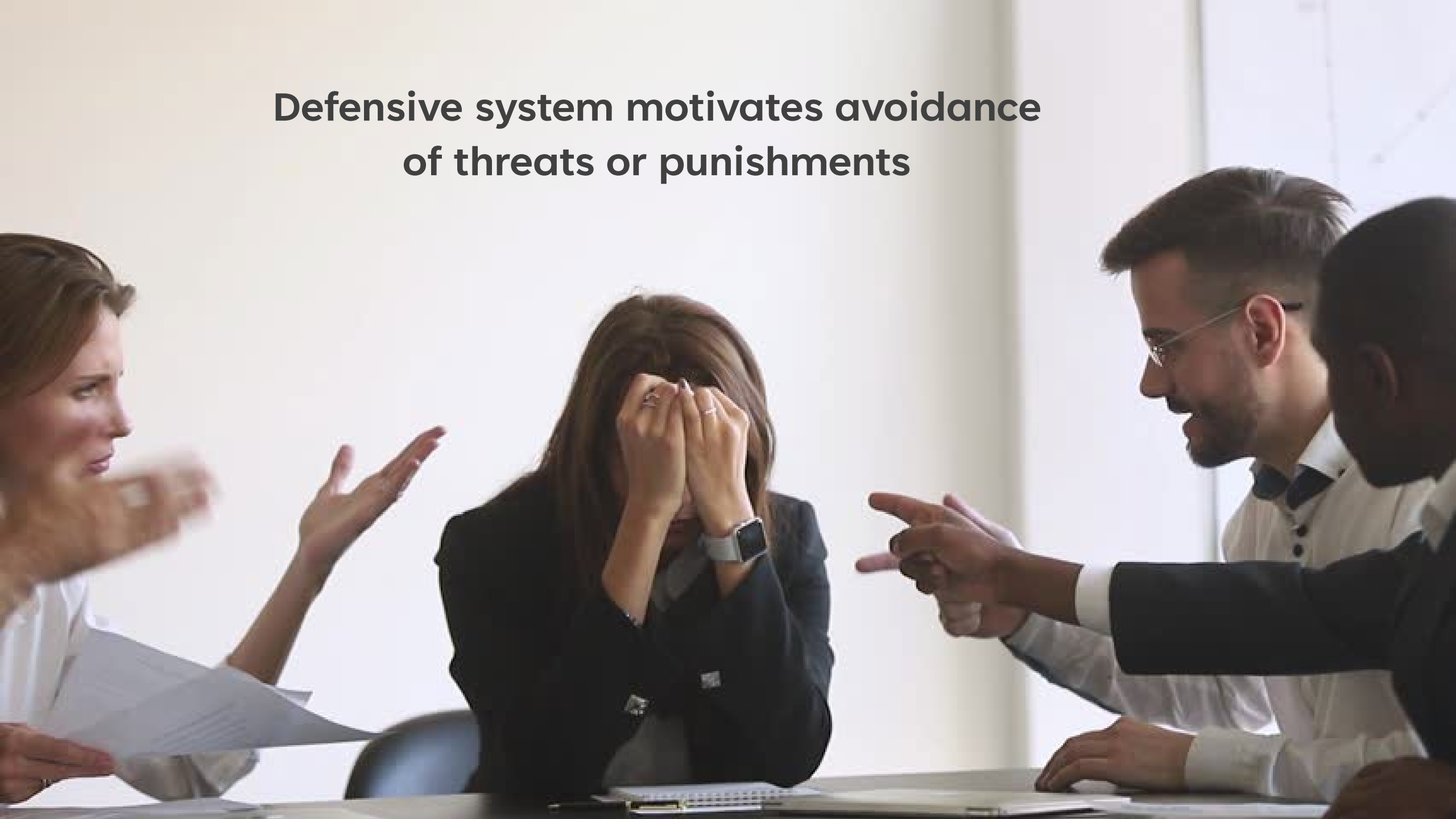
Targeting Threat & Reward Processes for Depression, Anxiety and Anhedonia: efficacy, mechanisms and community implementation

Michelle G. Craske, PhD, AO
UCLA
September, 2026

Defensive system motivates avoidance of threats or punishments



Appetitive system motivates approach towards goals and rewards

The Laboratory

Defensive threat mechanisms

Appetitive reward mechanisms

Targeted treatment

The Research Clinic

Precision matching

Community implementation with precision

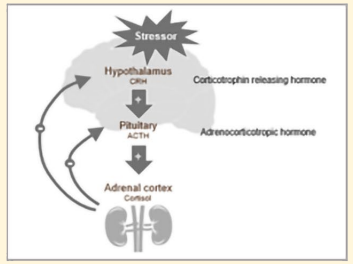
The Community

Threat Processes as Intervention Targets

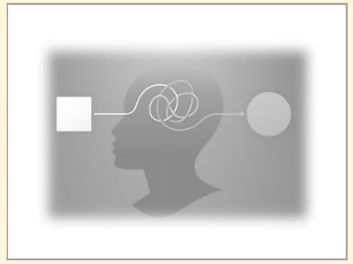
Anxiety: elevated threat reactivity as risk & predictor

Neuroticism

HPA



Cognitive biases



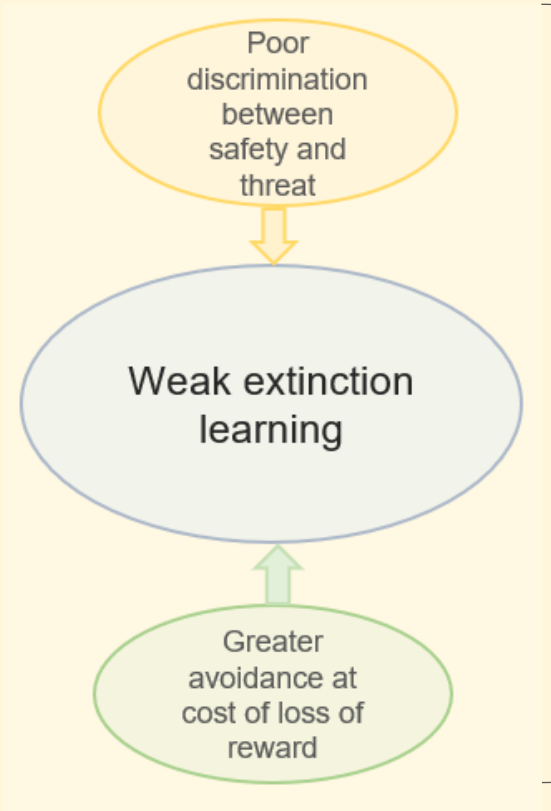
Zinbarg et al. (2016) *Clin Psych Sci*; Vinograd et al., (2020) *Clin Psych Sci*; Mineka et al (2020) *J Abnorm Psych*; Doane et al. (2013) *Devel & Psychopath*; Adam et al (2014) *Psychoneuroendicronology*; Gilbert et al (2017) *Clin Psych Sci;* Waters et al. (2007) *Beh Res & Ther*; Waters et al. (2008) *Beh Res & Ther*; McGlade et al. (2020) *J Beh Ther & Exp Psych*

Anxiety: subjective, autonomic and neural deficits in Pavlovian fear extinction

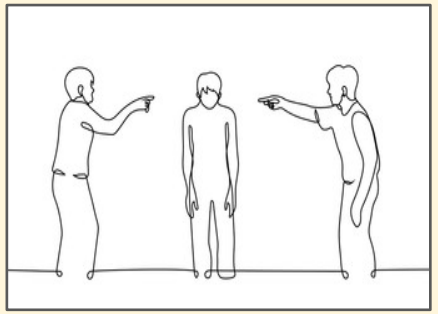
Craske et al. (2018) *Trans R Soc Lond B Biol Sci*; Treanor et al., (2021) *Biol Psych*; Craske et al. (2022) *Neurosci Biobeh Rev*; Davis et al. (2025) *Trends in Cog Sci*

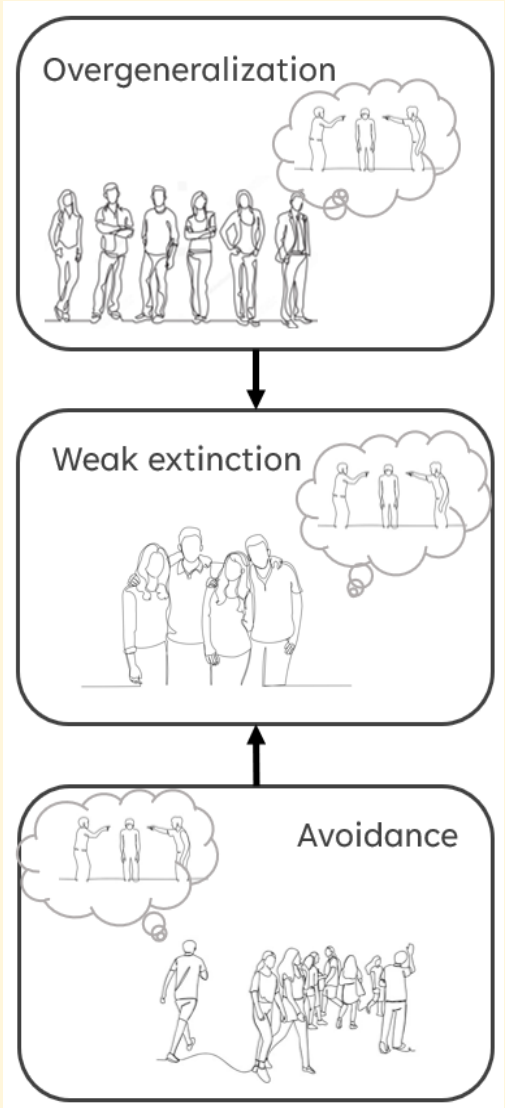
Threat Processes as Intervention Targets

Anxiety: subjective, autonomic and neural deficits in Pavlovian fear extinction



Innately aversive event





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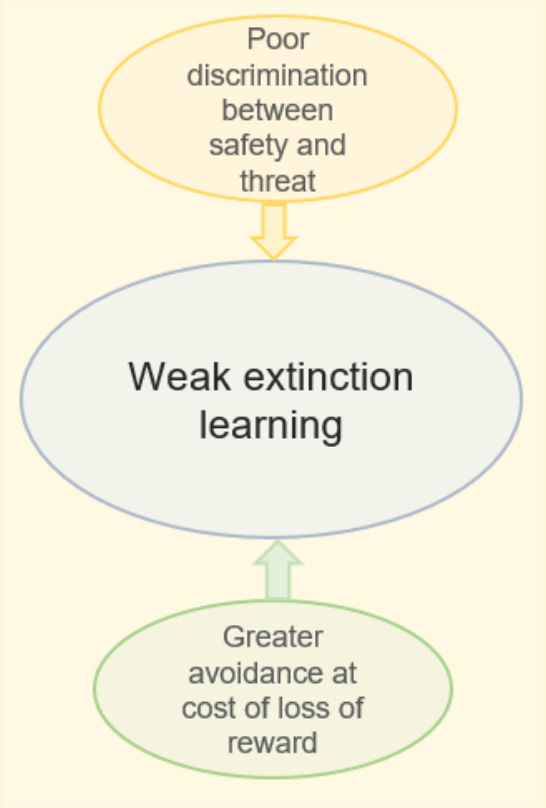
Threat Processes as Intervention Targets

Anxiety: subjective, autonomic and neural deficits in Pavlovian fear extinction



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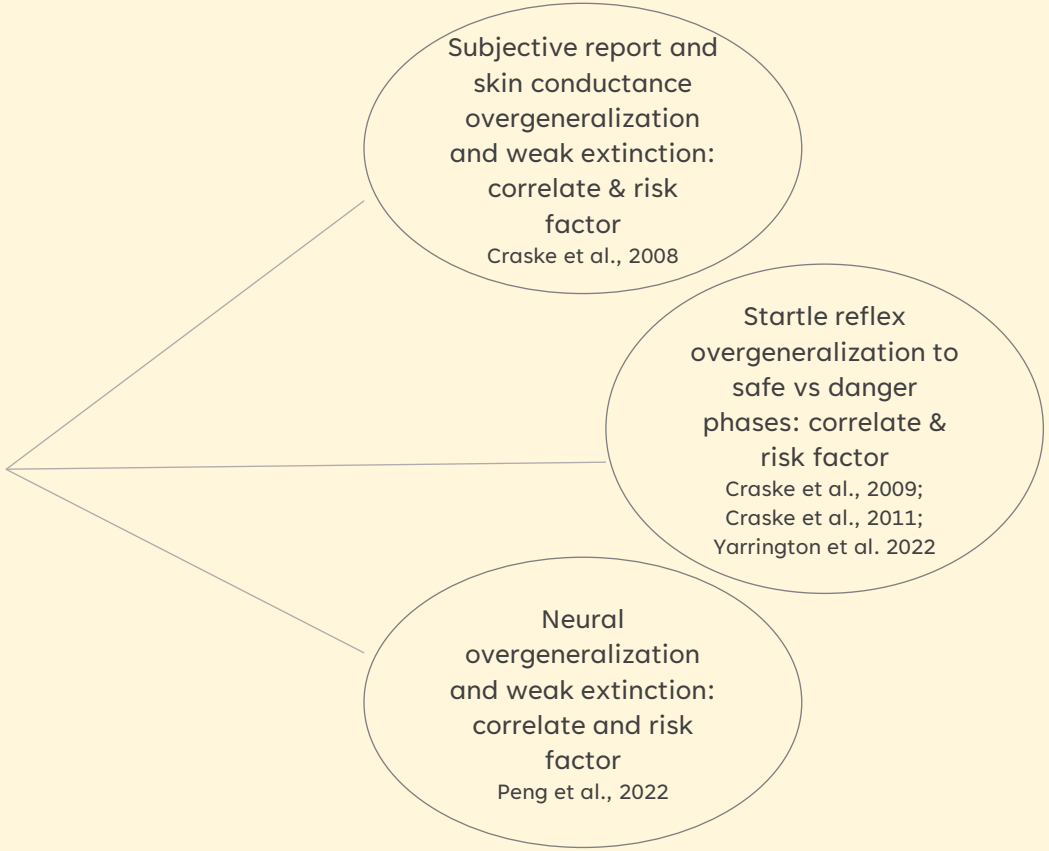
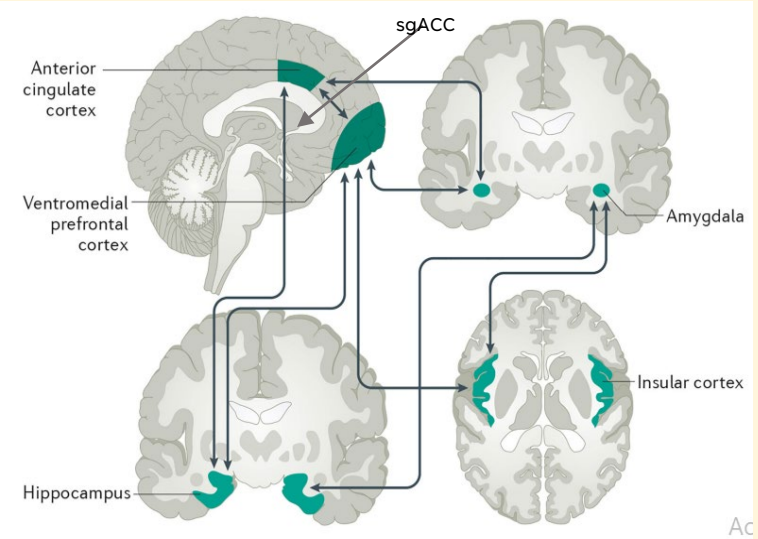


Craske et al., (2008) *Beh Res & Ther*; Craske et al. (2009) *Biol Psych*; Craske et al. (2011) *J of Ab Psych*; Yarrington et al. (2022) *J Affective Dis*; Peng et al. (2022) *Biol Psych:CNNI*

Threat Processes as Intervention Targets

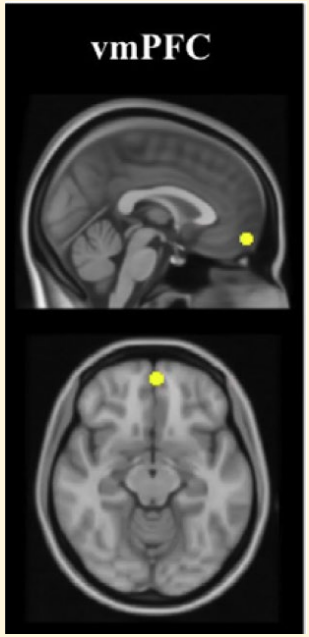


Craske et al., 2017

Neural activation in threat regions during fear acquisition → predicted increased fears over next 30 months,

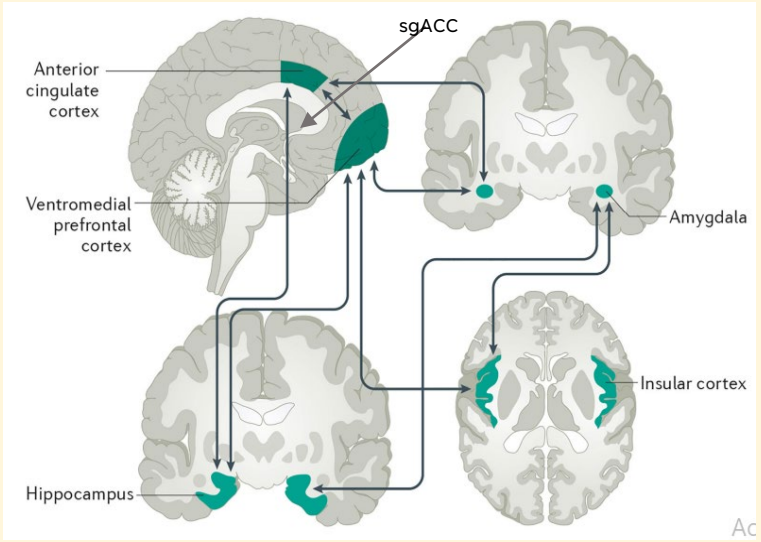
N=273, r=.33, p=.018

Effect primarily driven by fear overgeneralization (poor discrimination between stimulus paired with shock and stimulus not paired with shock) in vmPFC



Peng, Y., Knotts, J. D., Young, K. S., Bookheimer, S. Y., Nusslock, R., Zinbarg, R. E., Kelley, N. J., Echiverri-Cohen, A. M., & Craske, M. G. (2023). Threat neurocircuitry predicts the development of anxiety and depression symptoms in a longitudinal study. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 8*(1), 102–110.

