Pediatric Anxiety: Fear Learning and Extinction Recall

Alicia Henson[1], Lisa Williams[1], Ned Kalin[1]
Departments of Psychiatry[1], University of Wisconsin-Madison, Madison, WI, USA

HEALTHEmotions RESEARCH INSTITUTE UNIVERSITY OF WISCONSIN

Introduction

- Anxiety disorders are one of the most common psychiatric disorders in youth, with prevalence estimates between 10-20%,[1] and childhood anxiety is a risk factor for stress-related psychopathology in adulthood.[2]
- As anxiety disorders are significantly more prevalent in women,[3] this study focuses on girls as a high-risk population
- Fear learning, extinction and extinction recall may be altered in individuals with anxiety:
  - May have stronger responses in Conditioning and Extinction
  - May be less able to retain extinction learning
- Previous studies examining anxiety-related differences in fear learning and extinction use classical conditioning, and find some differences in both conditioning and extinction[4,5,6].
  - Few studies have been done with children.
- Previous research using an Extinction Recall task have found anxiety-related differences in brain imaging,[7,8] but none have examined physiological responses
- **Using data collected for an ongoing study, we conducted a preliminary analysis exploring fear conditioning, extinction, and extinction recall across a sample of girls aged 8-11 with a range of anxiety levels.**
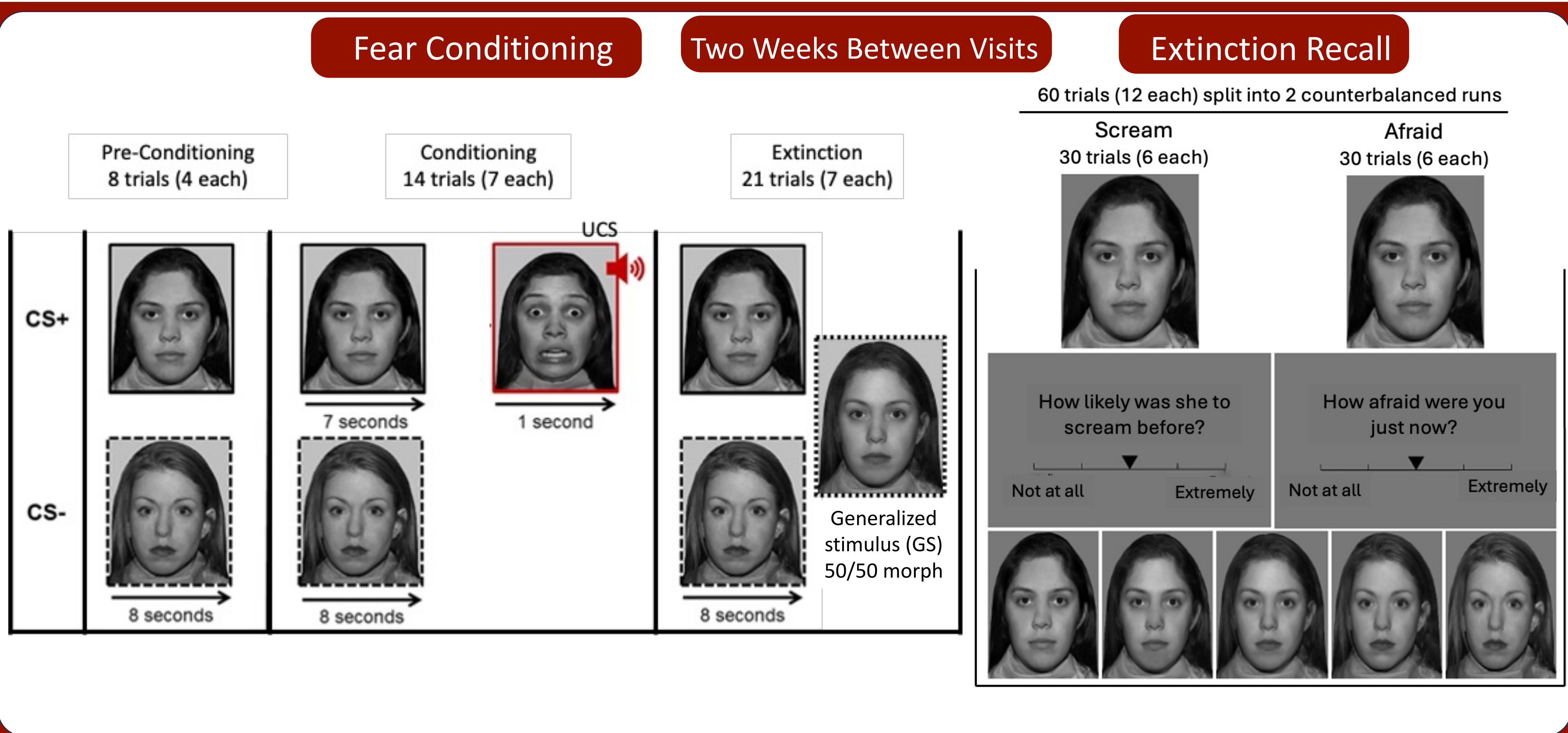
Participants

