Clinical Trials Protocol for "Reward Processes and Rehearsal in Exposure Therapy" (NCT06132425)

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Study Description:
The purpose of this study is to 1) examine the importance of self-reported relief following exposure and 2) test whether positive-focused rehearsal following exposure can improve treatment outcomes for participants who endorse fear of public speaking. Exposure therapy is an extinction-based behavioral technique, often employed in the context of cognitive behavioral therapy. It involves strategically exposing an individual to a feared stimulus in an effort to generate new non-fear associations with that stimulus. Relief refers to the positive, rewarding emotions associated with the absence of an expected aversive outcome following exposure to a feared stimulus. In the current study, participants will engage in a series of short public speaking exposures that take place over two sessions. After every two exposures, participants will be asked to complete either a positive or neutral rehearsal exercise, consisting of recalling either positive or neutral aspects of the speech exposures. At multiple points throughout the study, participants will complete ratings of reward sensitivity, positive affect, relief, and expectancy of the aversive outcome. We will test whether 1) participants with higher reward sensitivity and positive affect will report more relief after each exposure, and 2) participants who report experiencing more relief after each exposure will learn more quickly that the feared stimulus does not predict an aversive outcome (i.e., learning rate). We will also test whether participants who engage in the positive rehearsal exercise will show 1) greater reduction in public speaking anxiety symptoms at the end of the study, 2) greater improvements in reward sensitivity and positive affect, and 3) a faster learning rate and changes in relief over the course of the study. The sample will be volunteer UCLA undergraduates who endorse fear and avoidance of public speaking, measured by two Likert scale screening questions. They will come in at two time points: Visit 1 (first set of exposures) and Visit 2 (second set of exposures), and will complete a few short surveys one week after Visit 2.

Background & Significance:
Treatment response rates for cognitive behavioral therapy (CBT) across anxiety disorders average approximately 50% post-treatment and at follow-up (Loerinc et al., 2015). Thus, recent research has amplified efforts toward improving treatment methodology in an attempt to optimize clinical outcomes. Many efforts have targeted exposure therapy, an evidence-based behavioral technique during which a participant is strategically and repeatedly exposed to a feared stimulus in order to generate new non-fear associations with that stimulus.

Mechanisms of exposure therapy have been conceptualized using inhibitory retrieval models of extinction learning. These models, derived from Pavlovian conditioning, posit that extinction is dependent upon formation of an inhibitory association where the feared conditional stimulus (CS) no longer predicts the aversive unconditional stimulus (US). The new inhibitory CS-noUS association then competes with the original CS-US association. Research has demonstrated that greater expectation of US occurrence (US expectancy) followed by the unexpected omission of the US (i.e., expectancy violation) is associated with greater learning of the inhibitory association (Bouton, 1993). Exposure therapy is a clinical proxy of extinction; in order to compete with the original association between public speaking (CS) and rejection (US), participants engage in repeated exposures to the CS without the US (no rejection) and form a

new inhibitory association wherein public speaking no longer predicts rejection (Craske et al., 2022). Strategies to enhance this inhibitory learning process include mental rehearsal, where information from a previous exposure trial is recounted to reinforce the newly learned inhibitory association (McGlade & Craske, 2021).

There is also promising evidence which suggests that reward processes may facilitate extinction learning, though studies have yet to be conducted in a clinical sample. Experimental studies have demonstrated that greater relief, a positive emotion that occurs following US omission, is associated with greater expectancy violation (San Martín et al., 2020; Vervliet et al., 2017; Willems & Vervliet, 2021). This suggests that positive emotions during exposure (e.g., relief) may directly influence the extinction learning process. Reduced positive affect has been associated with decreased updating of US expectancies, leading to slower learning during extinction (Young et al., 2021). In contrast, elevated positive affect has been associated with enhanced encoding, rehearsal, and retrieval processes, which may lead to faster learning during extinction and prevent return of fear (i.e., relapse) (Zbozinek & Craske, 2017). Strategies designed to enhance reward sensitivity and positive affect may therefore be an important avenue of future research to improve exposure therapy outcomes. While not yet applied during exposure, strategies aimed to increase reward sensitivity via positive-focused rehearsal have led to decreased anxiety, depression, and negative affect and increased positive affect (Chen et al., 2021; Craske et al., 2019, in press; A. Waters et al., 2016; L. Waters & Stokes, 2015). Recent work has shown that rehearsal without a positive focus immediately following exposure leads to reductions in anxiety (McGlade & Craske, 2021). Therefore, rehearsal following exposure that specifically focuses on positive emotions to increase reward sensitivity has the potential to lead to even greater symptom improvement.