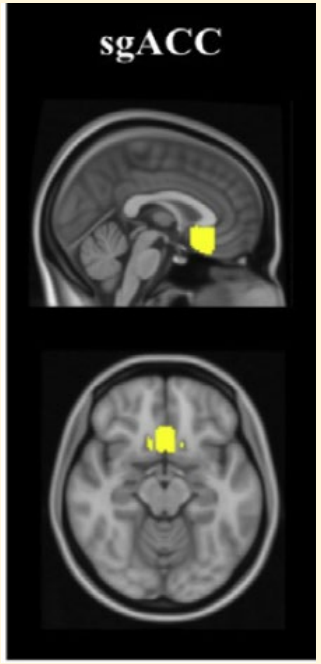
Threat Processes as Intervention Targets



Craske et al., 2017

Change in neural activation in threat regions during fear extinction recall covaried with increased general distress (anxiety/depression) over prior 30 months, N=273: r=-.48, p=.04

Effect primarily driven by weaker extinction (weaker inhibitory responding to extinguished stimulus) in subgenual ACC



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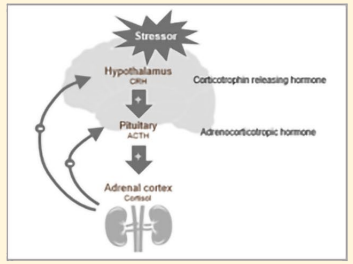
Threat Processes as Intervention Targets

Anxiety: elevated threat reactivity as risk & predictor

Neuroticism

HPA



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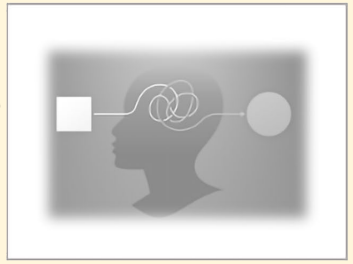

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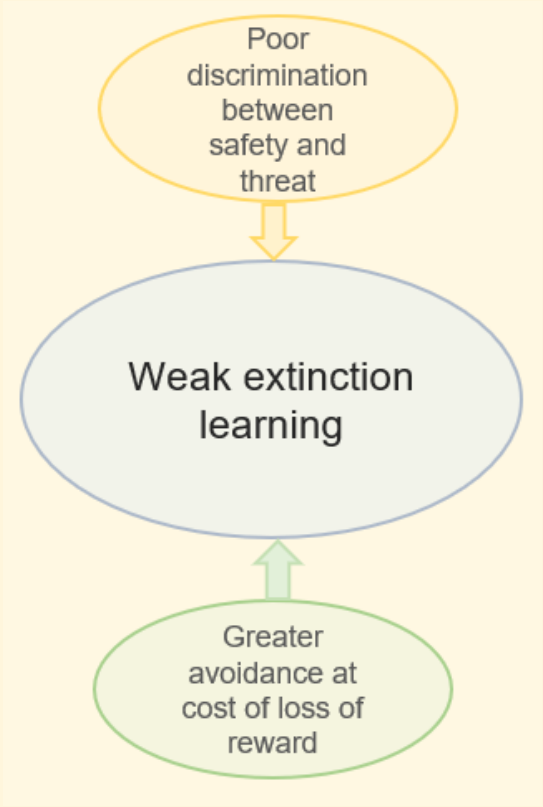

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Anxiety spreads and persists

Pervasive and chronic anxiety

Interventions that Target Threat Processes

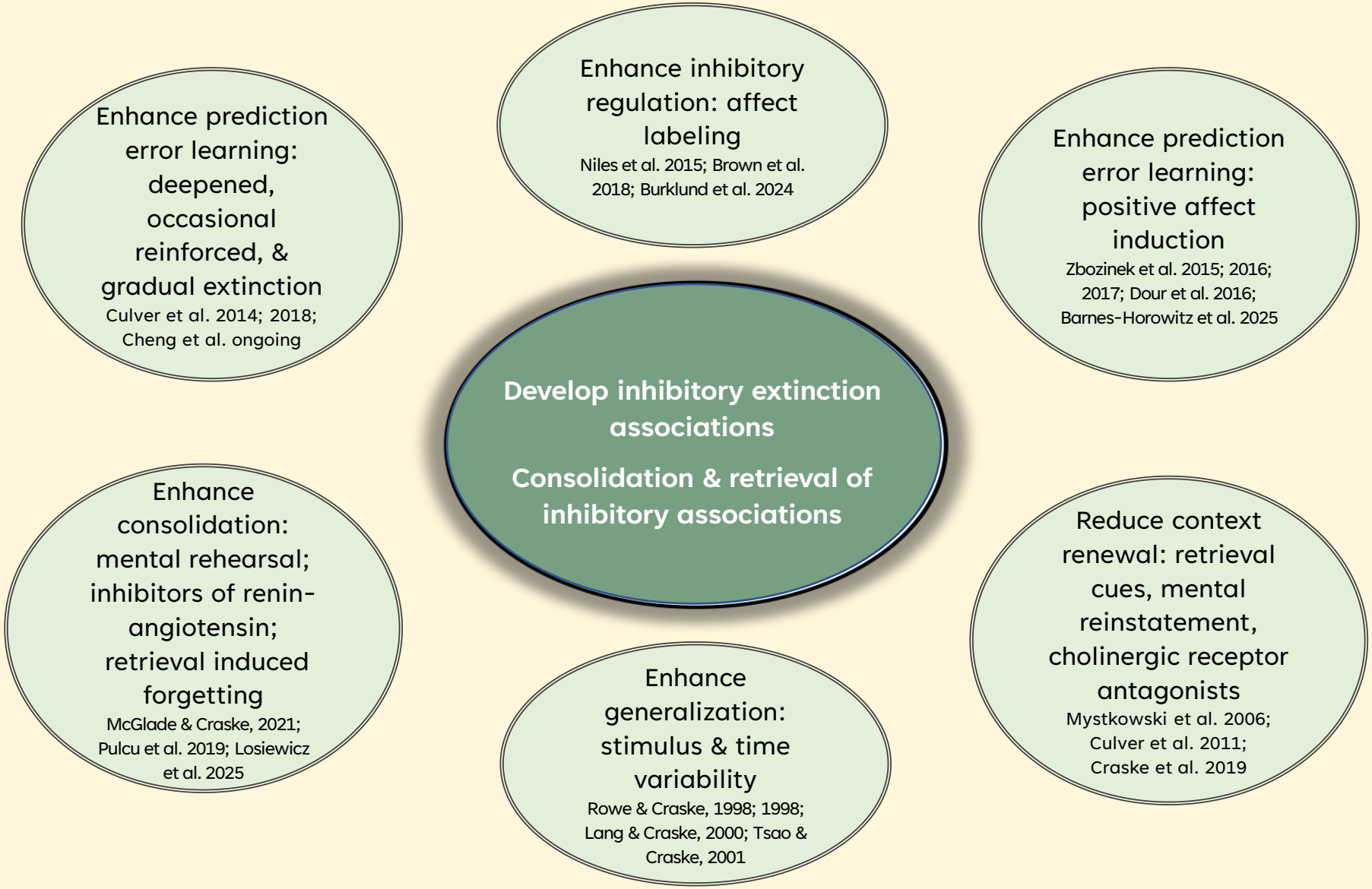
Interventions that Target Threat Processes

Exposure replaces avoidance with approach to enable extinction prediction error learning

But anxiety impedes extinction prediction error learning

→ ~50% remission and return of fear

Interventions that Target Threat Processes



Craske MG et al (2018) *Philos Trans R Soc Lond B Biol Sci.;* Treanor et al. (2021) *Biol Psych*; Craske et al. (2022) *Neurosci Biobeh Rev*; *Rosenberg et al., (2024) J Anx Dis;* Davis et al. (2025) *Trends in Cognitive Sciences*

Because positive and negative outcomes occur in real life....

Retrieval induced forgetting (RIF) (Anderson et al., 1994)

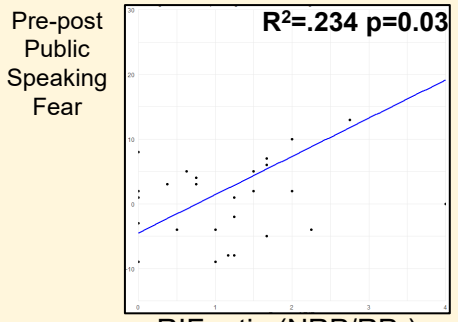
Losiewicz OM, Davis B, Craske MG. Remembering to forget fear: Augmenting exposure with retrieval-induced forgetting. Behav Res Ther. 2025 Jul 29;193:104829.

Interventions that Target Threat Processes

Retrieval of inhibitory (positive) memories induced forgetting of excitatory (negative) memories from the same exposure trial

NRP>RP-
t(29)=4.04, p<.01

RIF of excitatory (negative) memories improved outcomes from exposure therapy



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Interventions that Target Threat Processes

Inhibitory Retrieval Model of Exposure Therapy	
Active Ingredient	**Theoretical Construct**
Rationale	Associative learning
OptexNexus	Associative map
Expectancy violation	Prediction error
Wean safety signals and behaviors	Prediction error
Attention to primary stimuli (affect labeling)	Prediction error
Post-exposure consolidation and mental rehearsal	Consolidation
Varied stimuli	Generalization and retrieval
Varied contexts	Context generalization and retrieval
Deepened exposure	Prediction error
Occasional reinforced exposure	Prediction error and context generalization
Mental reinstatement	Context generalization

Craske MG, Treanor M, Zbozinek TD, Vervliet B. (2022) Optimizing exposure therapy with an inhibitory retrieval approach and the OptEx Nexus. *Behaviour Research and Therapy*. 2022 May;152:104069

Interventions that Target Threat Processes

Design exposures to violate expectancy
& generate prediction error

Interventions that Target Threat Processes

What do you expect to happen

What did you expect to happen?

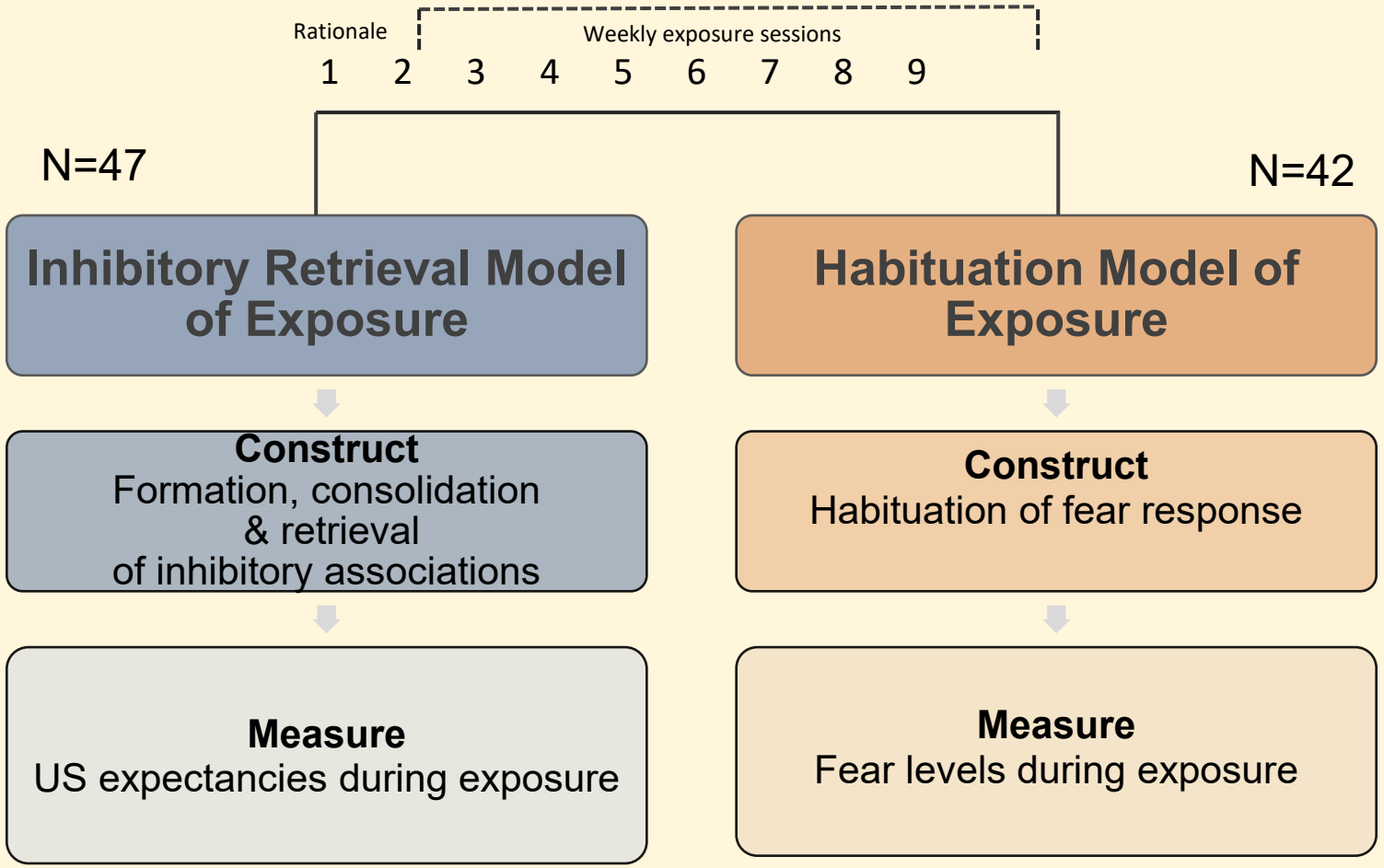
What actually happened?

What did you learn?

What surprised you?

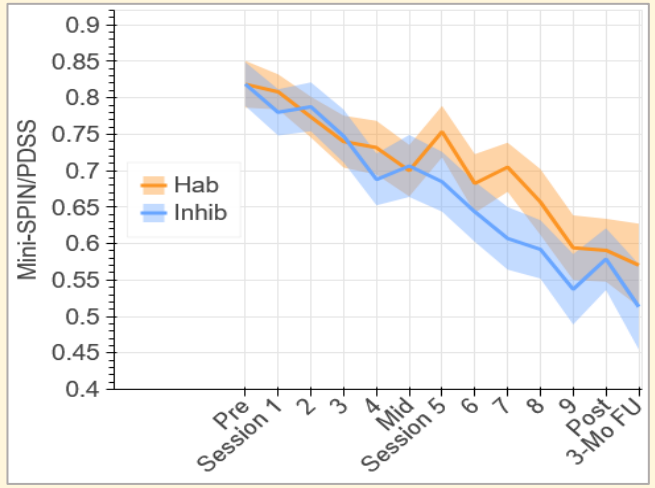
Interventions that Target Threat Processes

Social anxiety or panic disorder

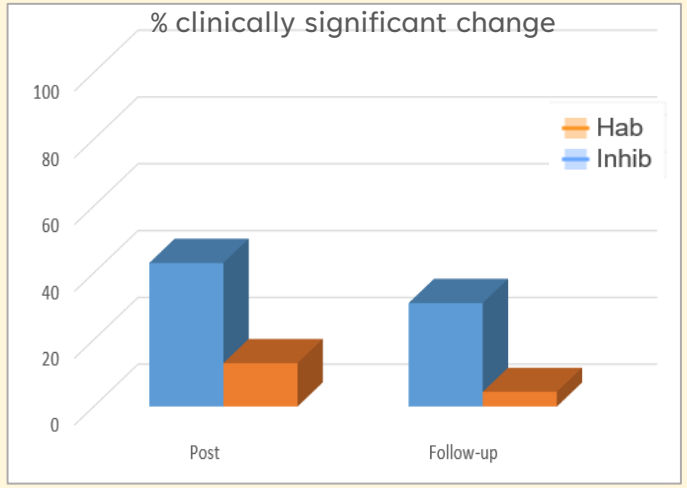


Treanor, M., Zbozinek, T. D., Rosenberg, B. M., Sewart, A., Sandman, C. F., Ruiz, J., & Craske, M. G. (2025). A randomized controlled trial comparing two processes of exposure therapy: Extinction learning and habituation. *Journal of Consulting and Clinical Psychology, 93*(10), 705–717.

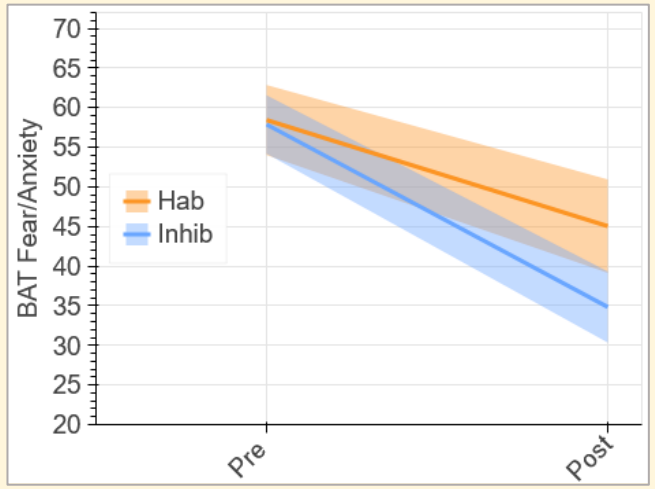
Interventions that Target Threat Processes



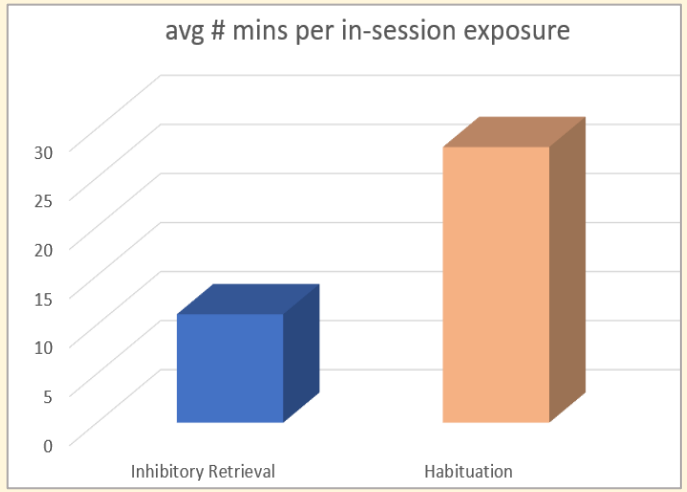
Steeper reduction:(b=.01, 95% CI:[.004,.02], $\chi^2(1)=12.33$, $p=.001$)



$\chi2(1)=5.406$, $p=.020$ $\chi2(1)=1.634$, $p=.201$



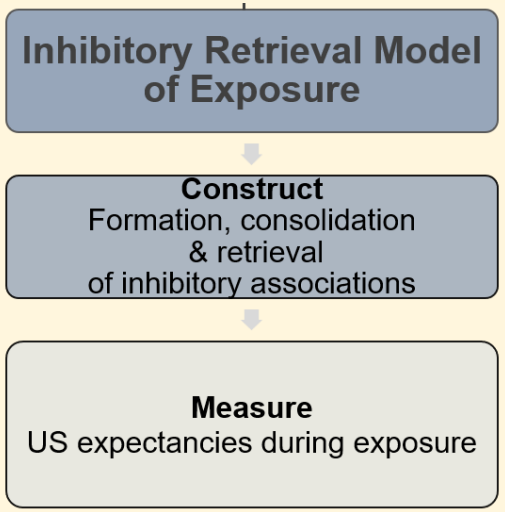
Steeper reduction: b=6.95, 95% CI:[.60,13.31], $\chi^2(1)=4.60$, $p=.032$



$t(82)=-5.96$, $p<.001$

Treanor, M., Zbozinek, T. D., Rosenberg, B. M., Sewart, A., Sandman, C. F., Ruiz, J., & Craske, M. G. (2025). A randomized controlled trial comparing two processes of exposure therapy: Extinction learning and habituation. *Journal of Consulting and Clinical Psychology, 93*(10), 705–717.

Interventions that Target Threat Processes



Expectancy change = learning from prediction error

Before starting your exposure, how likely is it that _____(feared outcome) will come true?

0----------25----------50----------75----------100
Not at all Possible 50/50 Probable Definite

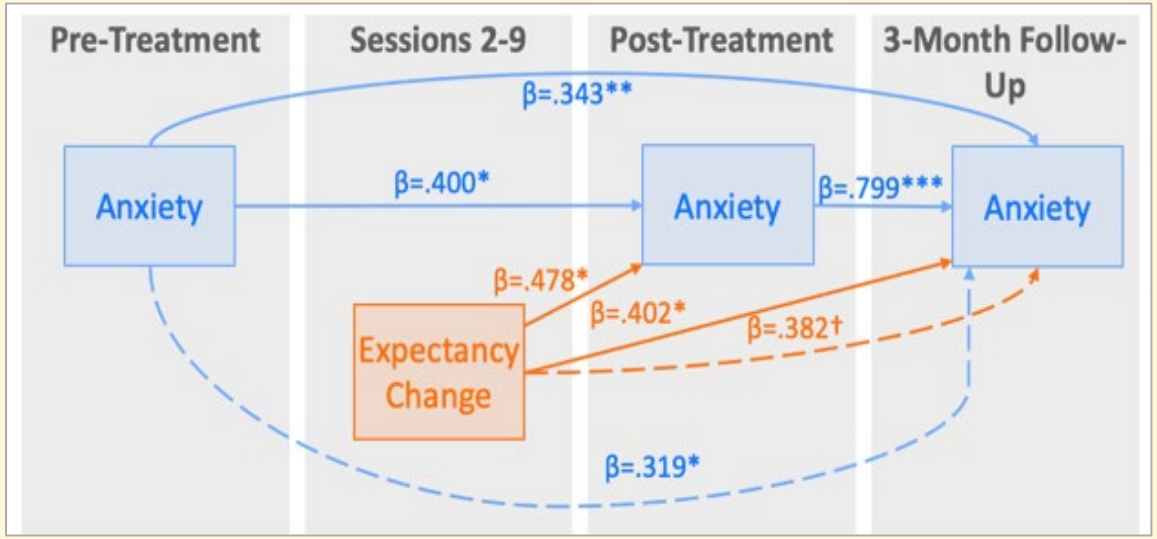
- - - - - - - - - - - - - -

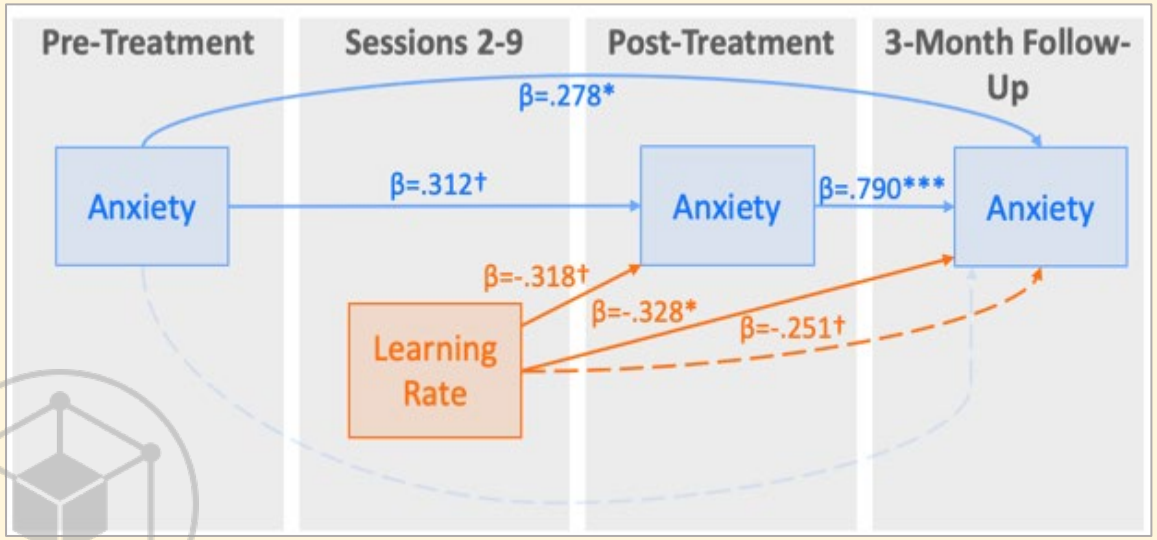
Imagine you did the same exposure again. How likely is it that _____(feared outcome) will come true this time?