- Girls between ages of 8-11 years old at time of first visit were recruited as part of a larger study. All participants were medication and therapy free.
  - Anxiety (AD): Met criteria for anxiety diagnosis (Separation, Generalized, or Social) based off KSADS interview
  - Sub-Threshold Anxiety (SubAD): No anxiety diagnosis, but notable levels of anxiety
  - Control: No diagnosis, typical level of anxiety
- In the Conditioning sample, 43 participants attempted the task. 18 withdrew, consistent with previous studies using this task in youth, resulting in a final sample size of 25.
- In the Extinction Recall sample, 21 participants attempted the task, 1 withdrew and 1 had an equipment error, resulting in a final sample size of 19.
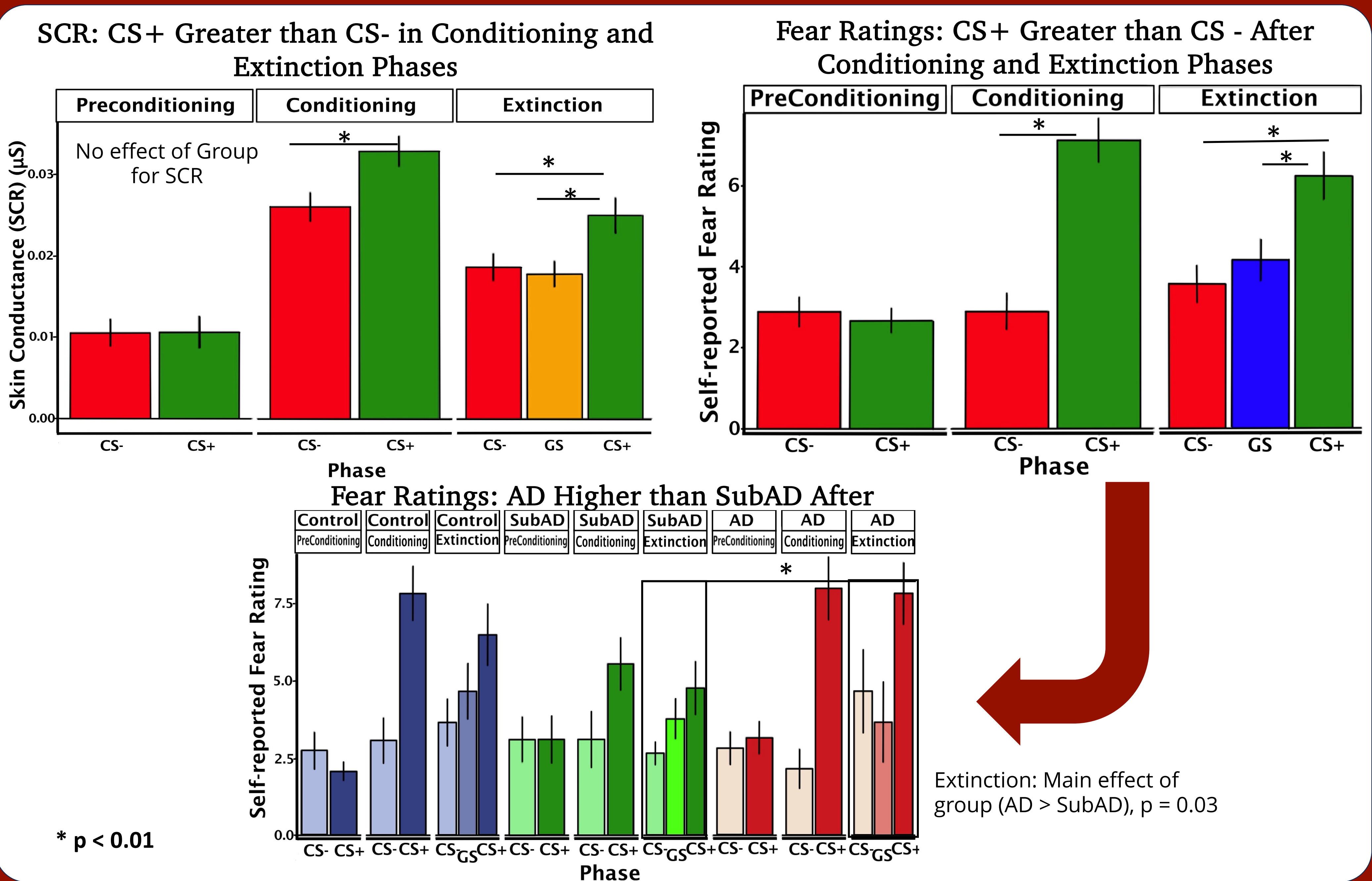
Group	Conditioning Task		Extinction Recall Task	
	N Participants	M Age	N Participants	M Age
Total	25	10.1	19	10.3
AD	5	10.7	5	10.8
SubAD	9	9.4	7	9.6
Control	11	10.3	7	10.7

