ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: April 4, 2022

ClinicalTrials.gov ID: NCT05203861

Study Identification

Unique Protocol ID:	R33MH115138
Brief Title:	Affect Treatment for Depression and Anxiety
Official Title:	Reward and Threat Sensitivity as Mediators of Positive and Negative Affect Treatment
Secondary IDs:	

Study Status

Record Verification:	April 2022
Overall Status:	Recruiting
Study Start:	November 22, 2021 [Actual]
Primary Completion:	May 31, 2024 [Anticipated]
Study Completion:	May 31, 2024 [Anticipated]

Sponsor/Collaborators

Sponsor:	University of California, Los Angeles
Responsible Party:	Principal Investigator Investigator: Michelle Craske [mcraske] Official Title: Principal Investigator Affiliation: University of California, Los Angeles
Collaborators:	Southern Methodist University

Oversight

U.S. FDA-regulated Drug:	No
U.S. FDA-regulated Device:	No
U.S. FDA IND/IDE:	No
Human Subjects Review:	Board Status: Approved Approval Number: 21-001788 Board Name: UCLA Medical Institutional Review Board 3 Board Affiliation: U. S. Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP) Phone: (310) 825-5221 Email: RUTH.TESFAMICHAEL@RESEARCH.UCLA.EDU Address:

11000 KINROSS AVENUE
STE 211
LOS ANGELES, CA 90095

Data Monitoring: Yes

FDA Regulated Intervention: No

Study Description

Brief Summary: The purpose of this study is to evaluate the efficacy and mediators of change in Positive Affect Treatment, a psychotherapy specifically aimed at enhancing reward sensitivity in individuals with low positive affect (a core feature of anhedonia) in the context of depression or anxiety.

Target enrollment is 100 male and female participants with low positive affect and depression or anxiety and impaired functioning, between the ages of 18 and 65 years, who will be randomized to either Positive Affect Treatment or Negative Affect Treatment (designed to reduce threat sensitivity). Participants will complete laboratory tests, psychiatric assessments, and self-report questionnaires as part of the study.

The total length of participation is around 5 months.

Detailed Description: Low positive affect in the context of depression or anxiety has been relatively resistant to pharmacological and psychological treatments. Newer treatments that focus upon positivity or reward sensitivity have shown promising results.

As a replication and extension of a prior NIMH funded R61 phase trial, the purpose of this R33 phase randomized controlled trial is to evaluate the efficacy and mediators of change of Positive Affect Treatment (designed to augment reward sensitivity) for individuals with low positive affect in the context of depression or anxiety symptoms. Mediators (targets) include behavioral, cognitive, physiological and experiential measures of two reward targets: reward anticipation and response to reward attainment. Specificity of target engagement is assessed by comparison with Negative Affect Treatment, designed to reduce threat sensitivity, and by including behavioral, cognitive, physiological and experiential mediators (targets) that assess threat sensitivity.

Clinical outcomes are assessed at baseline and either weekly or at Week 5, Week 10, Week 15 (post), and one-month follow-up. Mediators (targets) are assessed at baseline, Week 5, Week 10, Week 15 (post) and one-month follow-up. Mediational models will evaluate the degree to which change in the target measures explain change in the outcome measures.

Target enrollment is 100 male and female participants with low positive affect and depression or anxiety and impaired functioning between the ages of 18 and 65 who will be randomized to Positive Affect Treatment or Negative Affect Treatment, each comprising 15 individual psychotherapy sessions.

Participants will complete laboratory tests and psychiatric assessments and self-report questionnaires as part of the study. Total length of participation is around 5 months.

Conditions

Conditions: Depression
Anxiety

Keywords:

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	N/A
Interventional Study Model:	Parallel Assignment
Number of Arms:	2
Masking:	Single (Outcomes Assessor)
Allocation:	Randomized
Enrollment:	100 [Anticipated]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Positive Affect Treatment 15 sessions of psychotherapy designed to augment reward anticipation, reward attainment, and reward learning.	Behavioral: Positive Affect Treatment Sessions 1-7: Pleasurable activities + imaginal recounting and reinforcement of positive mood effects (continued for sessions 8-15) Sessions 8-10: Cognitive exercises focusing on identifying positive aspects of experience, taking responsibility for positive outcomes, and imagining future positive events Sessions 11-14: Exercises to cultivate and savor positive experiences Session 15: Relapse prevention.
Active Comparator: Negative Affect Treatment 15 sessions of psychotherapy designed to decrease threat avoidance, threat appraisal and arousal.	Behavioral: Negative Affect Treatment Sessions 1-7: Exposure therapy to feared or avoided situations, sensations, or memories (continued for sessions 8-15) Sessions 8-10: Cognitive restructuring of probability, cost, and attributional biases Sessions 11-14: Capnometry-assisted respiratory training Session 15: Relapse prevention

Outcome Measures

Primary Outcome Measure:

1. Positive and Negative Affect Schedule Expanded (PANAS-X) (General Dimensions Scales)
   Reported positive affect (general dimensions scale positive affect) and negative affect (general dimension scale negative affect) (score range for each scale: 10-50, higher scores represent higher levels of positive affect or negative affect).

   [Time Frame: Baseline to post-treatment (16 weeks) and follow-up (20 weeks)]
2. Depression Anxiety and Stress Scale (DASS-21)
   Reported symptoms of depression (score range: 0-21), anxiety (score range: 0-21), and stress (score range: 0-21), higher scores indicate higher severity and frequency.