0----------25----------50----------75----------100
Not at all Possible 50/50 Probable Definite

Interventions that Target Threat Processes

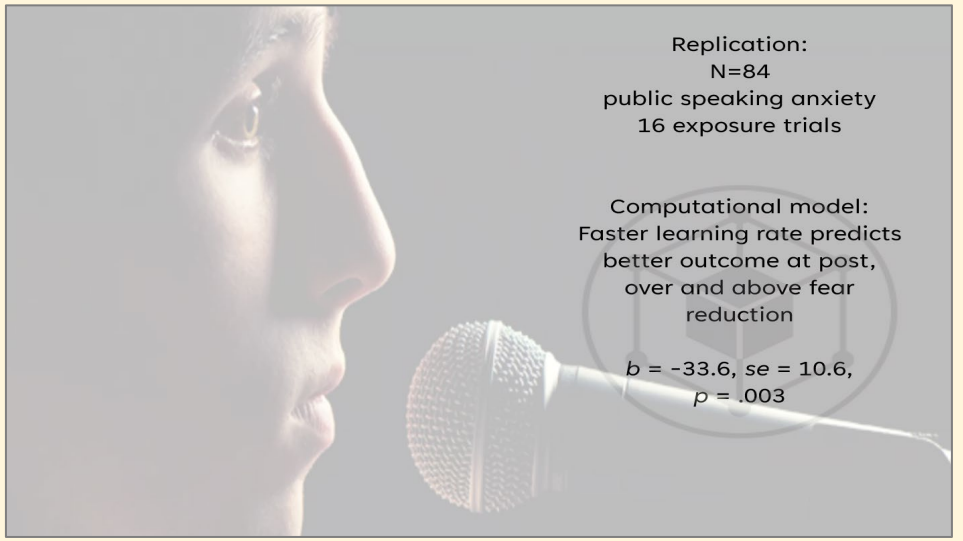
Inhibitory Retrieval Condition





Zbozinek, T., Rosenberg, B., Treanor, M., & Craske MG. (2026)
Behaviour Research and Therapy

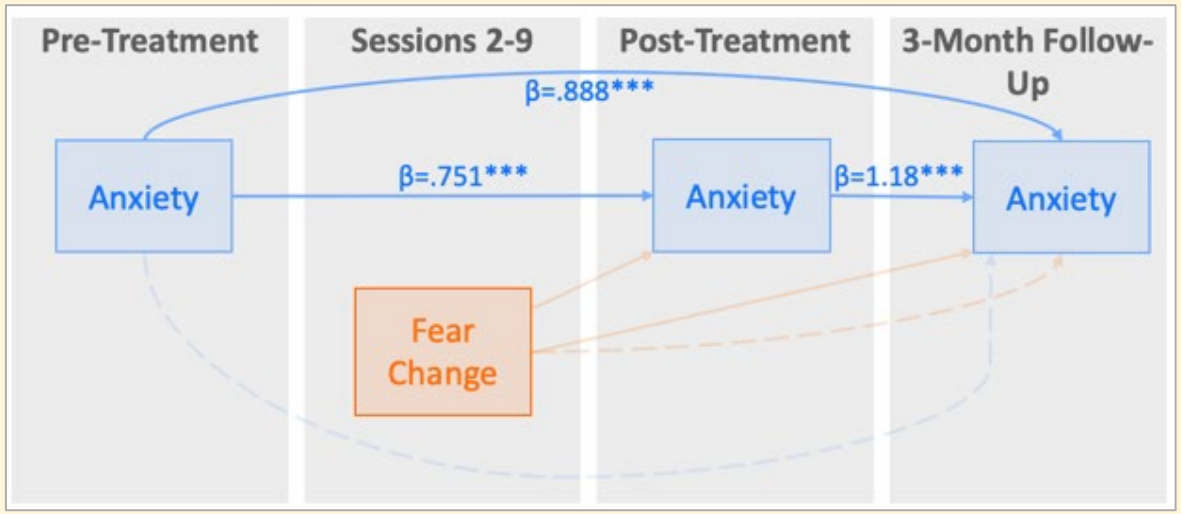
Expectancy change predicts therapeutic outcome, over and above fear reduction



Barnes-Horowitz NM, Zbozinek TD, & Craske MG. (2025)
Behaviour Research and Therapy

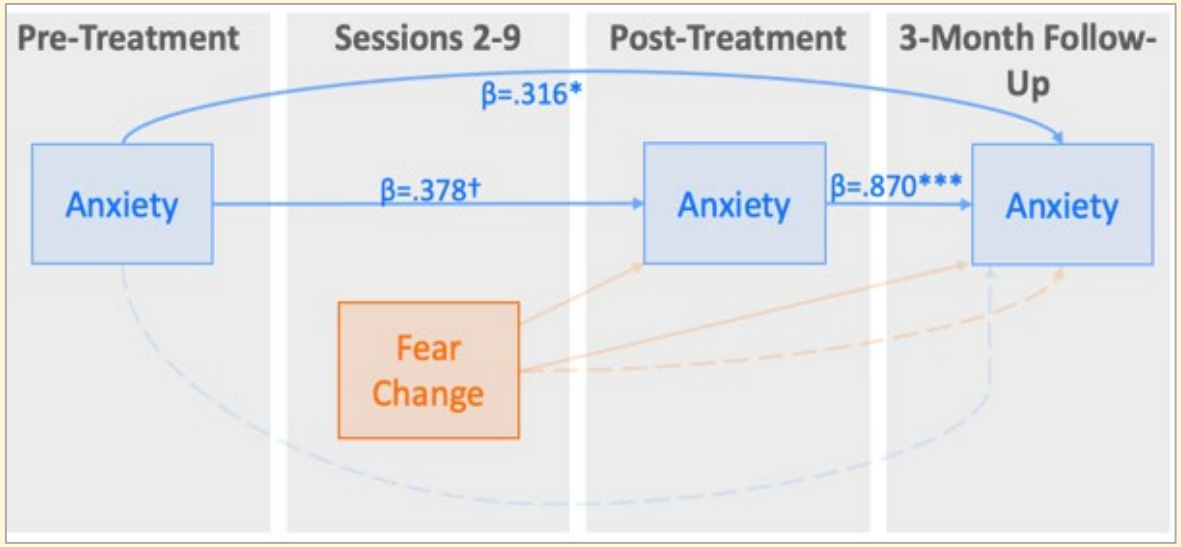
Interventions that Target Threat Processes

Habituation Condition



Fear habituation occurs but does not predict therapeutic outcome

Inhibitory Retrieval Condition



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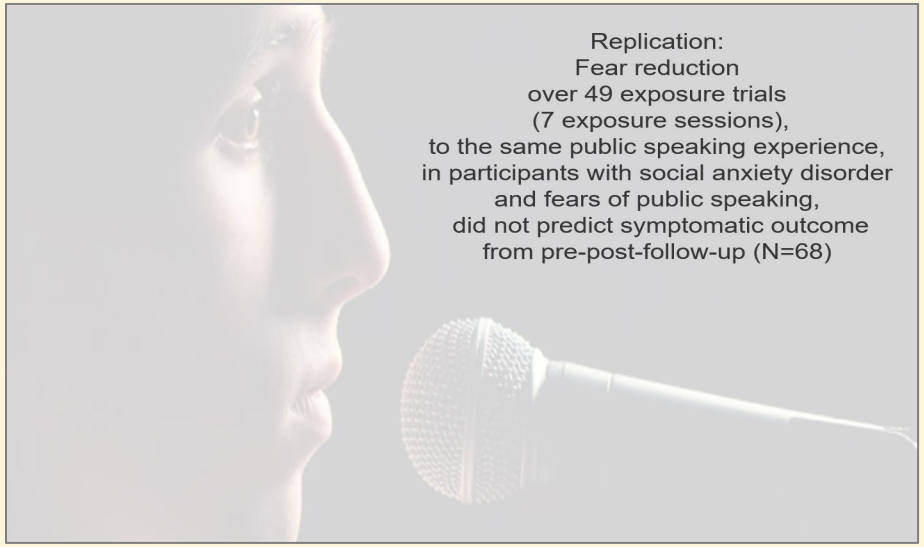
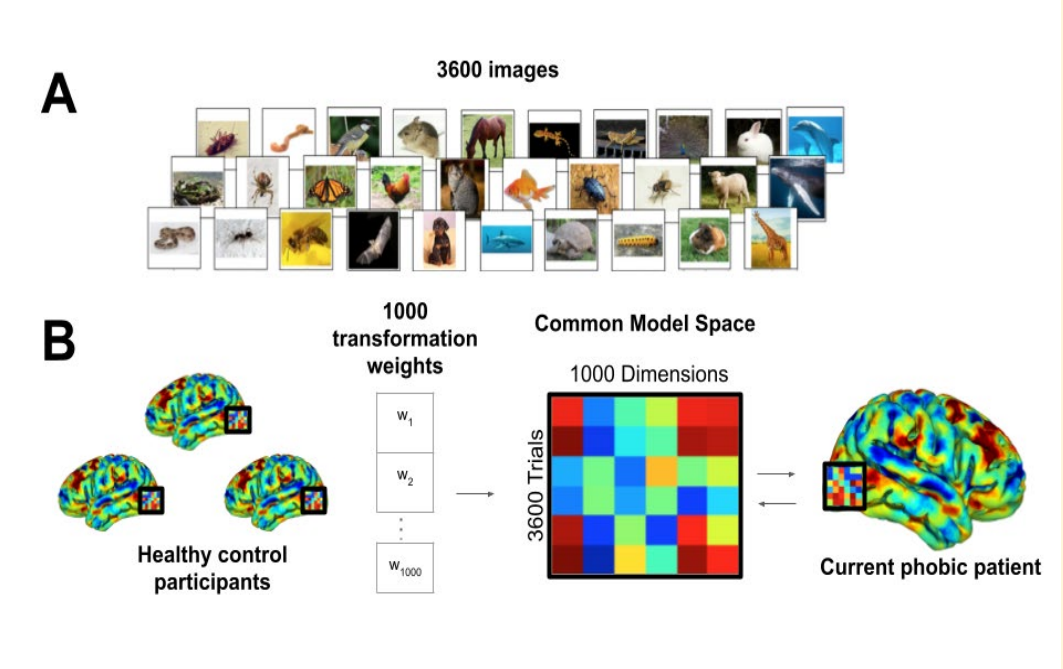


McGlade AL, Treanor M, Kim R, Craske MG. (2023) *Journal of Behaviour Therapy & Experimental Psychiatry*

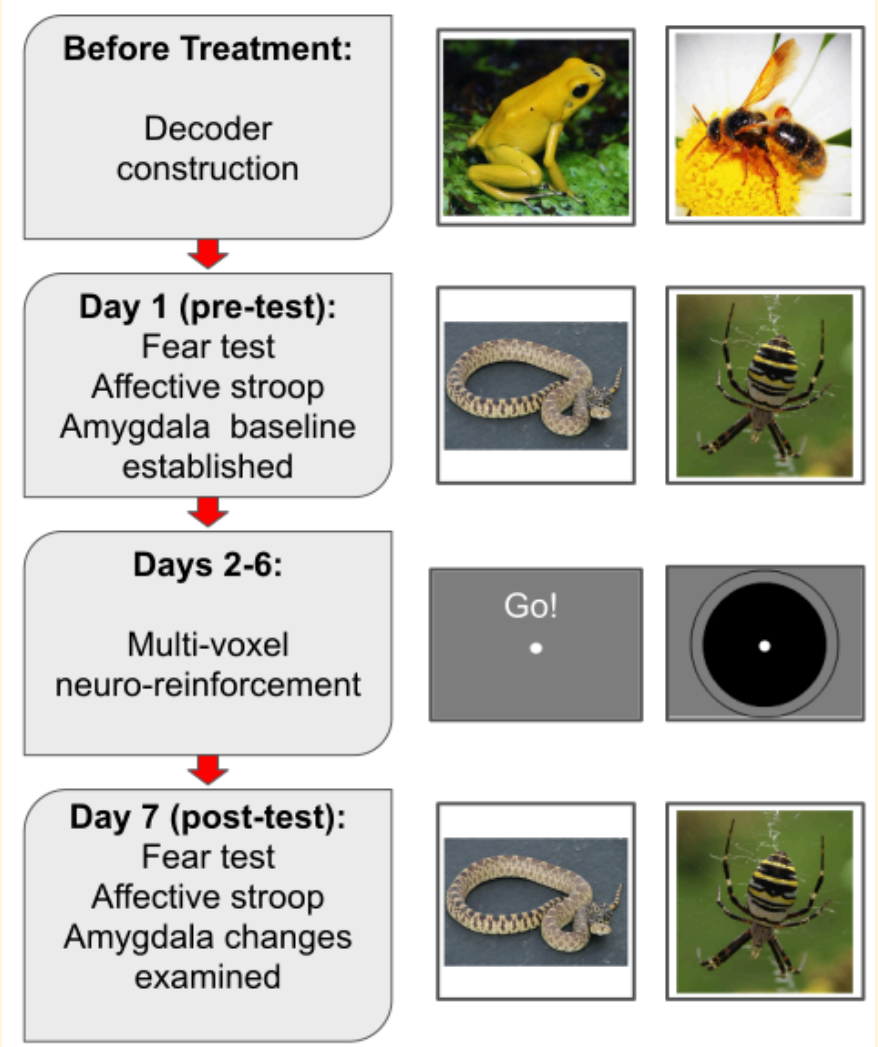
Interventions that Target Threat Processes



Functional alignment of brain data into phobic patient brain using hyperalignment

(A) Participants view 3600 images rapidly (0.98sec) in scanner
(B) Transformation parameters into functionally aligned common model space are determined with phobic image trials withheld. Data from all participants for all categories (including phobic categories) are transformed into common model space and reverse transformed into native space of current phobic participant. Machine-learning classifier is trained on phobic images in the patient's native brain space despite patient never having personally viewed the images

Unconscious exposure

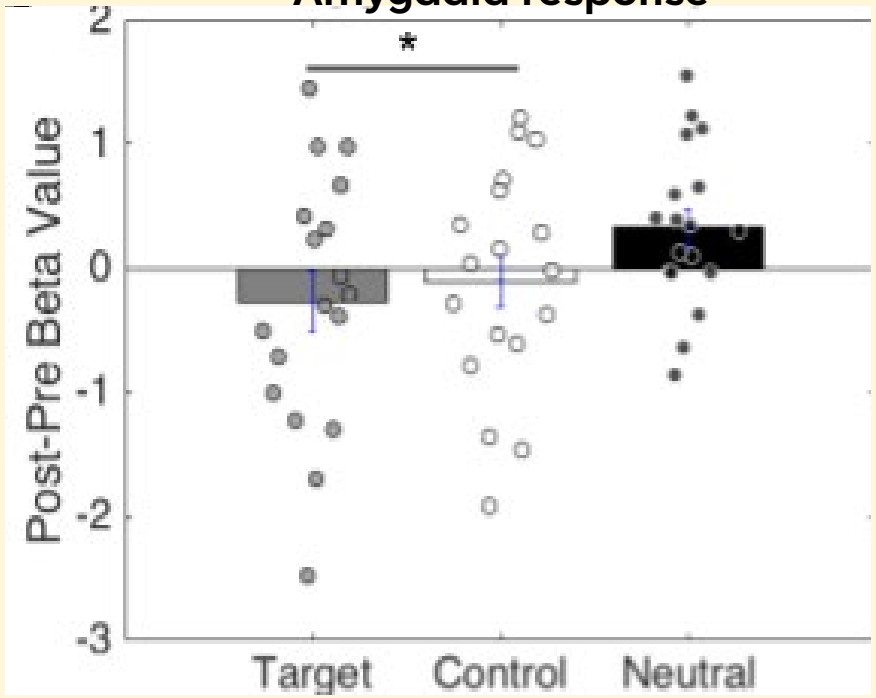


Cushing, C., Lau, H-W, Kawato, M., Craske, M.G., & Taschereau-Dumouchel, V (2024)
Psychiatry and Clinical Neurosciences

Interventions that Target Threat Processes

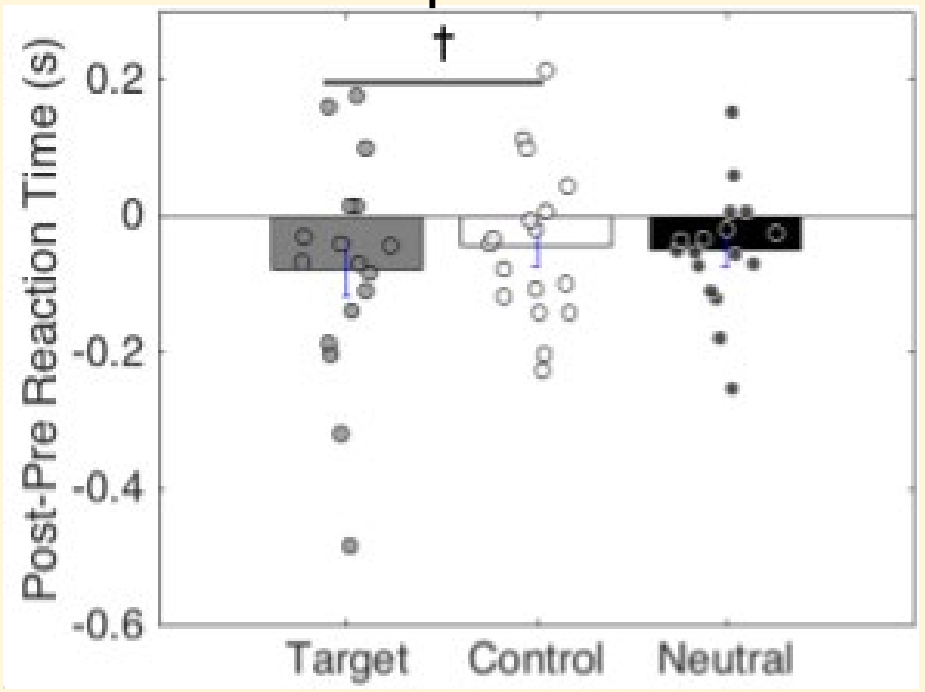
N=23, Specific Phobia, Animals x 2

Amygdala response



Greater amygdala decrease in Target vs Control phobias following neuro-reinforcement
* $p<0.05$ interaction Time (pre/post) x condition (target/control)

Stroop reaction time



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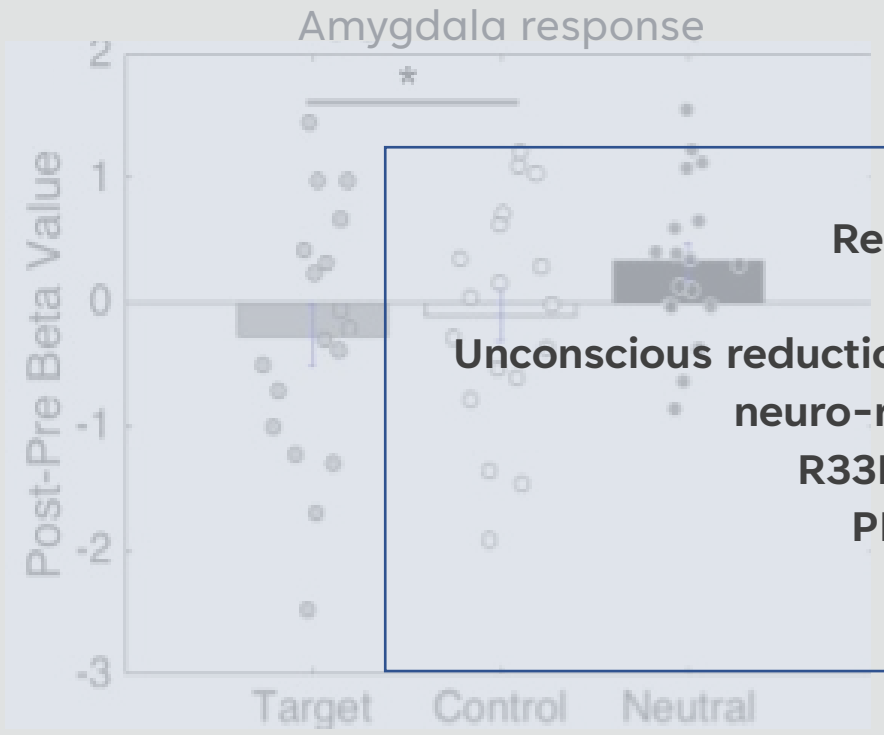

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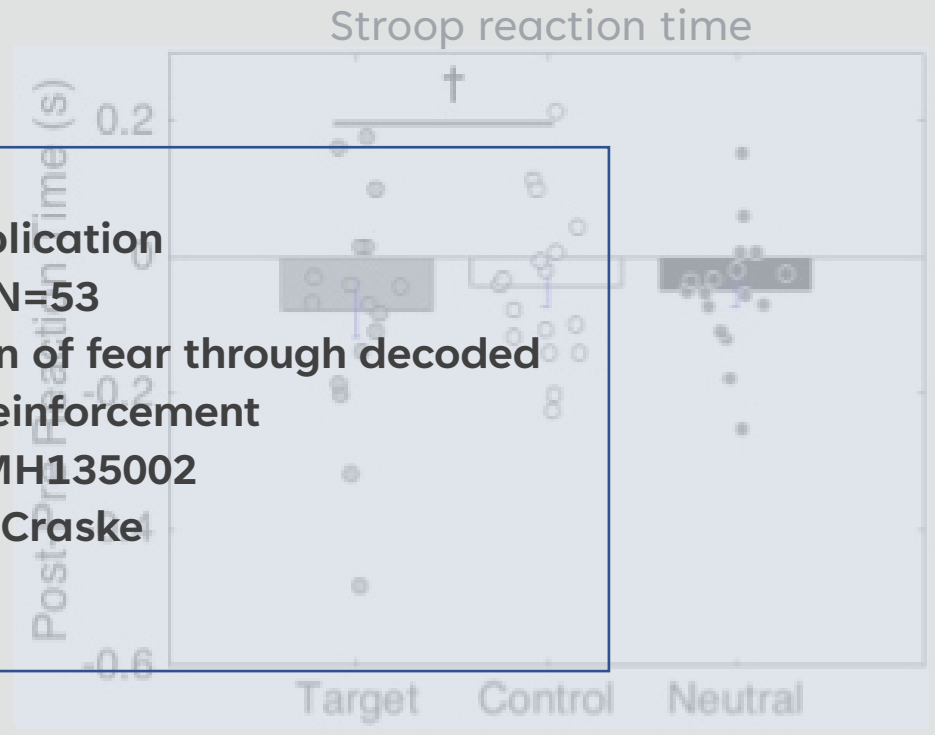