Methods

Fear Conditioning | Two Weeks Between Visits | Extinction Recall

Pre-Conditioning 8 trials (4 each) — Conditioning 14 trials (7 each) — UCS — Extinction 21 trials (7 each)
CS+ — 7 seconds — 1 second — 8 seconds
CS- — 8 seconds — 8 seconds
Generalized stimulus (GS) 50/50 morph

Extinction Recall: 60 trials (12 each) split into 2 counterbalanced runs
Scream 30 trials (6 each) | Afraid 30 trials (6 each)
How likely was she to scream before? Not at all — Extremely
How afraid were you just now? Not at all — Extremely
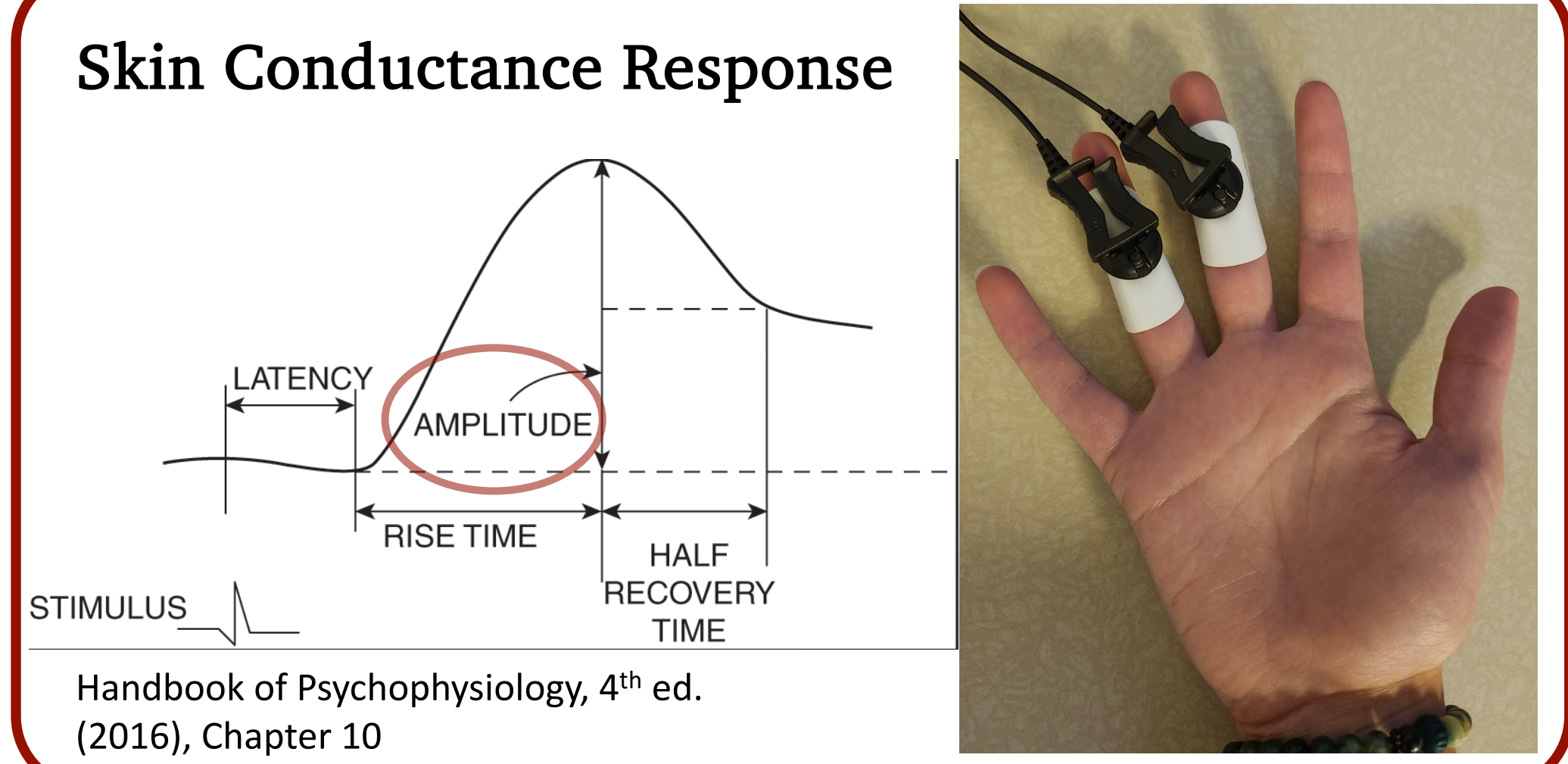
Methods

- Screaming Lady Paradigm, classical conditioning task for fear learning and extinction
  - The conditioned stimulus (CS) is a neutral face
  - The unconditioned stimulus (UCS) is a loud scream
    - CS+ is paired with UCS
    - CS- is never paired with UCS
- Two weeks later, participants return for the Extinction Recall Task to assess memory and salience of faces
  - 5 morphed faces between CS+ and CS-
  - Judge one of two Attention Conditions in blocks:
    - Scream: explicit memory of which face screamed
    - Afraid: appraisal of fear still associated with the face
  - **During both tasks we collect SCR and subjective fear ratings.**