Thus, the current study seeks to examine the role of relief during extinction learning and to test whether positive-focused rehearsal exercise may be implemented to improve treatment outcomes in exposure therapy in a population of individuals who demonstrate excessive fear of public speaking. There are three main goals of the study: 1) examine whether baseline reward sensitivity and positive affect predict relief following exposure, 2) examine whether relief predicts subsequent extinction learning across exposure trials., and 3) test the efficacy of a positive rehearsal exercise following exposure compared to a neutral rehearsal exercise. Participants will be randomized to either complete positive or neutral rehearsal exercises following exposure. Prior research has shown that mental rehearsal following exposure enhances treatment results (McGlade & Craske, 2021). Thus, all participants are expected to see positive results following exposure and rehearsal exercises, but participants who complete positive rehearsal exercises are expected to exhibit greater reward sensitivity and positive affect, thereby strengthening their learning of the new inhibitory association and exhibiting greater treatment effects.

Specific Aims:

The overall aim of this research is to evaluate methods for enhancing the effectiveness of exposure therapy for the treatment of anxiety disorders, and to better understand reward and relief mechanisms as they relate to extinction learning during exposure. Exposure therapy is an

extinction-based behavioral technique, often employed in the context of cognitive behavioral therapy (CBT). It involves strategically exposing a participant to a feared stimulus in an effort to generate new non-fear associations with that stimulus. Importantly, across anxiety disorders, treatment response rates for CBT average approximately 50% post-treatment and at follow-up, indicating a need for more effective treatment methodology (Loerinc et al., 2015).

The current research specifically aims to examine the role of relief during extinction learning and to test whether positive-focused rehearsal exercise may be implemented to improve treatment outcomes in exposure therapy in a population of individuals who demonstrate excessive fear of public speaking. This is a highly relevant population, given that the National Comorbidity Survey Replication estimated that 13% of Americans are estimated to experience social phobia at some point in their lives (Kessler et al., 2012). Further, a more recent study assessed over 1100 college students and 63.9% reported a fear of public speaking (Ferreira Marinho et al., 2017). The current study has three primary aims. First, the study seeks to examine whether baseline reward sensitivity and positive affect predict relief following exposure. Second, the study seeks to examine whether relief predicts subsequent extinction learning across exposure trials. Third, the study seeks to test the efficacy of a positive rehearsal exercise following exposure, characterized by technology-guided recall and rehearsal of positively-valenced emotional aspects of speech exposures done in session, relative to a neutral rehearsal exercise following exposure, characterized by technology-guided recall and rehearsal of non-emotional, factual aspects of speech exposures done in session.

Participants will complete rehearsal exercises after every two exposures to ensure there is sufficient content for rehearsal. Learning rate (change in expectancy of an aversive outcome across exposure trials) and relief rate (change in relief ratings across exposure trials) will be calculated based on self-reported expectancy and relief ratings provided after each exposure. We hypothesize that regardless of rehearsal group assignment, participants with reduced baseline reward sensitivity and positive affect will exhibit a slower relief rate relative to individuals with elevated baseline reward sensitivity and positive affect, and that lower positive affect will be associated with lower subsequent relief ratings relative to higher positive affect. We hypothesize that regardless of group assignment, higher relief ratings after the first exposure will be associated with a faster learning rate on subsequent exposure trials. Finally, we hypothesize that the positive rehearsal group will lead to significantly greater reductions in symptoms of social phobia and greater increases in reward sensitivity and positive affect at the end of the study, as well as faster learning and relief rates relative to the neutral rehearsal group.

Research Design & Methods:
Visits will either be conducted over HIPAA-compliant video conferencing platform Zoom or in person.

OVERVIEW
The experiment will consist of two study visits. Visit 1 will include informed consent and questionnaires. Participants will then complete a series of short 1-minute public speaking

exposures. After every two exposures, participants will complete a rehearsal task where the participant is asked to use a positive or neutral approach to remember and recount the exposures they have just completed (for a total of approximately 60-90 minutes). Visit 2 will occur approximately 1 week after Visit 1 and will consist of another series of short 1-minute public speaking exposures, followed by the same rehearsal task after every two exposures. Participants will then be asked to complete another series of questionnaires (for a total of approximately 60-90 minutes) For the rehearsal task in Visits 1 and 2, participant will be randomized to practice rehearsing a) focusing on positive emotional aspects of the exposures, or b) focusing on neutral, factual aspects of the exposures. One week after Visit 2, participants will be asked to complete a brief set of questionnaires (approximately 5-10 minutes).