Greater reaction time decrease in Target vs Control phobias following neuro-reinforcement
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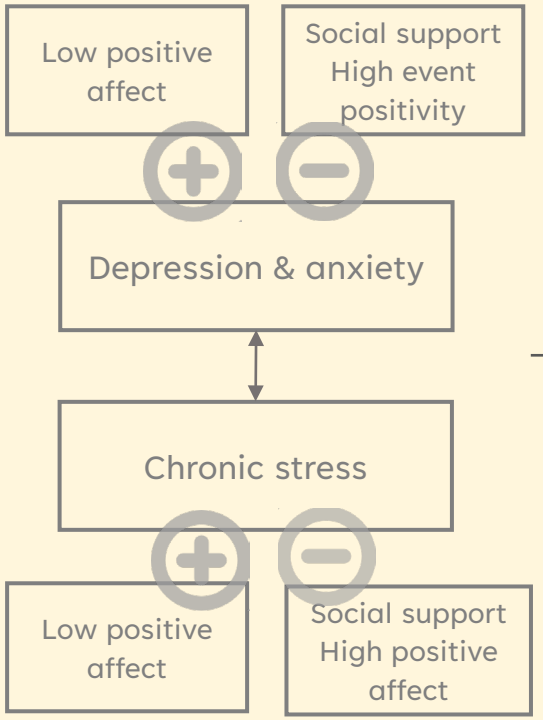
Replication
N=53
Unconscious reduction of fear through decoded neuro-reinforcement
R33MH135002
PI Craske

Reward Processes as Intervention Targets

Reward Processes as Intervention Targets

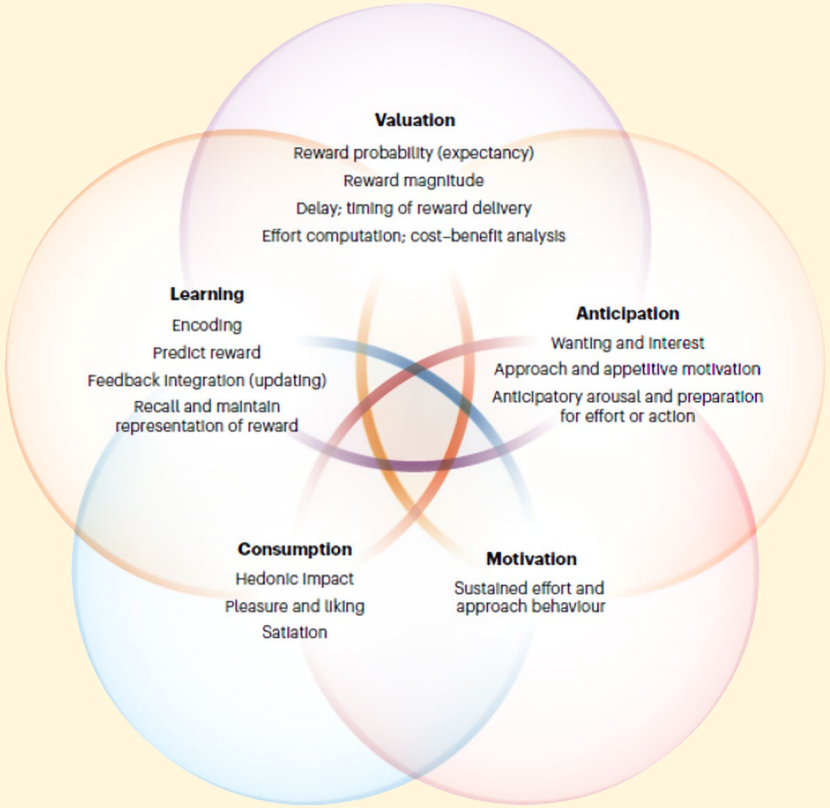
Reward Processes as Intervention Targets

Low positive affect as risk & high positive affect as protector for depression and anxiety



Kendall AD, et al. (2015) *J Abnorm Psychol*; Sewart, A.R. et al. (2019) *Clinical Psychological Science*; Metts, A., et al. (2021) *Journal of Abnormal Psychology*; Metts, AV et al. (2022) *Development and Psychopathology*; Yarrington, et al (2023) *Clinical Psychological Science*; Metts, A. et al (2024) *Clinical Psychological Science*

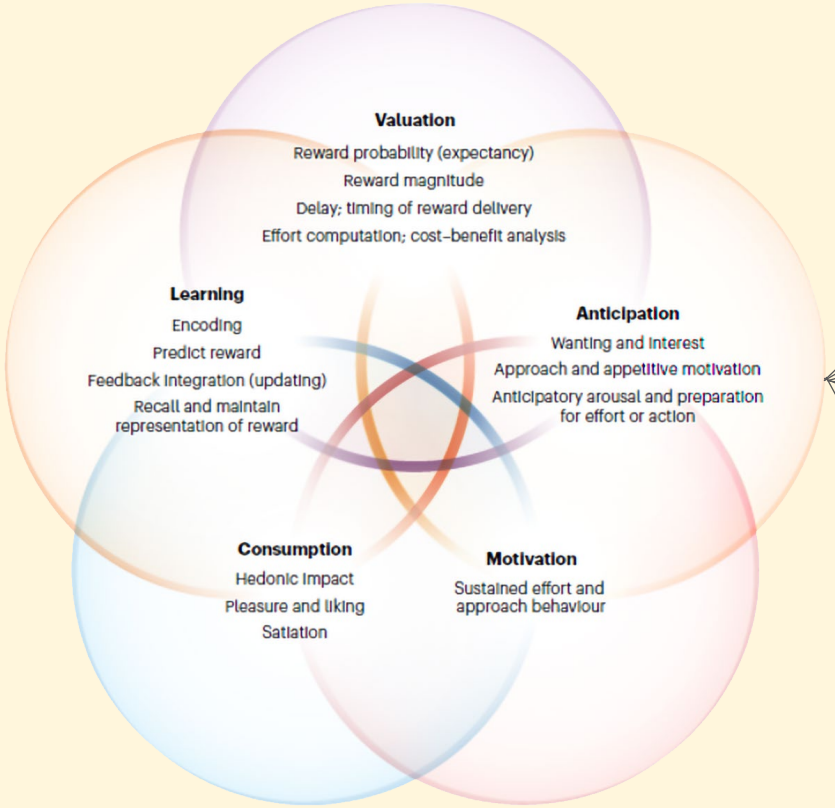
Anhedonia: subjective, cognitive, behavioral, autonomic and neural hypo-responsivity to reward



Craske, M.G. et al. (2024) *Nature Reviews Psychology*; Sandman CF & Craske MG. (2021) *Current Topics Behavioral Neuroscience*

Reward Processes as Intervention Targets

Anhedonia: subjective, cognitive, behavioral, autonomic and neural hypo-responsivity to reward



Craske, M.G. et al. (2024) *Nature Reviews Psychology*; Sandman CF & Craske MG. (2021) *Current Topics Behavioral Neuroscience*

Weaker neural reward activation to monetary gain
Peng et al. 2022; Nusslock et al (in review); Well Leap (PI Craske)

Less positive approach bias & sustained attention
Paulus et al. 2021

Less positive interpretations of ambiguous scenarios
Yarrington & Craske, 2024

Less effective reappraisal of negative scenarios
Metts & Craske, 2023

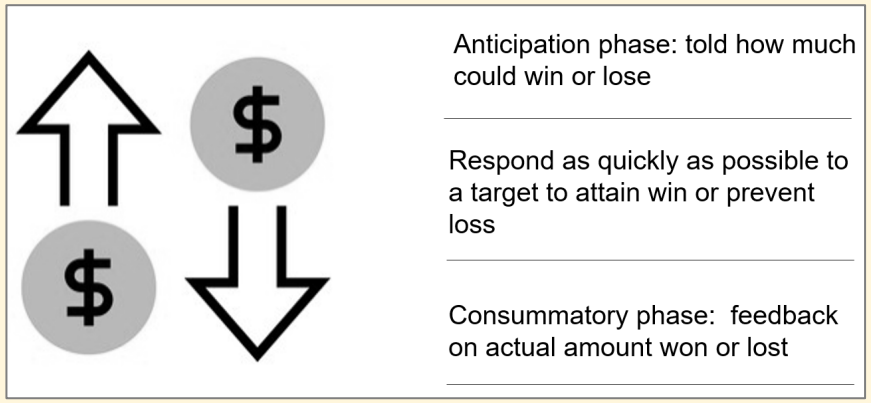
Less positive subjective experience positive stimuli
Peng et al. 2021

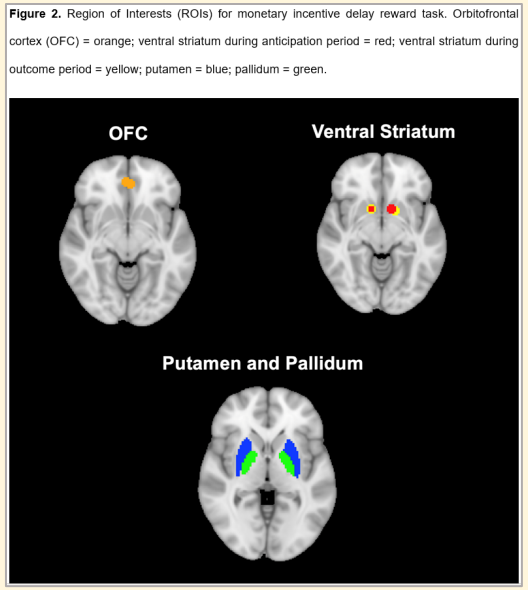
EMA report of lower reward motivation, effort, anticipation and joy in daily life
Well Leap (PI Craske); Null et al. (in review)

Yarrington & Craske (2024) *Behaviour Research & Therapy*; Metts, A & Craske, MG (2023) *Behaviour Research & Therapy*; Paulus, M., et al. (2017) *Journal of Affective Disorders;* Peng, Y., et al (2021) *Biological Psychiatry: CNNI*; Nusslock et al. (in review); Null et al. (in review); Wellcome Leap MCPsych Consortium

Reward Processes as Intervention Targets

Monetary Incentive Delay Task





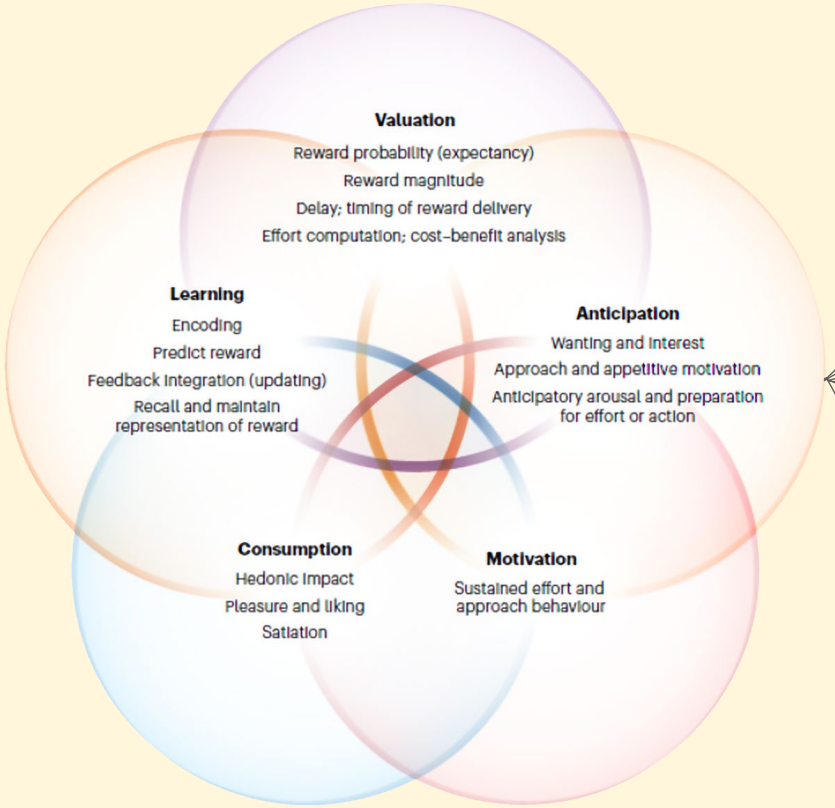
Anhedonia negatively associated with OFC during MID consummation phase (win vs no win), N=273 18-19 year olds, b=-.34, se=.147, p=.021

Specific to anhedonia vs negative affect or fears

Nusslock, R., Zinbarg, R., Young, K., Carrol, D., Chat, I., Cushing, C., & Craske, M.G. (under review)

Reward Processes as Intervention Targets

Anhedonia: subjective, cognitive, behavioral, autonomic and neural hypo-responsivity to reward



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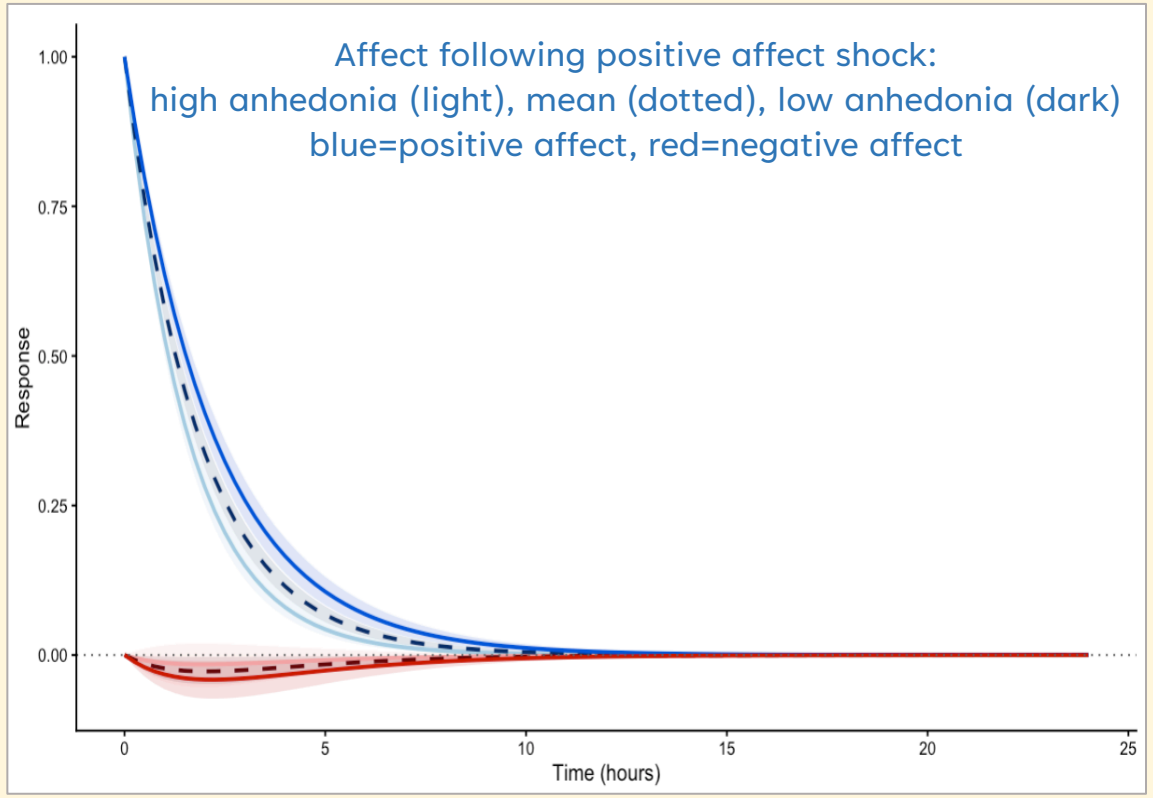
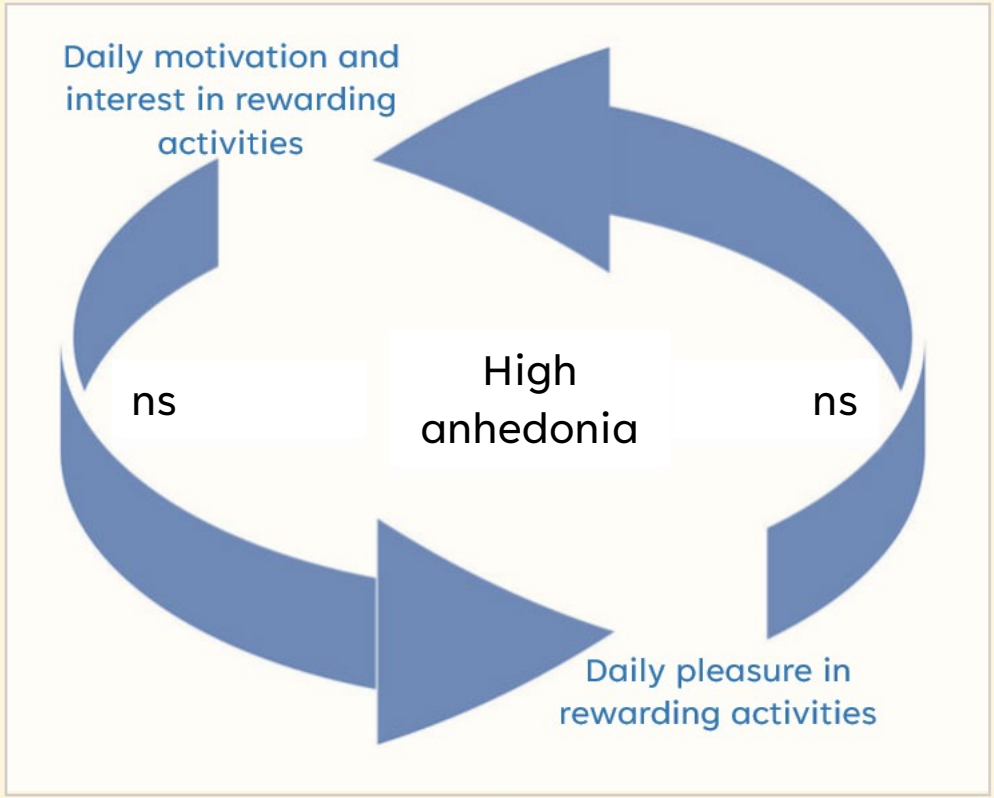
Reward Processes as Intervention Targets

Steeper decay in positive affect and disrupted reward cycles as function of anhedonia:
EMA, N=330 moderately to severely depressed participants

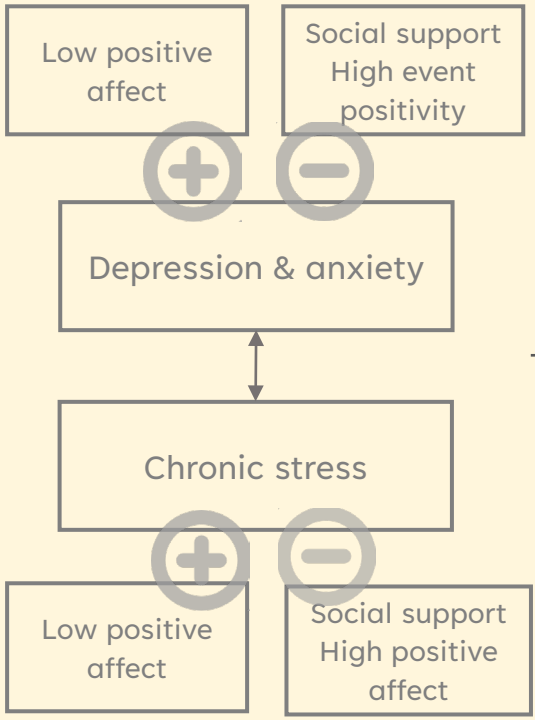




Null, K., West, A., Cohen, Z., Zbozinek, T., Jones, K., Bui, A., Welsh, R., & Craske, M.G. (in preparation)