   [Time Frame: Baseline to post-treatment (16 weeks) and follow-up (20 weeks)]

Secondary Outcome Measure:

3. Interviewer Anhedonia Ratings
   Interviewer ratings of interest, pleasure, and motivation in hobbies/pastimes, foods/drinks, social activities (score range: 1-12), higher scores indicate lower anhedonia

   [Time Frame: Baseline to post-treatment (16 weeks) and follow-up (20 weeks)]
4. Sheehan Disability Scale (SDS)

Reported impairment due to symptoms (score range: 0-30) with higher scores indicating greater impairment. Includes reported number of days of missed school/work and number of days of reduced productivity.

[Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

5. Beck Scale for Suicide Ideation
   Reported suicidal ideation (score range: 0-38), higher scores indicate higher suicidality

   [Time Frame: Baseline to post-treatment (16 weeks) and follow-up (20 weeks)]

6. Positive and Negative Affect Schedule Expanded (PANAS-X) Basic Positive Emotions Scales and Serenity
   Mediator: Reported positive affect (basic positive emotions scales and serenity) (score range: 19 – 95). Note: items which overlap with the general dimensions scale for positive affect (see Outcome 1) will not be included in this composite score. Excluded overlapping items include: alert, attentive, determined, enthusiastic, excited, proud, and strong.

   [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

7. Effort-Expenditure for Rewards Task (EEfRT)
   Mediator: behavioral effort for reward

   [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

8. Monetary Incentive Task
   Mediator: cardiac acceleration to anticipation of reward

   [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

9. Behavioral Inhibition/Behavioral Activation (reward drive subscale) (BAS-RD)
   Mediator: Reported reward sensitivity (score range: 4-16), and threat sensitivity (score range: 7-28), with higher scores indicating higher sensitivity

   [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

10. Dimensional Anhedonia Rating Scale
    Mediator: Reported reward desire, motivation, effort, and pleasure (score range: 0-68), with higher scores indicating higher degree of reward desire, motivation, effort, and pleasure

    [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

11. Modified Attentional Dot Probe Task
    Mediator: attentional engagement with positive and negative stimuli

    [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

12. International Affective Picture System Task
    Mediator: cardiac response to positive stimuli

    [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

13. Temporal Experience of Pleasure Scale (consummatory subscale)
    Mediator: Reported reward consummatory pleasure (score range: 8-48)

    [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

14. Anxiety Sensitivity Index
    Mediator: Reported threat appraisal of anxiety (score range: 0-64)

    [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

15. Probability and Cost Questionnaire for Social and Physical Outcomes
    Mediator: Reported threat appraisal of social and physical outcomes (score range: 0-80 for each subscale), with higher scores indicating higher cost/probability estimation

    [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

16. Mental Arithmetic Task
    Mediator: cardiorespiratory response to stress

    [Time Frame: Baseline, Week 5, Week 10, post-treatment (Week 16) and follow-up (Week 20)]

Eligibility

Minimum Age: 18 Years

Maximum Age: 65 Years

Sex: All

Gender Based: No

Accepts Healthy Volunteers: No

Criteria: Inclusion Criteria:

- English-speaking
- Low positive affect indexed by less than or equal to 24 on the positive affect subscale of the PANAS (i.e., PANAS-P); and scores of greater than or equal to 11 for depression, greater to or equal to 6 for anxiety, or greater to or equal to 10 for stress on the Depression, Anxiety, and Stress Scale; and scores of greater than or equal to 5 on any Sheehan Disability Scale subscale.
- Willingness to refrain from starting other psychosocial or pharmacological treatments until study completion.

Exclusion Criteria:

- Patient report of serious medical conditions - such as history of serious, uncontrolled medical illness, or instability (including significant cardio-pulmonary disease, organic brain syndrome, seizure disorder, cerebrovascular disease, thyroid dysfunction, and diabetes)
- Active suicidal ideation
- Lifetime history of bipolar disorder, psychosis, cognitive impairment, or organic brain damage
- Substance abuse in the last 6 months or dependence within last 12 months.
- Greater than 11 cigarettes per week or nicotine equivalent
- History of marijuana, cocaine or stimulant use 5-7 times/week or more before age 15 (e.g., amphetamine, cocaine, methamphetamine)
- Willingness to refrain from marijuana use 1 week before laboratory assessments
- Pregnancy
- Bupropion, dopaminergic or neuroleptic medications use in the past 6 months
- Heterocyclics and SSRIs are permitted if stabilized (3 months) and PRN benzodiazepines and beta-blockers are permitted but discouraged on laboratory assessment visits
- Refusal of video/audio-taping
- Prior participation in previous waves of this study

Contacts/Locations

Central Contact Person: Shawn Wang, B.A.
Telephone: (209) 800-8930
Email: shawnwang@psych.ucla.edu

Central Contact Backup: Michelle G Craske, Ph.D
Telephone: (310) 206-9191
Email: MCraske@mednet.ucla.edu

Study Officials:

Locations: **United States, California**
University of California, Los Angeles

[Recruiting]
Los Angeles, California, United States, 90095
Contact: Michelle G Craske, PhD 310-206-9191
MCraske@mednet.ucla.edu
Principal Investigator: Michelle G. Craske, Ph.D

United States, Texas
Southern Methodist University
[Recruiting]
Dallas, Texas, United States, 75205
Contact: Alicia E Meuret, PhD 214-768-3422 ameuret@mail.smu.edu
Principal Investigator: Alicia E Meuret, PhD
Principal Investigator: Thomas Ritz, PhD

IPDSharing

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References

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