Due Date*:	**September 23, 2019**

*Date a Continuing Review application is due to the IRB office if human subject activities covered under this protocol, including data analysis, are to continue beyond the Protocol Expiration Date.

ASSOCIATED FUNDING:

The table on the following page indicates whether grant proposals are related to this protocol, and which of the listed proposals, if any, have been compared to this protocol, if required.