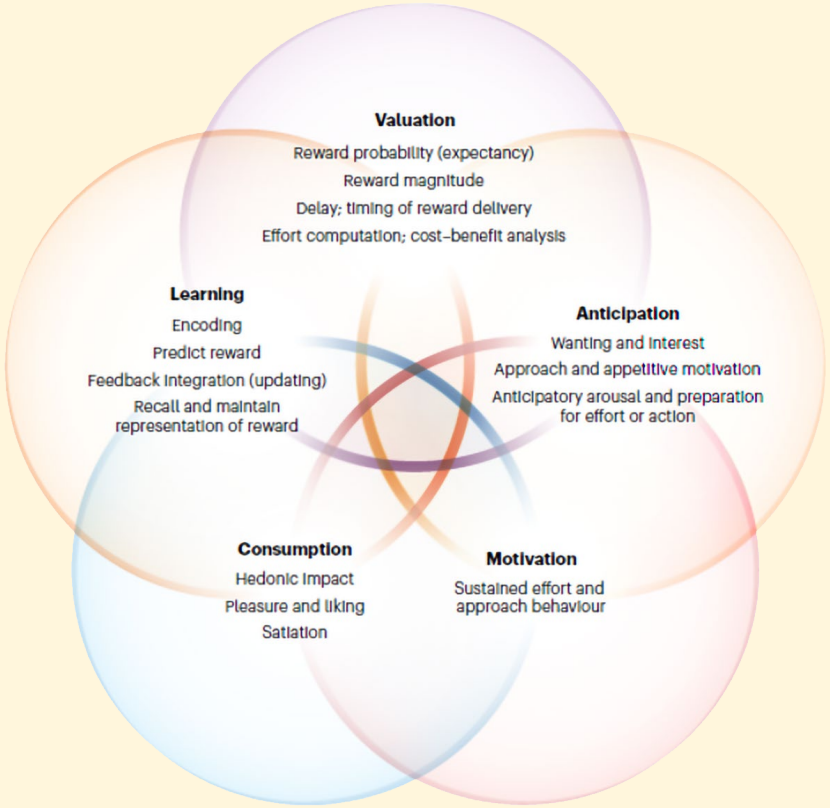
Reward Processes as Intervention Targets

Low positive affect as risk & high positive affect as protector for depression and anxiety



Kendall AD, et al. (2015) *J Abnorm Psychol*; Sewart, A.R. et al. (2019) *Clinical Psychological Science*; Metts, A., et al. (2021) *Journal of Abnormal Psychology*; Metts, AV et al. (2022) *Development and Psychopathology*; Yarrington, et al (2023) *Clinical Psychological Science*; Metts, A. et al (2024) *Clinical Psychological Science*

Anhedonia: subjective, cognitive, behavioral, autonomic and neural hypo-responsivity to reward



Craske, M.G. et al. (2024) *Nature Reviews Psychology*; Sandman CF & Craske MG. (2021) *Current Topics Behavioral Neuroscience*

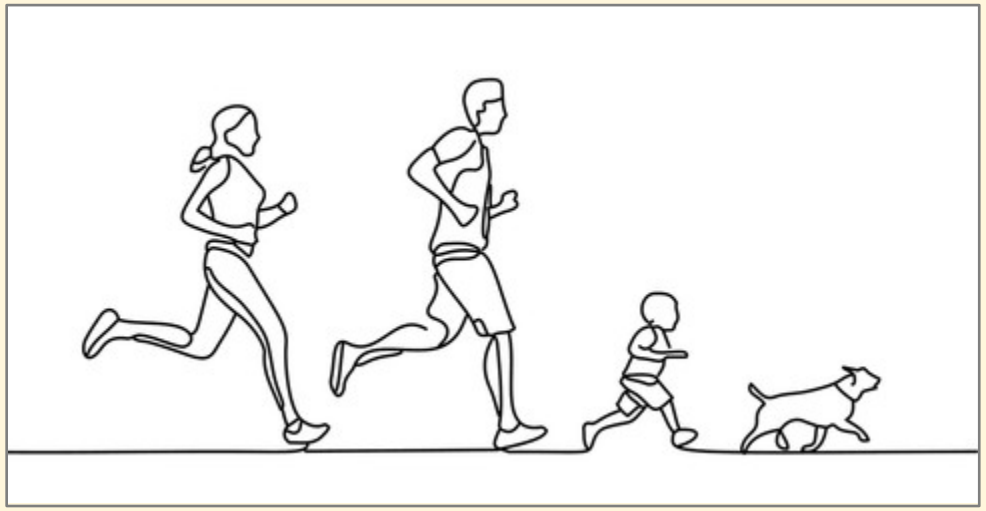
Less engagement in activities with reinforcement potential; less salience and reinforcement when reward is offered

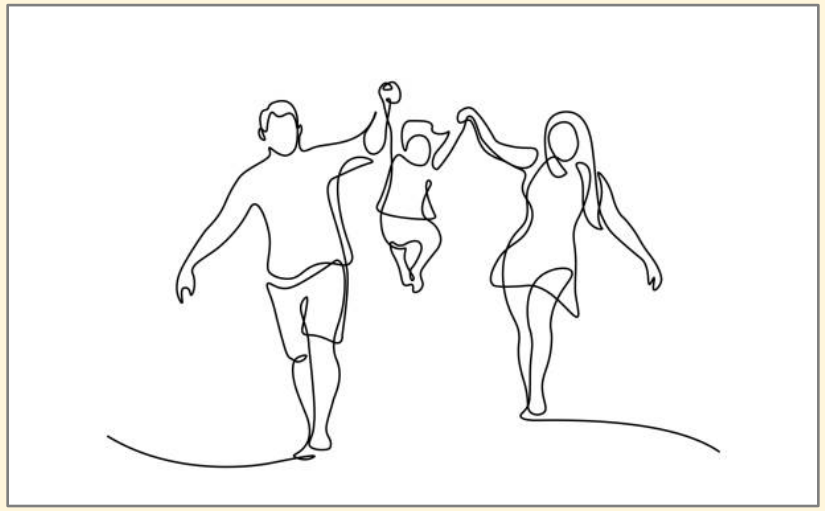
Pervasive and chronic anhedonia

Interventions that Target Reward Processes

Interventions that Target Reward Processes

Behavioral activation with pleasant activities → To experience more pleasure

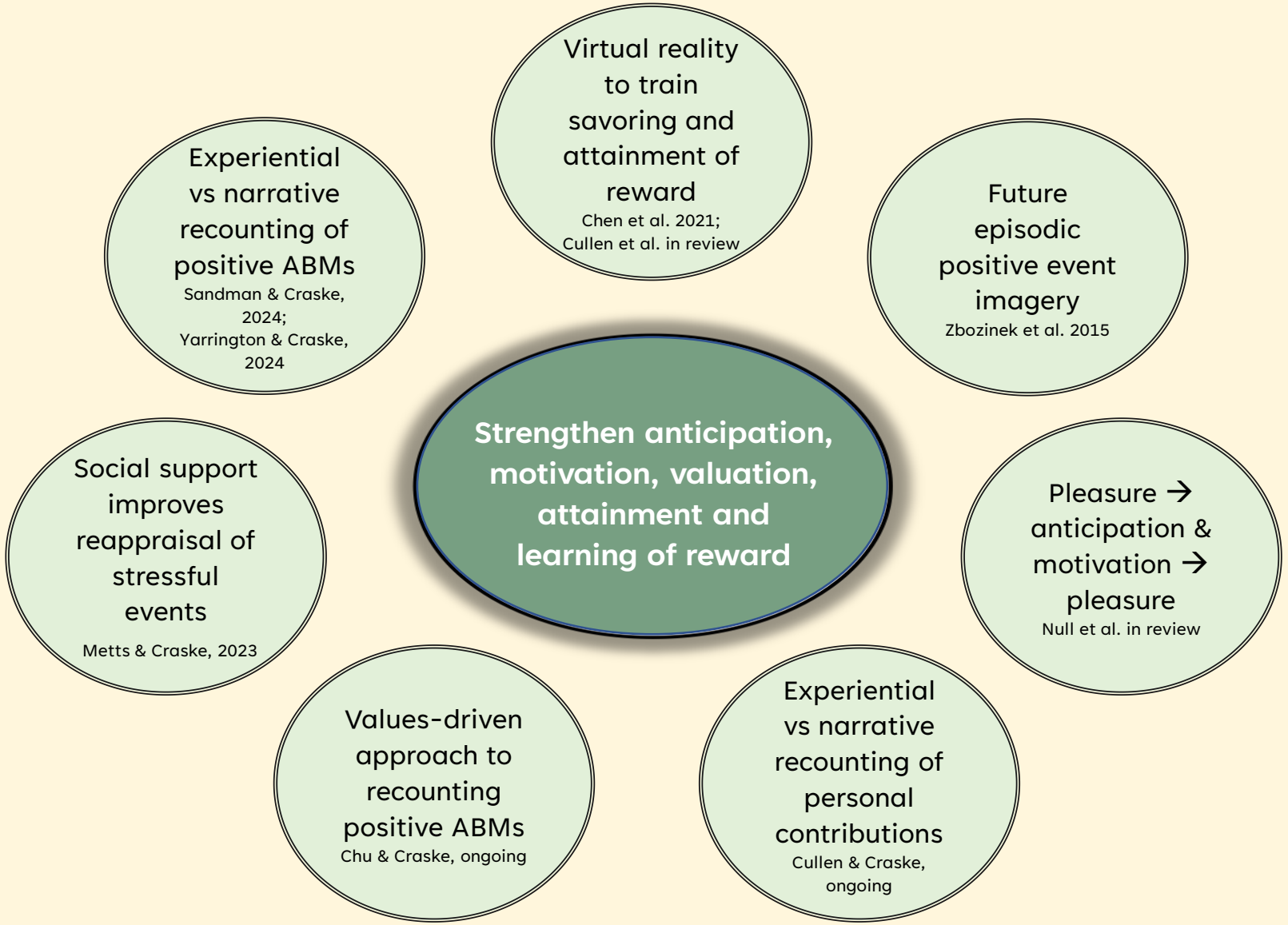




Deficits in reward processing inhibit enjoyment & sustainment of pleasure

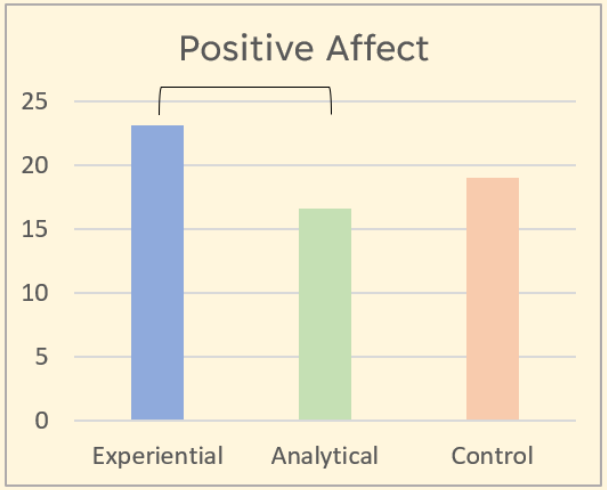
→ BA fails to substantially improve positive affect

Interventions that Target Reward Processes

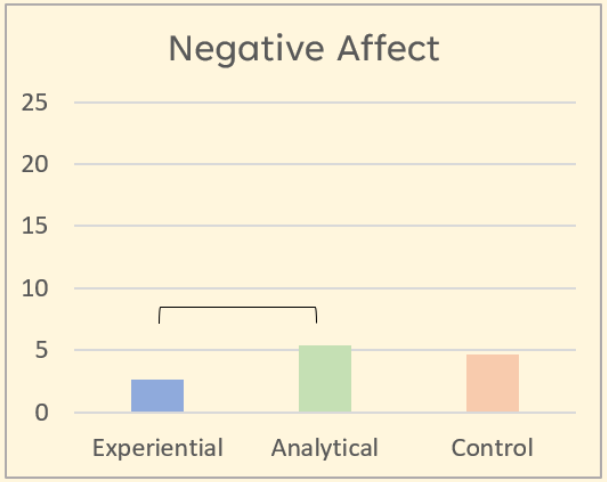


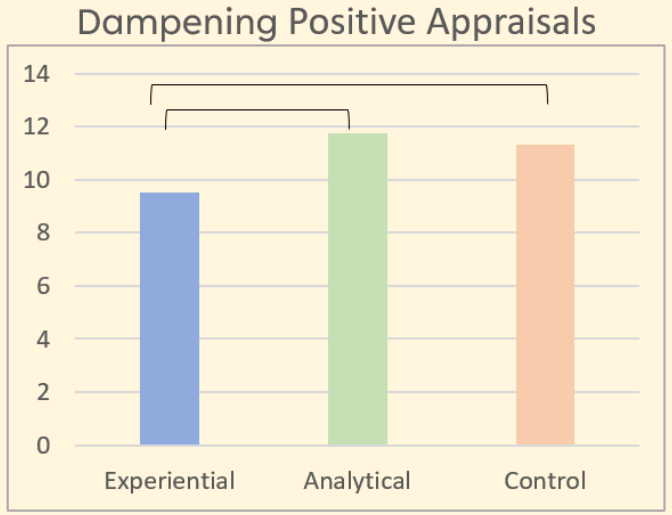
Zbozinek et al. (2015). *Behaviour Research and Therapy;* Sandman, C. F., & Craske, M. G. (2024) *Behaviour Research and Therapy;* Metts AV & Craske MG. (2023) *Behaviour Research and Therapy;* Yarrington & Craske (2024) *Behaviour Research and Therapy*; Chen et al. (2021) *Frontiers in Psychology;* Null et al. (in review); Cullen et al., (in review); Chu & Craske (ongoing); Cullen & Craske (ongoing)

Interventions that Target Reward Processes



Effect of experiential vs analytic vs control processing of positive autobiographic memories,
N=96 high anhedonia





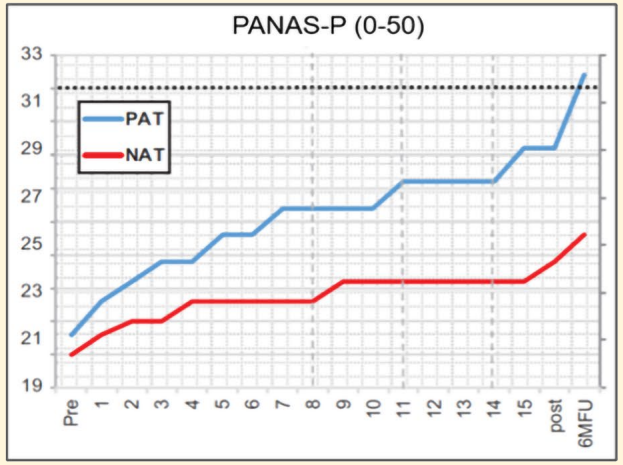
Sandman CF, Craske MG. Experiential processing increases positive affect and decreases dampening appraisals during autobiographical memory recall in an anhedonic sample. Behav Res Ther. 2024 Oct;181:104606.

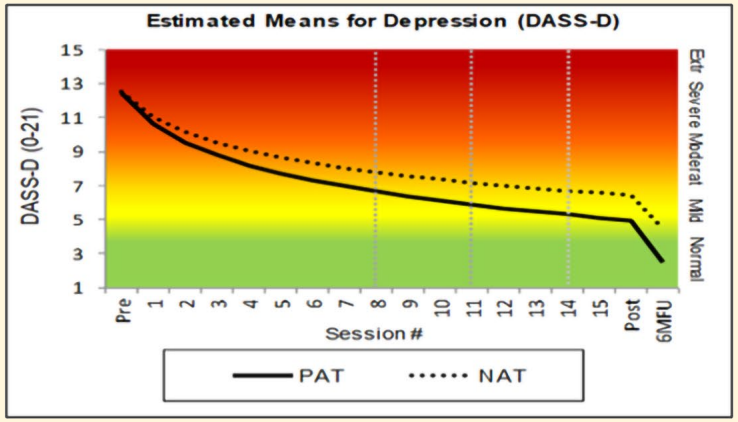
Interventions that Target Reward Processes

Positive Affect Treatment	
Active Ingredient	**Reward Mechanism**
Shades of positive emotions	Anticipation + Consumption
Mood–activity monitoring	Learning
Behavioral activation planning	Anticipation
Behavioral activation implementation	Consumption + Learning
Imaginal recounting	Consumption + Learning
Finding silver linings	Consumption + Learning
Taking ownership	Consumption + Learning
Imagining positive outcomes	Anticipation + Learning
Loving kindness	Consumption + Learning
Gratitude	Consumption + Learning
Generosity	Consumption + Learning
Appreciative joy	Consumption + Learning

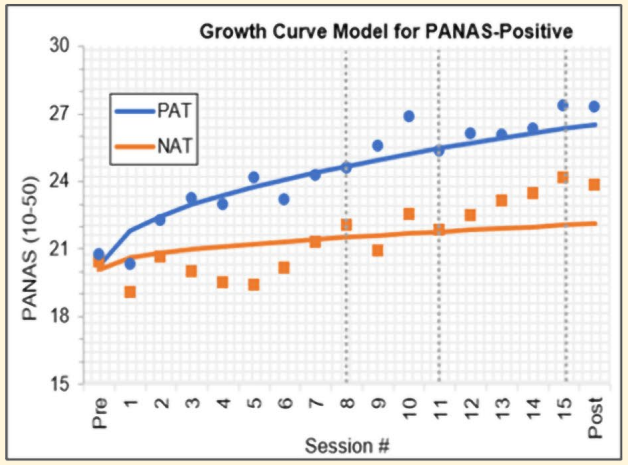
Craske MG, Meuret AE, Ritz T, Treanor M, Dour H, Rosenfield D. Positive affect treatment for depression and anxiety: A randomized clinical trial for a core feature of anhedonia. *Journal of Consulting and Clinical Psychology* 2019 May;87(5):457-471.

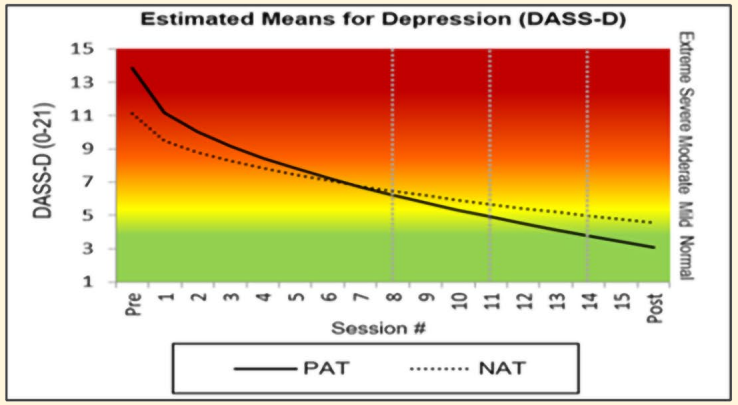
Positive Affect Treatment



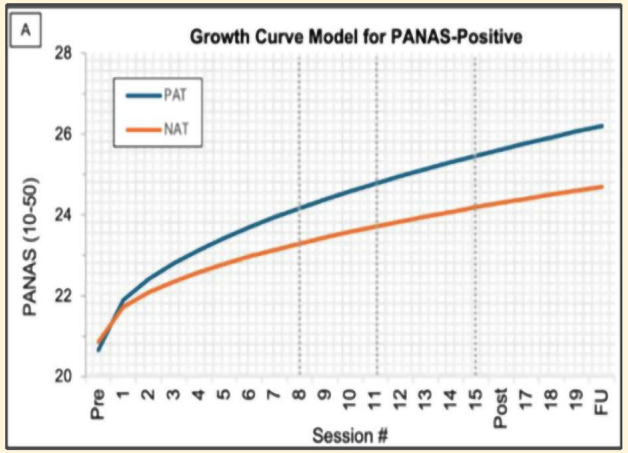


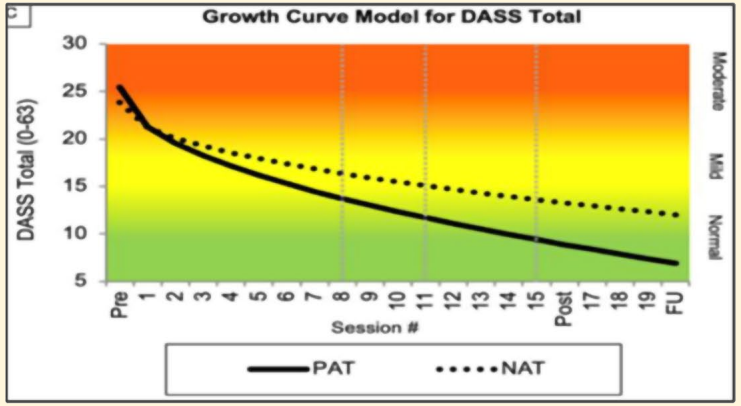
Craske, M.G., Meuret, A., Ritz, T., Treanor, M., Dour, H., & Rosenfield, D. (2019). *Journal of Consulting and Clinical Psychology*, 87(5), 457-471. doi: 10.1037/ccp0000396





Craske, M.G., Meuret, A., Echiverri-Cohen, E., Rosenfield, D., & Ritz, T. (2023). *Journal of Consulting and Clinical Psychology.* 2023 Mar 9. doi: 10.1037/ccp0000805