Prospective participants will be recruited through the UCLA Psychology Department Subject Pool (i.e., SONA). Prior to signing up for the study, prospective participants recruited through SONA will complete two public speaking anxiety screening questions as part of SONA's prescreening process to determine eligibility for participation. The questions are "How anxious would you feel giving a formal speech before a live audience?" and "How likely would you be to avoid taking a class that required an oral presentation?" Both questions are rated from 0 to 8, with zero indicating no anxiety/never avoid and 8 indicating extreme anxiety/aways avoid. Eligible participants must report a score of 6 or higher on the first question and a score of 5 or higher on the second question. Participants will be assigned course credit after participating in the study. Participants will sign up for the study only if they are able to make both visits of the experiment. If the participant does not attend both visits, course credit will still be given for the amount of time the participant spent doing the experiment (i.e., 1 credit for 1 hour).

VISIT 1

On Visit 1, participants will first provide informed consent after the nature of the study has been fully explained and the participant has had time to ask questions. After obtaining informed consent participants will complete a demographics and eligibility questionnaire, which will be reviewed by the researcher upon completion. Ineligible participants (i.e., participants with scores below a 6 on public speaking anxiety and below a 5 on public speaking avoidance, who do not speak English, or are below 18 years of age) will be informed that they do not meet criteria and the research session will be terminated at this time. Participants participating for credit who are found to be ineligible will still receive .5 credits for their time.

Participants will then complete the remaining study questionnaires, the Liebowitz Social Anxiety Scale (LSAS, Leibowitz, 1987), Personal Report of Public Speaking Anxiety (PRPSA, McCroskey, 1970), 8-item version (excluding the suicide item) of the Patient Health Questionnaire-9 (PHQ-9, Kroenke et al., 2001), Positive Valence System Scale (PVSS, Khazanov et al., 2020), Behavioral Activation Scale (BAS, Carver & White, 1994), and a visual analog scale that assesses current positive and negative emotions on a scale from 1-9 (1=neutral/no emotion, 9=extreme emotion; adapted from Lang, 1980).

Eligibility Questionnaire

Demographics Questionnaire

Liebowitz Social Anxiety Scale (LSAS, Leibowitz, 1987)
Personal Report of Public Speaking Anxiety (PRPSA, McCroskey, 1970)
8-item version (excluding the suicide item) of the Patient Health Questionnaire-9 (PHQ-9, Kroenke et al., 2001)
Positive Valence System Scale (PVSS, Khazanov et al., 2020)
Behavioral Activation Scale (BAS, Carver & White, 1994)
Visual Analog Scale (adapted from Lang, 1980)

All participants will then engage in a series of exposure practices. They will undergo 8 exposure trials for durations of 1 minute each. Prior to the first exposure, participants will be asked to record their feared negative outcome (i.e., unconditioned stimulus [US]), such as social rejection, to be used for reference during future US expectancy and relief ratings. During each exposure trial, they will first complete self-reported current fear/anxiety ratings ("How fearful and anxious are you right now about giving this speech?" where 0 = not at all, 50 = moderately, and 100 = very) and US expectancy ratings ("How likely is it that the feared outcome will occur?" where 0 = certain the feared outcome will not occur, 50 = completely uncertain, and 100 = certain the feared outcome will occur). Participants will then have 10 seconds to look at a speech topic followed by one minute of giving this speech to an audience of two confederates. Immediately after the exposure, participants will complete self-reported current fear/anxiety ratings ("How fearful and anxious are you right now after giving this speech?" where 0 = not at all, 50 = moderately, and 100 = very), US expectancy ratings ("If you were to complete the same exact speech again, how likely is it that the feared outcome would occur?" where 0 = certain the feared outcome will not occur, 50 = completely uncertain, and 100 = certain the feared outcome will occur; and "Did the feared outcome occur?" where 0 = no, and 1 = yes), and relief ratings ("How relieved are you that the feared outcome did not occur?" where 0 = not at all, 50 = moderately, and 100 = very). Participants will then be given another speech topic and will follow the same procedure.

Participants will be randomized at the start of the study to a positive or neutral rehearsal group. After every two exposure trials, participants will then complete a rehearsal exercise. Before the rehearsal exercise, participants will complete the visual analog scale to assess current mood. Participants will then be presented with instructions to complete a verbal rehearsal of the two exposures they just completed, followed by a written rehearsal of the two exposures they just completed. After the rehearsal exercise, participants will again rate their current mood using the visual analog scale, US expectancy ratings ("If you were to complete the same exact speech again, how likely is it that the feared outcome would occur?" where 0 = certain the feared outcome will not occur, 50 = completely uncertain, and 100 = certain the feared outcome will occur; and "Did the feared outcome occur?" where 0 = no, and 1 = yes), and relief ratings ("How relieved are you that the feared outcome did not occur?" where 0 = not at all, 50 = moderately, and 100 = very).

This entire process will be repeated four times, resulting in a total of 8 exposure practices and 4 rehearsal exercises. The visit is expected to take approximately 60-90 minutes to complete.