    - **SCR is a measure of general autonomic arousal, evidence for physiological conditioning**
    - **Subjective ratings let us examine emotional reactions**
- This preliminary analysis uses linear mixed effects models to examine task and anxiety-related effects with subject as a random effect. Significance is set at $p<0.05$.

Skin Conductance Response

LATENCY — AMPLITUDE — RISE TIME — HALF RECOVERY TIME — STIMULUS

Handbook of Psychophysiology, 4th ed. (2016), Chapter 10

Conditioning Task Results

SCR: CS+ Greater than CS- in Conditioning and Extinction Phases

No effect of Group for SCR

Skin Conductance (SCR) (µS) — Preconditioning | Conditioning | Extinction
Phase — CS- CS+ | CS- CS+ | CS- GS CS+

Fear Ratings: CS+ Greater than CS - After Conditioning and Extinction Phases

Self-reported Fear Rating — PreConditioning | Conditioning | Extinction
Phase — CS- CS+ | CS- CS+ | CS- GS CS+

Fear Ratings: AD Higher than SubAD After

Self-reported Fear Rating — Control PreConditioning | Control Conditioning | Control Extinction | SubAD PreConditioning | SubAD Conditioning | SubAD Extinction | AD PreConditioning | AD Conditioning | AD Extinction
Phase — CS- CS+ | CS- CS+ | CS- GS CS+ | CS- CS+ | CS- CS+ | CS- GS CS+ | CS- CS+ | CS- CS+ | CS- GS CS+