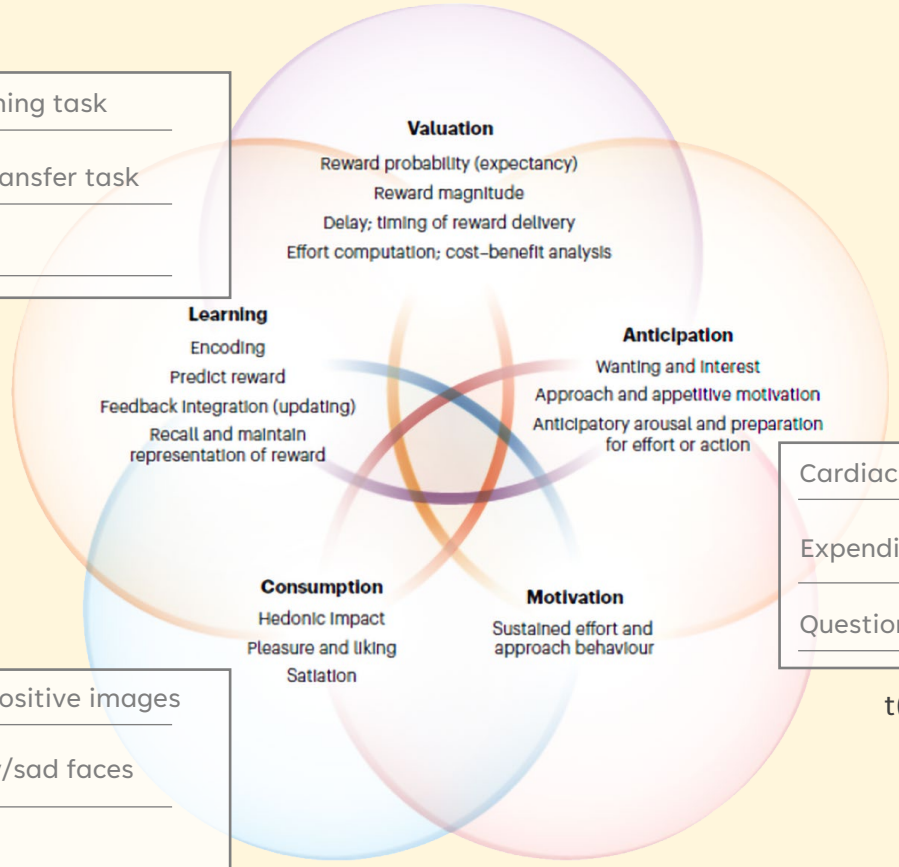
Meuret AE, Rosenfield D, Wang E, Hough CM, Ritz T, Craske MG. *JAMA Netw Open.* 2026;9(4):e267403. doi:10.1001/jamanetworkopen.2026.7403

Interventions that Target Reward Processes

Probabilistic reward learning task

Pavlovian instrumental transfer task

Questionnaires



Cardiac acceleration to anticipation of $

Expenditure of effort for reward task

Questionnaires

t(223)=1.99, p=.048, d=.27
b=.10, z=2.76, p=.006

Cardiac acceleration to positive images

Attentional bias to happy/sad faces

Questionnaires

t(273)=2.04,p=.042, d=.25
b=.07, z=2.18, p=.03

Increased reward processing
PAT > NAT

Correlated with clinical improvement

Craske, M.G., Meuret, A., Echiverri-Cohen, E., Rosenfield, D., & Ritz, T. (2023). Positive affect treatment targets reward sensitivity: a randomized controlled trial. *Journal of Consulting and Clinical Psychology.*

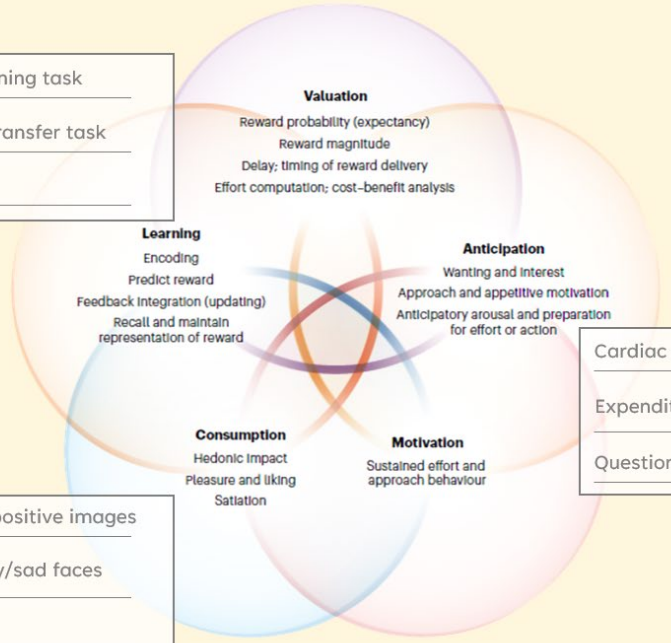
Interventions that Target Reward Processes

Reward Processes

Probabilistic reward learning task

Pavlovian instrumental transfer task

Questionnaires



Cardiac acceleration to anticipation of $

Expenditure of effort for reward task

Questionnaires

Cardiac acceleration to positive images

Attentional bias to happy/sad faces

Questionnaires

Threat Processes

Cardiac response to math stressor

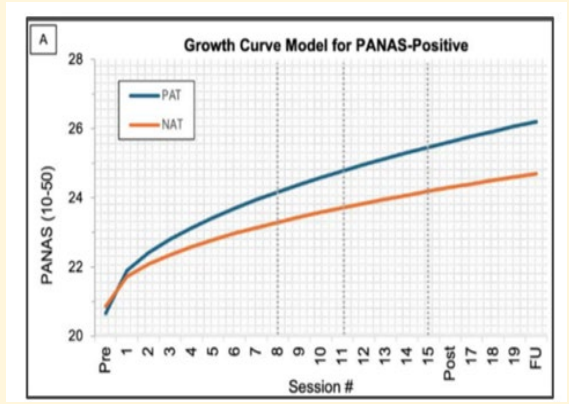
Cardiac response to negative images

Attentional bias to negative faces

Questionnaires

Increased reward processing
PAT = NAT

Mediated clinical improvement
PAT = NAT



t_{1356} = 1.55;P = .12;d = 0.26

Decreased threat responding
NAT = PAT

Mediated clinical improvement
NAT = PAT

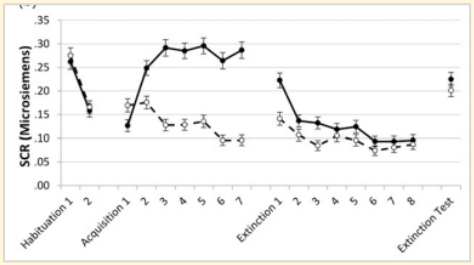
Larger reductions in depression & anxiety for PAT vs NAT

Increases in positive affect → decreases in dep & anx
(Barnes-Horowitz et al., 2023)

Meuret AE, Rosenfield D, Wang E, Hough CM, Ritz T, Craske MG. Positive Affect Treatment for Depression, Anxiety, and Low Positive Affect: A Randomized Clinical Trial. *JAMA Netw Open.* 2026;9(4):e267403.

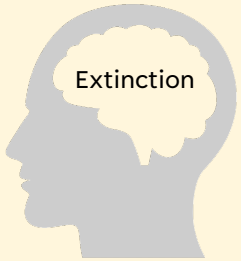
Precision by matching intervention to mechanism

Low positive affect impedes extinction



Zbozinek et al. (2015) *Beh Res & Ther*

Zbozinek & Craske (2016) *Cog & Emot*



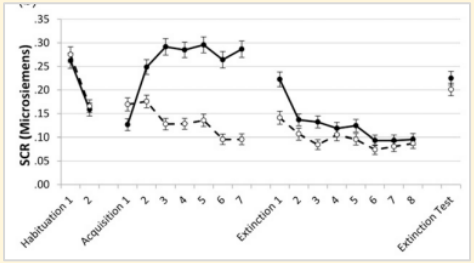
Young et al. (2021) *Neuropsychopharmacology*

Rosenberg et al. (2021) *Biol Psych: CNNI*

Nusslock et al. (under review)

Precision by matching intervention to mechanism

Low positive affect impedes extinction



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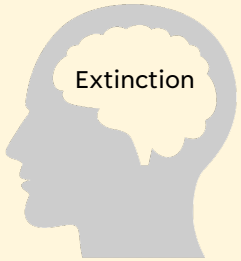
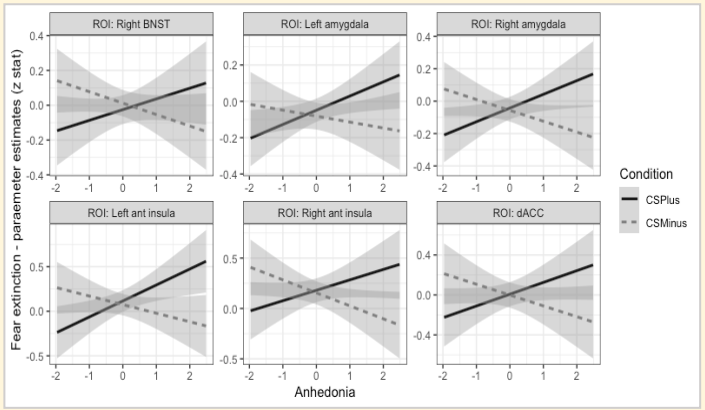


Young et al. (2021) *Neuropsychopharmacology*

Rosenberg et al. (2021) *Biol Psych: CNNI*

Nusslock et al. (under review)

Anhedonia associated with stronger neural threat activation to stimulus that should be extinguished



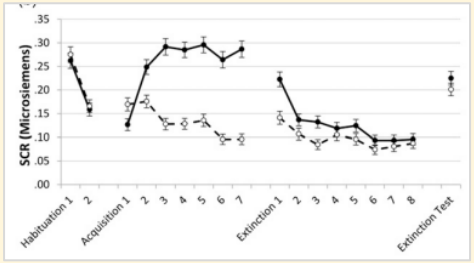
(Young et al., 2021)

Specific to anhedonia (vs negative affect and fears) and to extinction (vs acquisition)
b=.21, se=.066, p=.001
(Nusslock et al., under review)

Whole-brain multivoxel pattern analysis decoder: extinction decoded patterns associated with anhedonia (not negative affect or fears) (n=123), R^2 = 0.168. Decoder predicted anhedonia in cross-validation sample (n=136), R^2=.047, r=.276, p=.002
(Rosenberg et al., 2021)

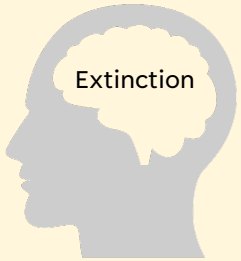
Precision by matching intervention to mechanism

Low positive affect impedes extinction



Zbozinek et al. (2015) *Beh Res & Ther*

Zbozinek & Craske (2016) *Cog & Emot*



Young et al. (2021) *Neuropsychopharmacology*

Rosenberg et al. (2021) *Biol Psych: CNNI*

Nusslock et al. (under review)

Potential mechanisms

Prediction error during fear extinction (point at which expected US does not occur) is better-than-expected outcome that generates positive hedonic value

(Vervliet et al., 2017; Willems & Vervliet, 2021)

Silencing of dopaminergic neurons in ventral tegmental area (site of prediction error) at US omission blocks extinction

(Shultz et al., 2016; Kalisch et al., 2019)

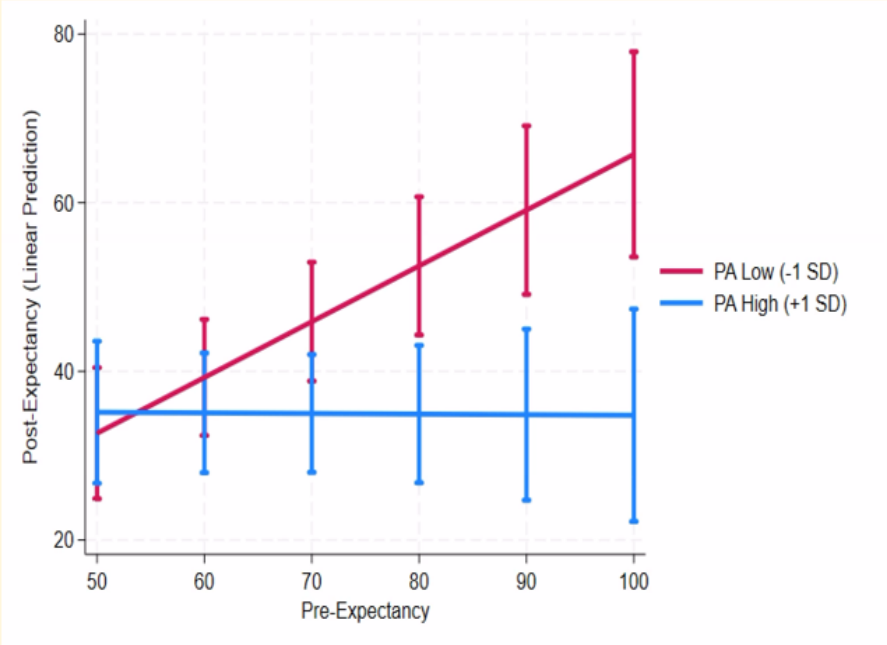
Anhedonia/low positive affect associated with less hedonic value and dopaminergic dysregulation

(Wang et al., 2021)

Anhedonia → impaired prediction error learning during exposure therapy??

Precision by matching intervention to mechanism

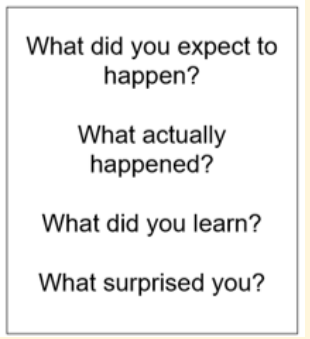
At higher pre-exposure expectancy, higher positive affect predicts lower post-expectancy



PA x pre-expectancy → post-expectancy: $f = .162$, $Z = -2.15$, $p = .032$
Within-subjects: $f = .202$, $Z = -2.61$, $p = .009$
Over and above NA: $f = .168$, $Z = -2.26$, $p = .024$

Rosenberg, Zbozinek, Treanor & Craske (2026)
J of Anxiety Disorders

Higher positive sentiment during exposure consolidation predicts greater expectancy change



BERT linguistic sentiment analyses:
i) written text ($b = 21.76$, SE = 9.69, $t(42.31) = 2.25$, $p = .030$)
ii) session transcripts ($b = 8.12$, SE = 3.25, $t(285.90) = 2.49$, $p = .013$)

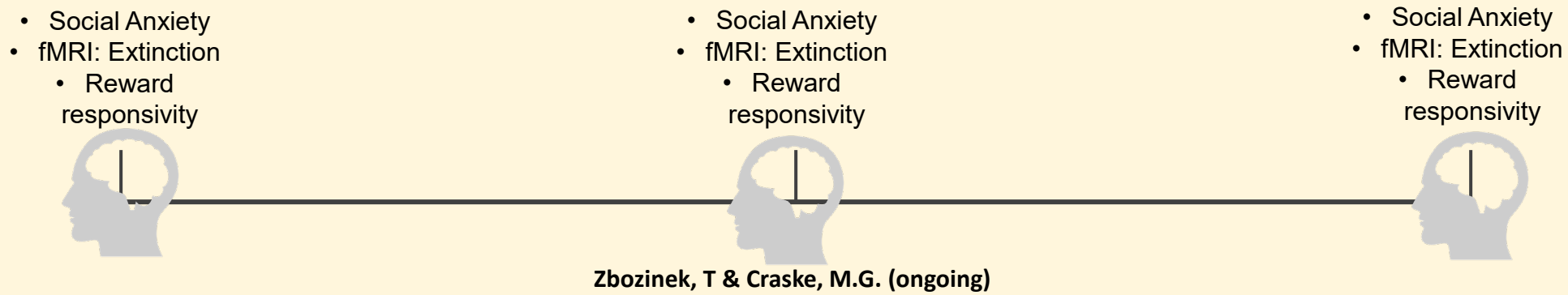
Barnes-Horowitz, Losiewicz, Treanor & Craske (2026)
Behaviour Research & Therapy

Expectancy change is a positive predictor of therapeutic outcome (Zbozinek et al., 2026; Barnes-Horowitz et al., 2025)
→ Reward-targeted therapy may augment exposure therapy for anxiety with anhedonia

Precision by matching intervention to mechanism

Social anxiety disorder with anhedonia

8 therapy sessions, 4 weeks		8 exposure sessions, 4 weeks
Positive Affect Treatment	+	Positive affect induction prior to each exposure trial
Arousal Reduction (breathing, PMR, mindfulness)	+	Arousal regulation induction prior to each exposure trial



Zbozinek, T & Craske, M.G. (ongoing)

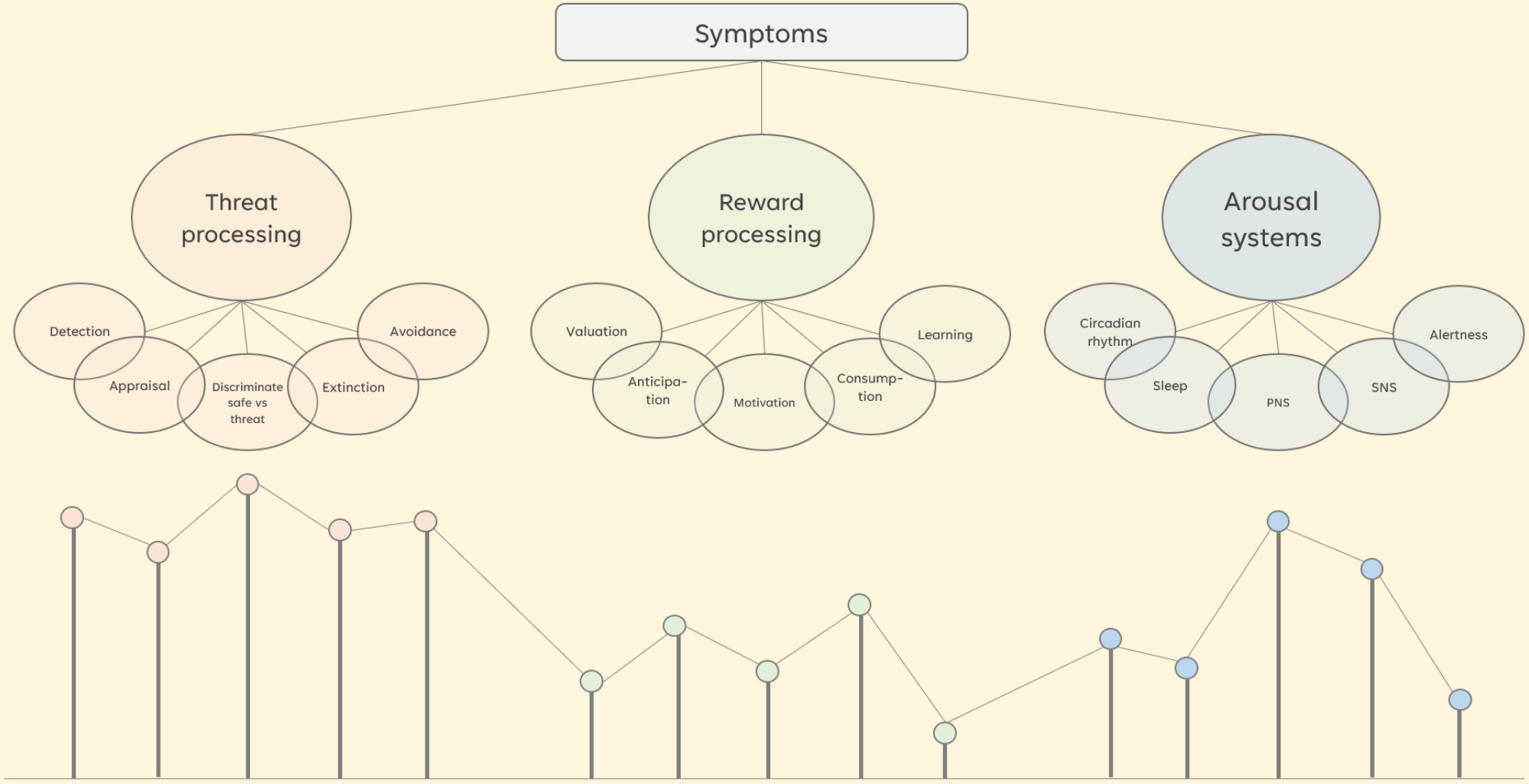
Precision by matching intervention to mechanism

	Psychological Treatment	*Biological Treatment/Augmentation*
Anhedonia and reward dysregulation	Positive Affect Treatment	Pramipexole[2] Kappa opioid antagonists[3]
Anxiety and extinction dysregulation	Inhibitory Retrieval Exposure Therapy	Scopolamine[4] Decoded neuroreinforcement[5]
Reward and extinction dysregulation	Positive Affect Treatment + Inhibitory Retrieval Exposure Therapy[1]	Amisulpride[6]

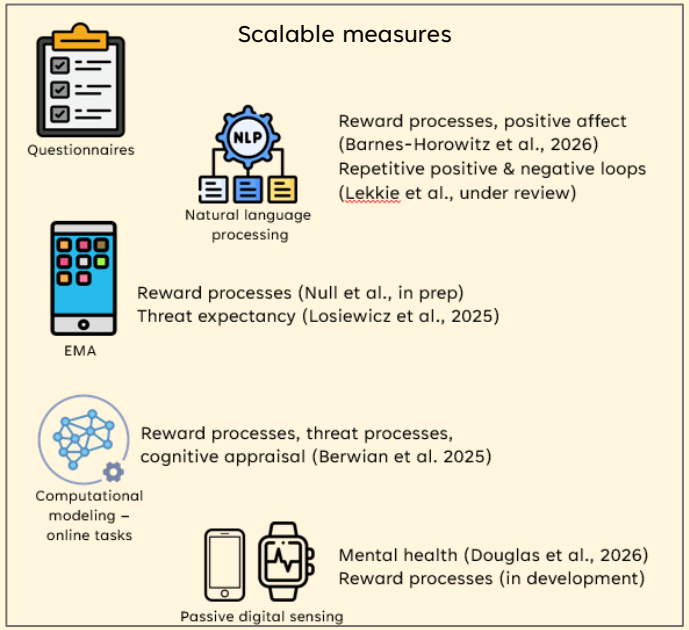
[1] Zbozinek & Craske, ongoing [2]Browning et al. Lancet Psychiatry. 2025. 0(0). doi:10.1016/S2215-0366(25)00194-4 [3]Krystal AD et al. *Nat Med.* 2020 May;26(5):760-768; [4]Craske et al. *Biological Psychiatry*. 2019. [5]Cushing CA, Lau H, Kawato M, Craske MG, Taschereau-Dumouchel V. *Psychiatry Clin Neurosci.* 2024 Nov;78(11):678-686. [6]Zbozinek, Rosenberg, Kahlsa, Pizzagalli & Craske (application)