VISIT 2

Visit 2 will occur approximately one week after Visit 1. Participants will first complete ratings on the visual analog scale to assess current mood. Participants will then undergo 8 exposure trials for durations of 1 minute each. Prior to the first exposure, participants will be asked to record their feared negative outcome (e.g., social rejection). During each exposure trial, they will first complete self-reported current fear/anxiety ratings ("How fearful and anxious are you right now about giving this speech?" where 0 = not at all, 50 = moderately, and 100 = very) and US expectancy ratings ("How likely is it that the feared outcome will occur?" where 0 = certain the feared outcome will not occur, 50 = completely uncertain, and 100 = certain the feared outcome will occur). Participants will then have 10 seconds to look at a speech topic followed by one minute of giving this speech to an audience of two confederates. Immediately after the exposure, participants will complete self-reported current fear/anxiety ratings ("How fearful and anxious are you right now after giving this speech?" where 0 = not at all, 50 = moderately, and 100 = very), US expectancy ratings ("If you were to complete the same exact speech again, how likely is it that the feared outcome would occur?" where 0 = certain the feared outcome will not occur, 50 = completely uncertain, and 100 = certain the feared outcome will occur; and "Did the feared outcome occur?" where 0 = no, and 1 = yes), and relief ratings ("How relieved are you that the feared outcome did not occur?" where 0 = not at all, 50 = moderately, and 100 = very). Participants will then be given another speech topic and will follow the same procedure.

After every two exposure trials, participants will then complete a rehearsal exercise (either positive or neutral rehearsal depending on their group assignment). Before the rehearsal exercise, participants will complete the visual analog scale to assess current mood. Participants will then be presented with instructions to complete a verbal rehearsal of the two exposures they just completed, followed by a written rehearsal of the two exposures they just completed. After the rehearsal exercise, participants will again rate their current mood using the visual analog scale, US expectancy ratings ("If you were to complete the same exact speech again, how likely is it that the feared outcome would occur?" where 0 = certain the feared outcome will not occur, 50 = completely uncertain, and 100 = certain the feared outcome will occur; and "Did the feared outcome occur?" where 0 = no, and 1 = yes), and relief ratings ("How relieved are you that the feared outcome did not occur?" where 0 = not at all, 50 = moderately, and 100 = very).

This entire process will be repeated four times, resulting in a total of 8 exposure practices and 4 rehearsal exercises. Participants will then complete a brief set of questionnaires including the LSAS, PRPSA, PVSS, and BAS. The visit is expected to take approximately 60-90 minutes to complete.

FOLLOW-UP

After completion of Visit 2, approximately one week later participants will be sent a short list of questionnaires to be completed independently. Surveys include the public anxiety screening questions, PRPSA, PVSS, and BAS and are expected to take 5-10 minutes to complete.

After completion of the follow-up surveys, participants will be compensated for their time one credit per hour of study participation. All participants will additionally be provided with a referral list at the end of the study.

Statistics & Data Analysis:

Sample size. The sample size will be 74 participants (37 per group). An a priori analysis using G*Power (Faul et al., 2007) indicated that a sample size of 74 would be sufficient to detect a significant effect based on a similar previous study (d=.30; Craske et al., 2019) with a power of .80 and an alpha of .05.

Reward sensitivity and positive affect predicting relief. Linear mixed models will be utilized to assess whether baseline reward sensitivity, measured by the Positive Valence System Scale (PVSS, Khazanov et al., 2020) and the Behavioral Activation Scale (BAS, Carver & White, 1994), and positive affect, measured by a visual analog scale, predict relief rate over the course of exposures. Relief rate will be calculated using a computational model derived from the Rescorla-Wagner model (Rescorla & Wagner, 1972) to capture change in self-reported relief ratings over time. A linear mixed model will also be utilized to assess whether positive affect before an exposure trial predicts subsequent relief on the same trial.

Relief predicting learning rate. A linear mixed model will be utilized to assess whether relief after the first exposure trial predicts learning rate for subsequent exposure trials. Learning rate will be calculated using a computational model derived from the Rescorla-Wagner model (Rescorla & Wagner, 1972) to capture change in self-reported US expectancy ratings over time.

Comparison of positive and neutral rehearsal exercises. A repeated measures between-subjects ANOVA will be utilized to test whether participants in the positive rehearsal intervention show greater reductions in anxiety symptoms (public speaking anxiety screening questions; LSAS, Liebowitz, 1987; PRPSA, McCroskey, 1970) or greater increases in positive affect or reward sensitivity relative to participants in the neutral rehearsal intervention. We will use paired samples t-tests to test whether participants in the positive rehearsal intervention show a faster learning rate or relief rate relative to participants in the neutral rehearsal intervention.