* p < 0.01

Extinction: Main effect of group (AD > SubAD), p = 0.03

Conclusion

- Overall results indicate that the Conditioning paradigm is effective for eliciting differential physiological and subjective responses to CSs
  - Physiological and subjective responses to CS+ are consistently higher than to CS- after Conditioning, which persists in Extinction
- In this first study examining SCR during Extinction Recall, SCR continues to have a differential response to CS+ and CS- two weeks after Conditioning and Extinction.
- Minimal anxiety-related differences with preliminary sample, but some AD-specific effects are beginning to emerge for subjective responses after Extinction

Extinction Recall Task Results

SCR: Increasing from CS- to CS+

Run 1 | Run 2
In Run1, main effect of Stimuli, p = 0.021

Skin Conductance (SCR) (µS)
Stimuli — CS- CS-.25.75 CS-.50.50 CS-.75.25 CS+ | CS- CS-.25.75 CS-.50.50 CS-.75.25 CS+

No effect of group for SCR or Fear and Memory Ratings

Fear and Memory Ratings: Effects of Faces and Attention Condition

Scream — How likely was she to scream before? | Afraid — How afraid are you?

Rating
Stimuli — CS- CS-.25.75 CS-.50.50 CS-.75.25 CS+ | CS- CS-.25.75 CS-.50.50 CS-.75.25 CS+

Main Effect of Stimuli, p < 0.001
Main effect of Attention Condition, p < 0.001
Interaction of Stimuli x Attention Condition, p < 0.001

References

1. Waters, A. M., & Craske, M. G. (2016). Towards a cognitive-learning formulation of youth anxiety: A narrative review of theory and evidence and implications for treatment. *Clinical Psychology Review, 50*, 50–66. https://doi.org/10.1016/j.cpr.2016.09.008
2. Bittner, A., Egger, H. L., Erkanli, A., Jane Costello, E., Foley, D. L., & Angold, A. (2007). What do childhood anxiety disorders predict? *Journal of Child Psychology and Psychiatry and Allied Disciplines, 48*(12), 1174–1183. Scopus. https://doi.org/10.1111/j.1469-7610.2007.01812.x
3. Farhane-Medina, N. Z., Luque, B., Tabernero, C., Castillo-Mayén, R. (2022). Factors associated with gender and sex differences in anxiety prevalence and comorbidity: A systematic review. *Science Progress, 105*(4). doi:10.1177/00368504221135469
4. Lissek, S., Powers, A. S., McClure, E. B., Phelps, E. A., Woldehawariat, G., Grillon, C., Pine, D. S. (2005). Classical fear conditioning in the anxiety disorders: a meta-analysis. *Behaviour Research and Therapy, 43*(11), 1391-1424. https://doi.org/10.1016/j.brat.2004.10.007.
5. Duits, P., Cath, D. C., Lissek, S., Hox, J. J., Hamm, A. O., Engelhard, I. M., van den Hout, M. A., & 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
6. Dvir, M., Horovitz, O., Aderka, I. M., Shechner, T., (2019). Fear conditioning and extinction in anxious and non-anxious youth: A meta-analysis. *Behaviour Research and Therapy, 120*. https://doi.org/10.1016/j.brat.2019.103431.
7. Gold, A. L., Abend, R., Britton, J. C., Behrens, B., Farber, M., Ronkin, E., Chen, G., Leibenluft, E., & Pine, D. S. (2020). Age Differences in the Neural Correlates of Anxiety Disorders: An fMRI Study of Response to Learned Threat. *American Journal of Psychiatry, 177*(5), 454–463. https://doi.org/10.1176/appi.ajp.2019.19060650
8. Britton, J. C., Grillon, C., Lissek, S., Norcross, M. A., Szuhany, K. L., Chen, G., Ernst, M., Nelson, E. E., Leibenluft, E., Shechner, T., & Pine, D. S. (2013). Response to learned threat: An FMRI study in adolescent and adult anxiety. *The American journal of psychiatry, 170*(10), 1195–1204. https://doi.org/10.1176/appi.ajp.2013.12050651