Precision by matching intervention to mechanism: future directions

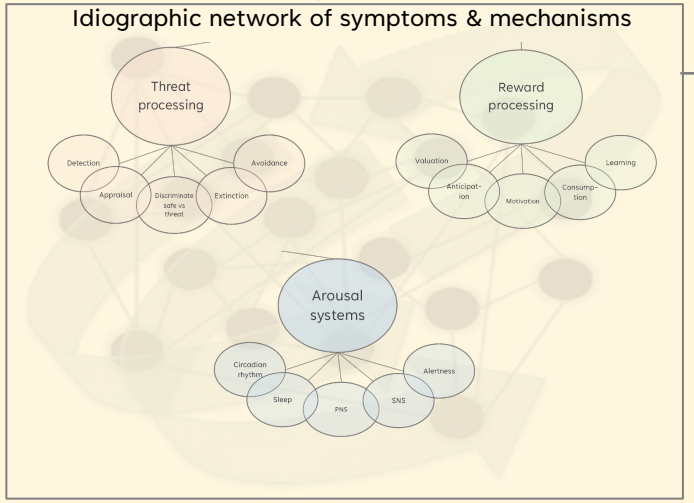
Idiographic symptom & mechanism profile



Precision by matching intervention to mechanism: future directions



Repeated measurement



Identify central drivers of spread of symptoms (network control theory)

	Psychological Treatment	*Biological Treatment*
Anhedonia and reward dysregulation	Positive Affect Treatment	Pramipexole[2] Kappa opioid antagonists[3]
Anxiety and extinction dysregulation	Inhibitory Retrieval Exposure Therapy	Scopolamine[4] Decoded neuroreinforcement[5]
Reward and extinction dysregulation	Positive Affect Treatment + Inhibitory Retrieval Exposure Therapy[1]	Amisulpride[6]

UCLA

Part of the Depression Grand Challenge

STAND

the STAND program

About STAND | @ ELAC | @ UCLA | for All | Tips

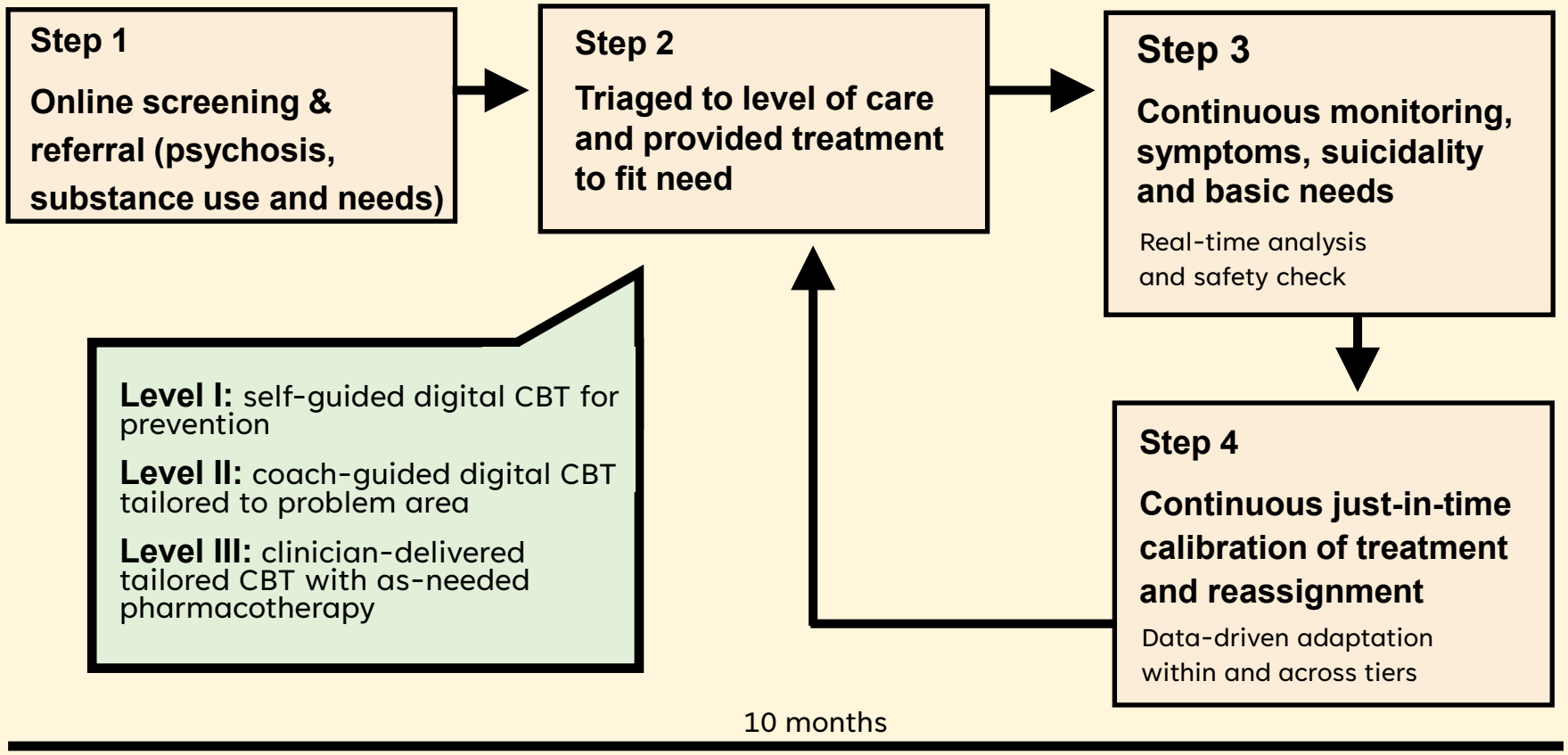
STAND: Screening & Treatment for Anxiety & Depression

A strategy to increase access to care.

When the UCLA Depression Grand Challenge started our work in 2015, we realized that if we wanted to reach the goal of cutting the global burden of depression, we needed to take action to develop a new way to effectively reach and treat more people. This was the impetus for the development of the STAND system of care.

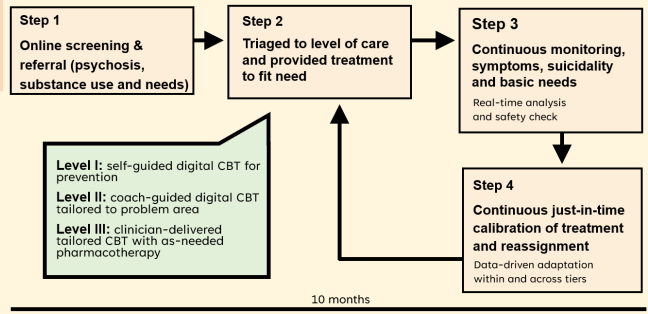
The STAND system of care is an all-in-one, end-to-end system, which includes screening, treatment and ongoing monitoring of mood and symptoms. Leveraging an online screening tool, participants are screened for symptoms of anxiety, depression and suicidality and triaged to the level of care matching their needs. Participants begin care in the recommended tier and are routinely screened with just-in-time calibration of their treatment level as their needs change. To learn more about the STAND program, review the STAND

STAND System of Care



Wolitzky-Taylor K, Wen A, Freimer N, Craske MG. Anxiety and depression in emerging adults: The STAND program as a model of scalable screening and intervention. Neuropsychopharmacology. 2026 Jan;51(1):244-258.

STAND System of Care



STAND: Step 1 Online Screening

Computerized adaptive testing (Gibbons et al. 2016)

- depression severity
- anxiety severity
- suicidality.....24/7 crisis team triggered, reach out, assess, action, fu

Psychosis screener.....LCSW alerted, assessment, linked to specialty services

Substance use screener.....LCSW alerted, assessment, linked to specialty services

Basic needs.....upon request, LCSW assessment, linked to local food, housing, finances, & safety services

STAND: Step 2 Triage to Level of Care

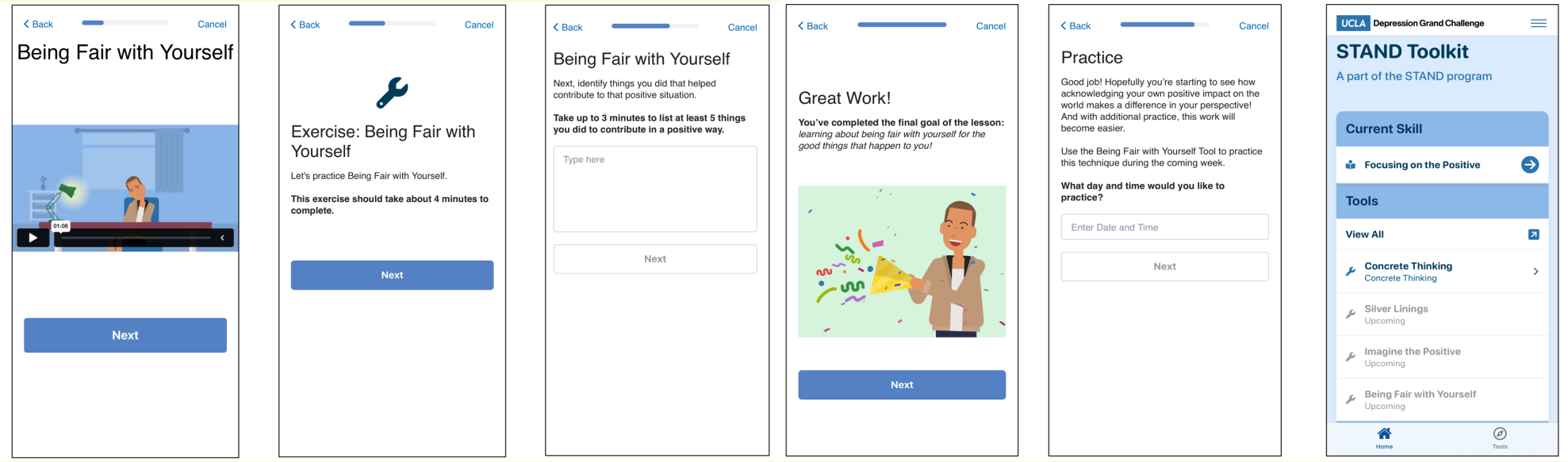
Level 1: self-guided digital CBT targeting negative rumination/worry, for prevention & wellness

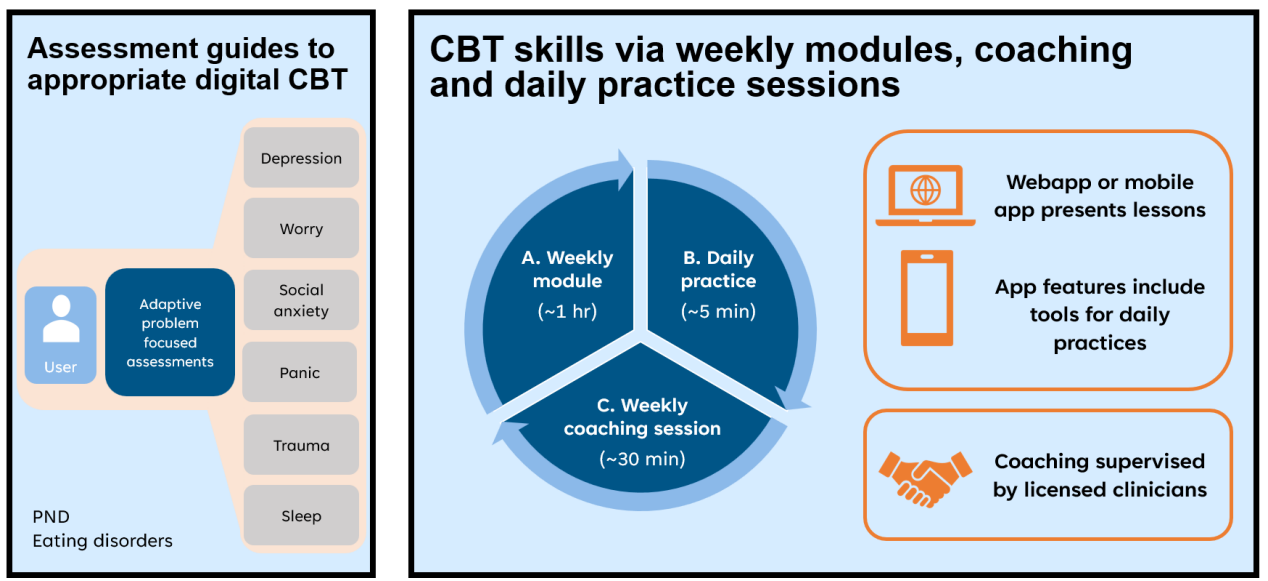
Level II: digital CBT adaptively tailored to specific problem areas with coach guidance, via telehealth

Level III: clinician-delivered CBT adaptively tailored to specific problem areas with pharmacotherapy as needed, via telehealth

STAND System of Care

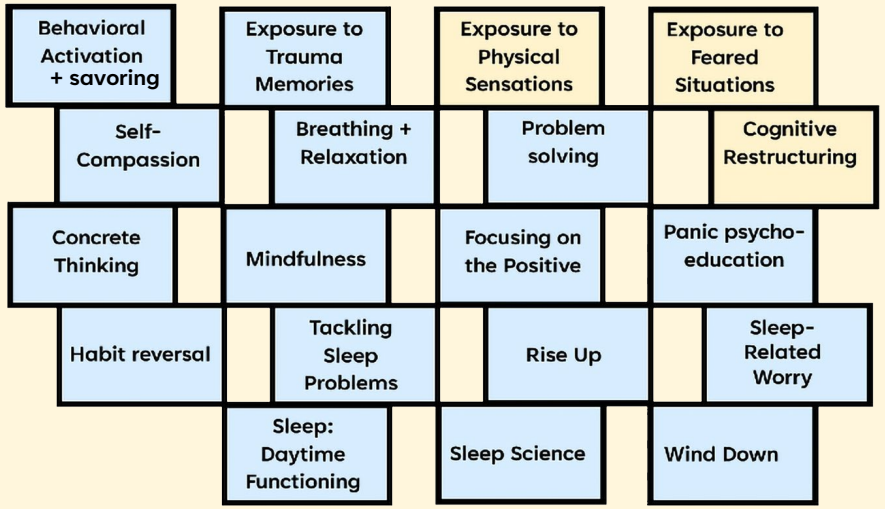
Level I:
self-guided digital CBT





Level II:
coach-guided, tailored digital CBT

- Coaching/support increases engagement
- Peer coaches: trained, certified, supervised, fidelity assessed (digitized protocols)
- Encourage CBT, problem solve barriers
- ≤ 8 videoconference visits with LCSW supervisor available

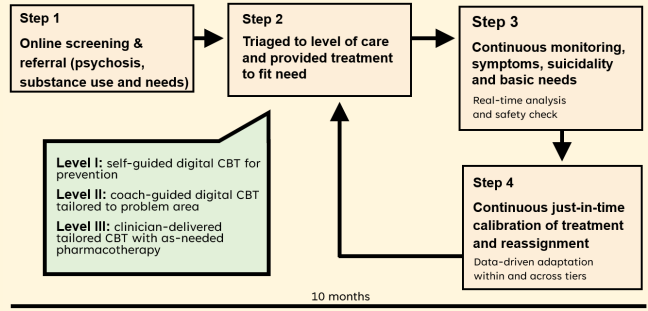


Level III: clinician-delivered, tailored CBT with medication as needed

- Community clinicians trained, certified, supervised & fidelity assessed (digitized protocols)
- Standardized questionnaires & functional assessment guide CBT strategy selection
- Psychiatry consultation & medication management as needed
- Measurement-based care
- Teleheath

Symptoms	CBT Strategy (+ medication as appropriate)
Anhedonia	Behavioral activation with savoring (PAT)
Fear/phobia	Inhibitory Retrieval Exposure therapy
Worry/rumination	Cognitive restructuring or acceptance/mindfulness
Sleep dysregulation	Brief behavioral therapy for insomnia
Trauma: fear	Imaginal/in vivo exposure
Trauma: guilt, shame, cognitive distortions	Trauma narrative with cognitive restructuring
Social skills	Interpersonal effectiveness training
Chronic suicidality/self harm/affective instability	Distress tolerance skills
Mania	Sleep regulation

STAND System of Care



STAND: Step 3 Monitoring

Weekly/biweekly symptom monitoring via computerized adaptive testing

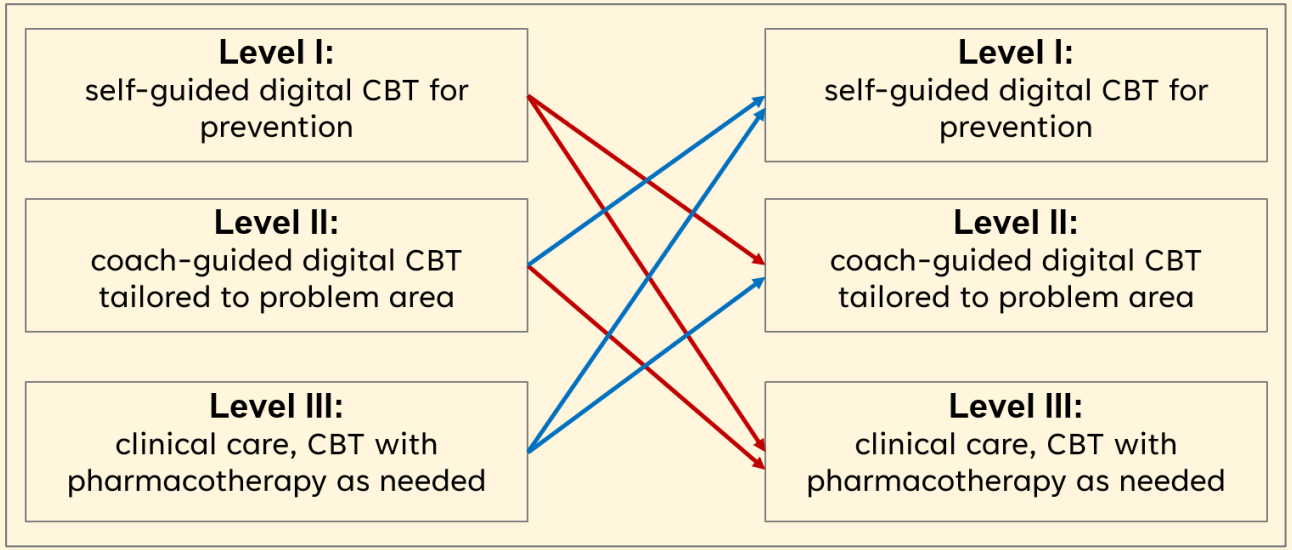
- depression
- anxiety
- suicidality.....24/7 crisis team triggered, reach out, assess, action, fu

Monthly basic needs self report

- finances
- food
- housing
- safety

.....upon request, LCSW assess & link to local resources

STAND: Step 4 Adaptation

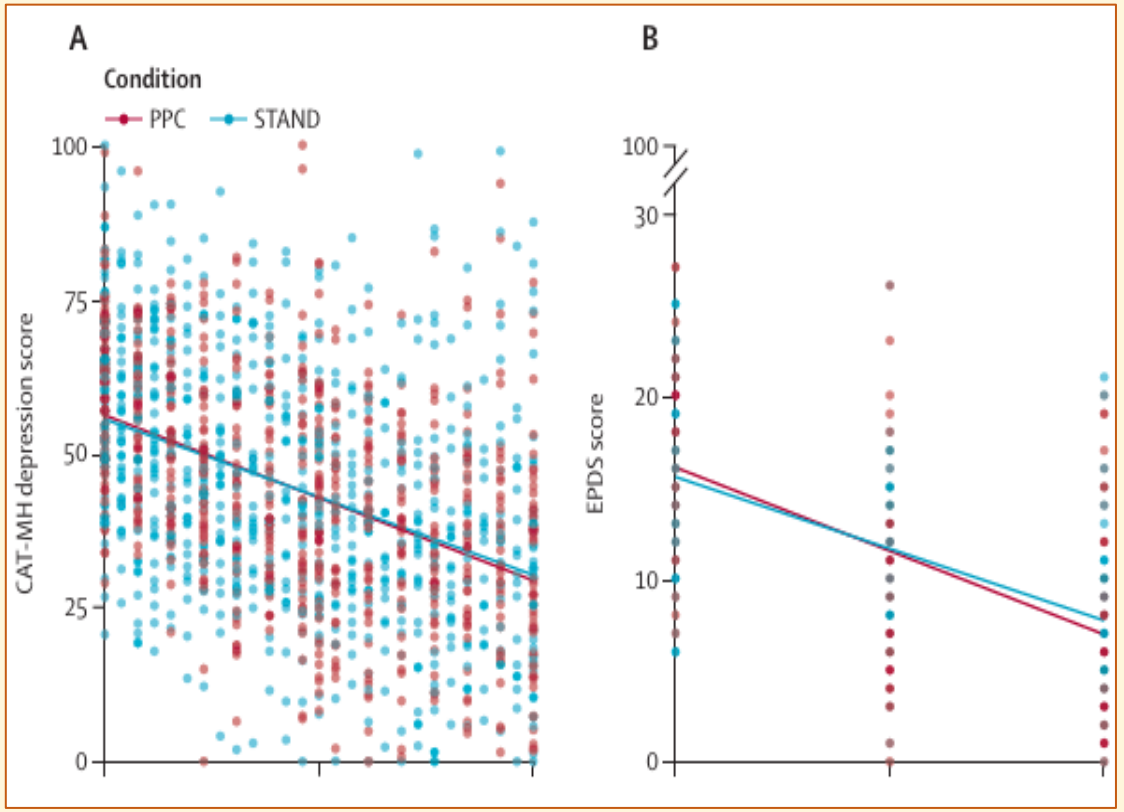


During active treatment or follow-up

STAND System of Care: Perinatal depression

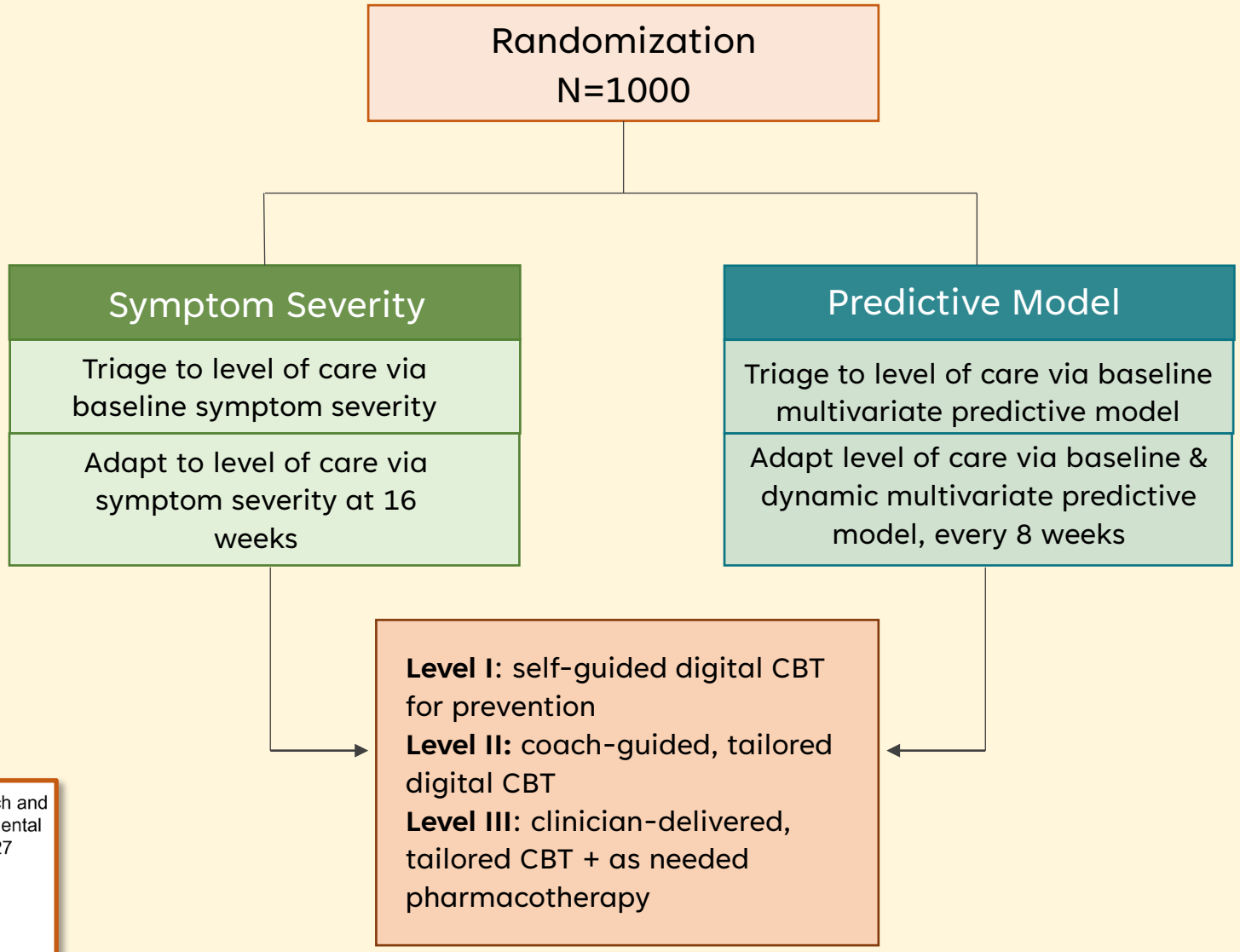
RCT; N=168 obstetrics clinic patients
with moderate to severe perinatal depression

- STAND (N=78)
  - Level II: digital CBT + coaching..... 75.8%
  - Level III: clinician-delivered CBT... 24.2%
  - Medication management..... 7.6%
- Reproductive Psychiatrist (N=88)
  - Supportive therapy..... 100%
  - Medication management..... 75.7%



Wolitzky-Taylor K, Richards, M.C., Metts, A., Welborn, A., McDonald, V., Arnaudova I., Fears S., Balliu, B., Huang, F., O'Mahen, H., Newby, J.M., Millard, M.R., Stein, A., Freimer, N., & Craske, M.G. (2026) An integrated system of digital therapy and clinician care versus perinatal psychiatric care for women with perinatal depression and anxiety in the USA: a single-centre, randomised controlled trial. *Lancet Obstetrics, Gynaecology, & Women's Health*

STAND System of Care: Increasing precision to needs



Advanced Laboratories for Accelerating the Reach and Impact of Treatments for Youth and Adults with Mental Illness (ALACRITY) Research Centers 2022-2027

Screening, tracking and treating anxiety and depression in community colleges

M.G. Craske & K. Wolitzky-Taylor

NIH National Institute of Mental Health

Randomization
N=1000

Symptom Severity

Triage to level of care via baseline symptom severity

Adapt to level of care via symptom severity at 16 weeks

Predictive Model

Triage to level of care via baseline multivariate predictive model

Adapt level of care via baseline & dynamic multivariate predictive model, every 8 weeks

Level I: self-guided digital CBT for prevention
Level II: coach-guided, tailored digital CBT
Level III: clinician-delivered, tailored CBT + as needed pharmacotherapy

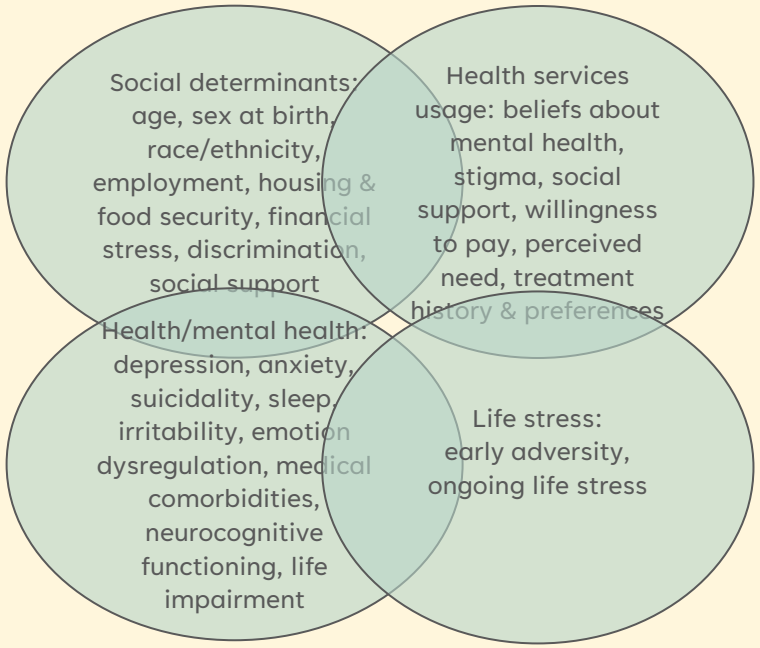
Computerized adaptive testing: anxiety, depression, suicidality

Level I: none to mild

Level II: moderate depression, up to severe anxiety

Level III: severe depression, suicidality

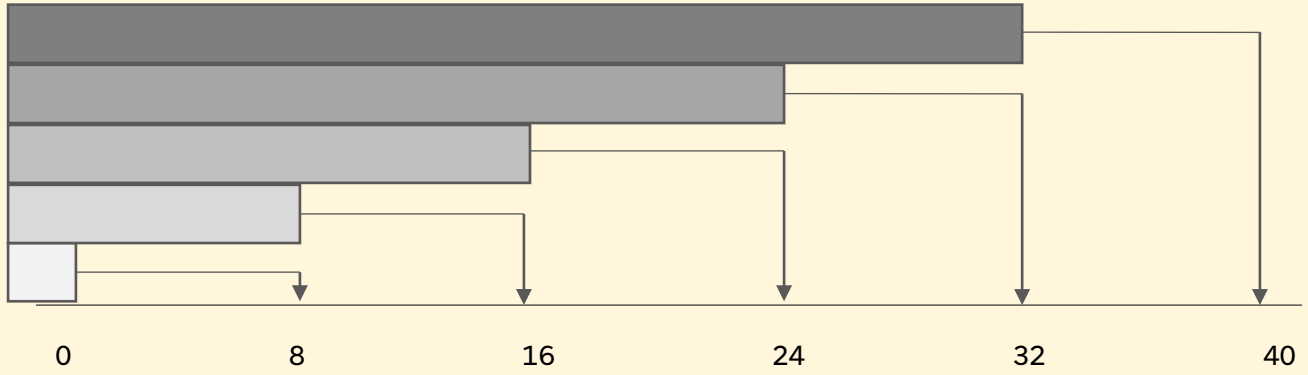
Baseline Predictors



Dynamic Predictors

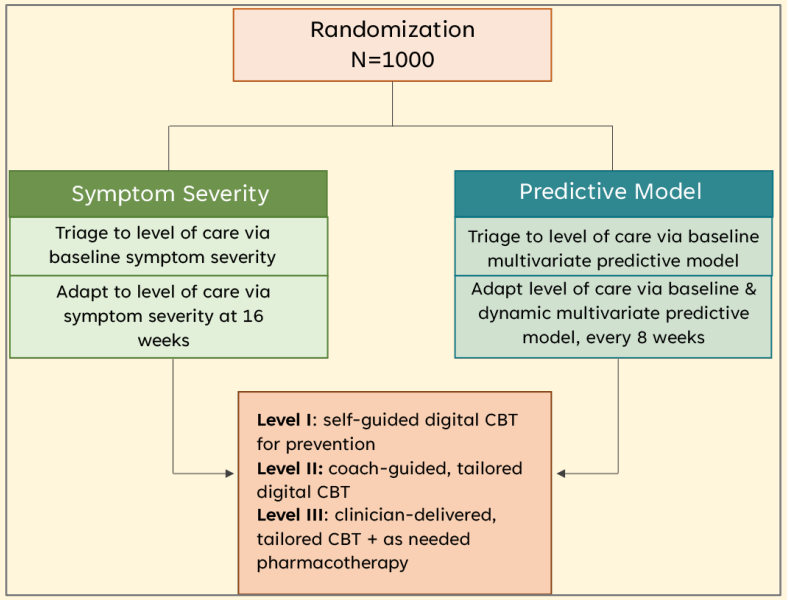
Pilot: digital sensing

Baseline & dynamic data predict symptoms 8 weeks later if switched vs stayed Level II vs III

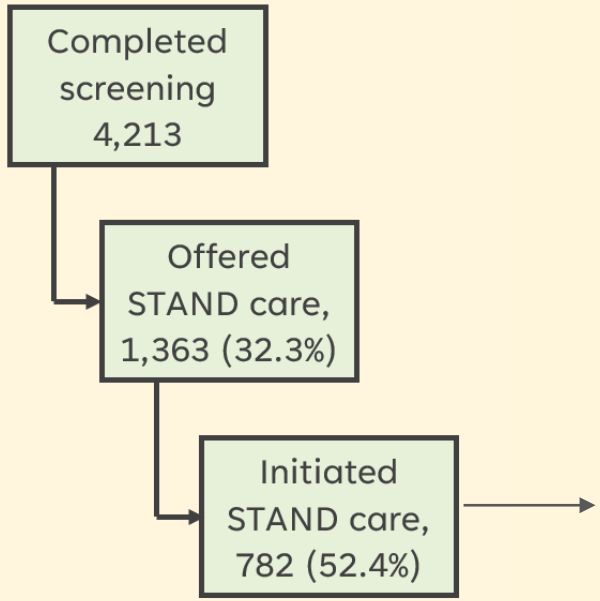


Baseline data predict symptoms at 8 weeks if triaged to Level II vs III

STAND System of Care: Increasing precision to needs



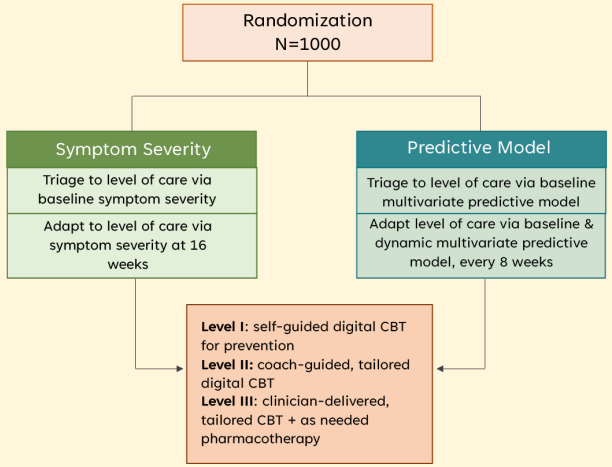
Unable to afford balanced meals in past week	50.0%
Eat less than should due to insufficient money for food in past week	34.9%
Difficulty paying rent in past week	31.2%
Houseless in past week	6.4%
Financial difficulties that could significantly impact life	45.9%



Triaged

Level I: 18%
Level II: 56%
Level III: 26%

STAND System of Care: Increasing precision to needs



To date (N=782).....predictive model leads to better outcomes than symptom severity

Uptake

Engagement

Symptoms

Academics

STAND System of Care: Increasing precision by matching intervention to mechanism

Symptoms

Questionnaires

Clinical functional assessment

CBT Strategy Digital or Clinician
Behavioral activation with savoring
Attending to the positive
Mindfulness & acceptance
Inhibitory Retrieval Exposure therapy
Cognitive restructuring
Trauma imaginal exposure
Relaxation/breathing
Distress tolerance skills
Problem solving/concrete thinking
Brief behavioral therapy for insomnia

STAND System of Care: Increasing precision by matching intervention to mechanism

Symptoms

Questionnaires

Clinical functional assessment

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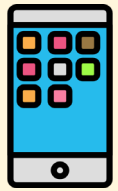
Trauma imaginal exposure
Relaxation/breathing
Distress tolerance skills
Problem solving/concrete thinking
Brief behavioral therapy for insomnia

Scalable Mechanism Measures

Questionnaires

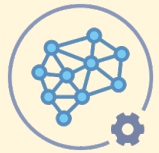
Natural language processing

Reward processes, positive affect (Barnes-Horowitz et al., 2026)
Repetitive positive & negative loops (Lekkie et al., under review)



EMA

Reward processes (Null et al., in prep)
Threat expectancy (Losiewicz et al., 2025)



Computational modeling – online tasks

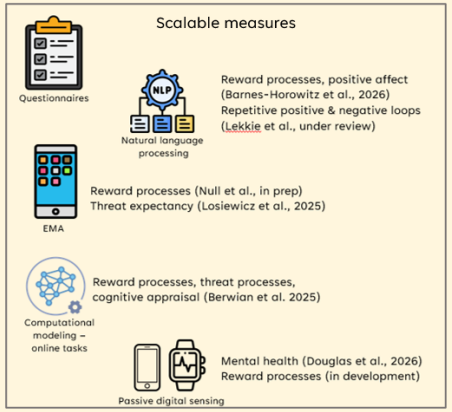
Reward processes, threat processes, cognitive appraisal (Berwian et al. 2025)

Passive digital sensing

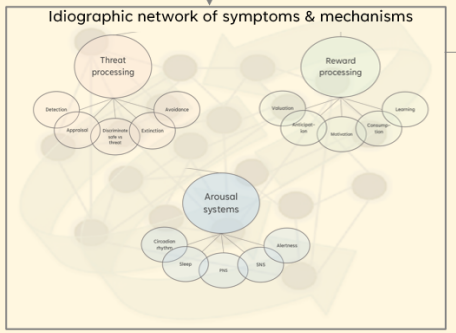
Mental health (Douglas et al., 2026)
Reward processes (in development)

STAND System of Care: Precision to mechanism and to needs

Idiographic matching of therapy to symptom and mechanism



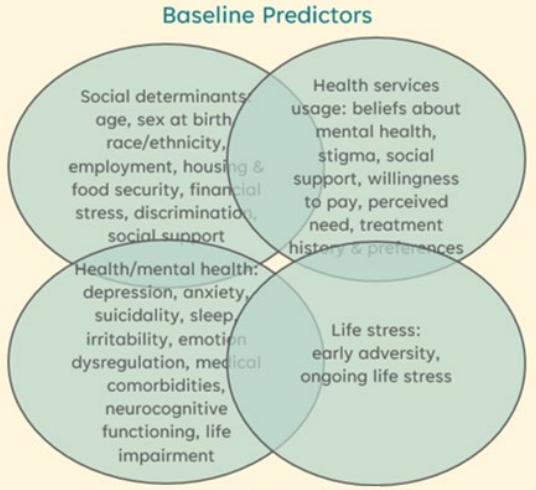
Repeated measurement



Identify central drivers of spread of symptoms (network control theory)

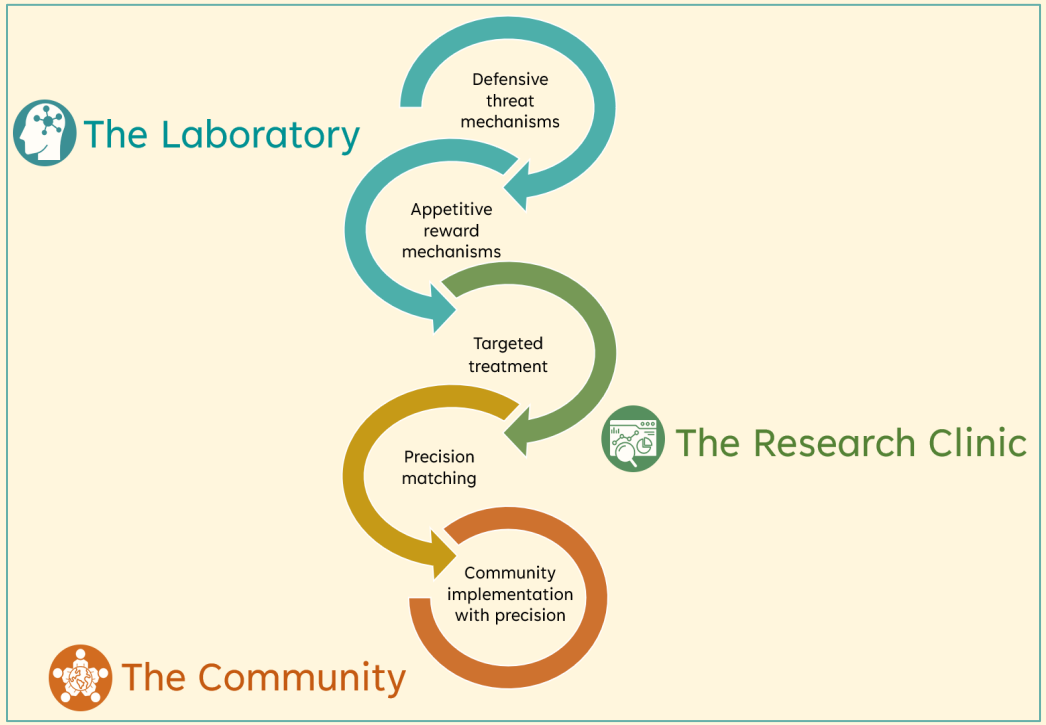
	Psychological Treatment	*Biological Treatment*
Anhedonia and reward dysregulation	Positive Affect Treatment	Pramipexole[2] Kappa opioid antagonists[3]
Anxiety and extinction dysregulation	Inhibitory Retrieval Exposure Therapy	Scopolamine[4] Decoded neuroreinforcement[5]
Reward and extinction dysregulation	Positive Affect Treatment + Inhibitory Retrieval Exposure Therapy[1]	Amisulpride[6]

Predictive modeling for selecting which level of care is likely to be most effective for a given person



Level I: self-guided digital CBT for prevention
Level II: coach-guided, tailored digital CBT
Level III: clinician-delivered, tailored CBT + as needed pharmacotherapy

Thank you



Acknowledgements:

Funding: UCLA Depression Grand Challenge, NIMH, DARPA, Wellcome Leap

Inhibitory Retrieval Exposure: Michael Treanor, Tomislav Zbozinek, Ben Rosenberg, Nora Barnes-Horowitz

Positive Affect Treatment: Alicia Meuret, Thomas Ritz, David Rosenfield, Christina Hough

STAND/ALACRITY: Kate Wolitzky-Taylor, Denise Chavira, Robert Gibbons, John Cursio, Joan Asarnow, Jocelyn Meza, Daniel Eisenberg, Alison Hamilton, Rebecca Collins, Amelia Welborn, Matthew Wong, Michelle Popowitz, Nelson Freimer, Gayane Gregorian, Alainna Wen, Francisco Segovia, Zachary Cohen, Tamar Kodish, numerous UCLA clinicians and student coaches, East Los Angeles College students, faculty and staff

ADRC: Research Scientists, Postdoctoral Fellows, Graduate Students, Research Coordinators