

Fear conditioning in preadolescent children with and without anxiety disorders

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INTRODUCTION

- Impaired fear acquisition and extinction are key components in the maintenance of anxiety disorders (ADs).¹
- A feature of pathological anxiety is exaggerated fear of anticipated threats and aberrant threat learning.²
- The current study compared physiological and subjective to a fear conditioning and extinction task, which was adapted the "screaming lady" paradigm³, between preadolescent children with and without ADs to examine potential differences in fear conditioning, extinction, and generalization.

PARTICIPANTS

- 126 preadolescent (8 to 12 years) boys and girls with and without ADs. Data were collected from four sites: University of Wisconsin-Madison, Vanderbilt University, National Institute of Mental Health, University of Nebraska.
- Diagnoses were determined with the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) semi-structured interview, which was administered by a trained study team member.
 - AD participants met DSM-5 criteria for current generalized, separation, and/or social AD, Control participants had no current or past psychopathology.

	Anxiety disorder	Control	T-test
Measure	(n = 71)	(n = 55)	P value
Age, years, mean (±SD)	10.90 (1.63)	10.88 (1.57)	0.952
Female, n (%)	43 (60.56)	28 (50.91)	0.282
Parent SCARED (Anxiety), mean (±SD)	30.77 (13.80)	5.65 (4.74)	<.001
Child SCARED (Anxiety), mean (±SD)	31.76 (13.61)	8.79 (6.99)	<.001
Parent MFQ (Depression), mean (±SD)	6.27 (5.13)	0.35 (0.68)	<.001
Child MFQ (Depression), mean (±SD)	6.14 (5.51)	0.85 (1.15)	<.001
CPRS (ADHD)	57.07 (11.15)	44.22 (4.04)	<.001
Diagnosis, n (%)			
Generalized anxiety disorder	57 (80.28)	-	-
Separation anxiety disorder	25 (35.21)	-	-
Social anxiety disorder	32 (45.07)	-	-
Anxiety disorder not otherwise specified	1 (1.41)	-	-
Specific phobia	13 (18.31)	-	-
Attention-deficit/hyperactivity disorder	11 (15.49)	-	-

TASK STRUCTURE

- Participants completed a differential threat learning paradigm.
- Images of two women with neutral expressions were used as the CS+ and the CS-.
- The unconditioned stimulus (UCS), which occurred at the offset of the CS+, was a 1-second 85-dB female scream presented with the CS+ woman displaying a fearful expression.
- The paradigm had three phases: preconditioning, conditioning, and extinction
- During extinction, a generalization stimulus (GS) was introduced, which was a 50/50 morph of the CS+ and the CS-.
- Outcome measures:
 - Skin conductance response (SCR), a non-specific measure of physiological arousal, was collected continuously throughout the task using two electrodes on the participant's non-dominant hand. SCR to stimuli was quantified as the average SCR across a 7-second window after stimulus onset.
 - Self-reported fear (i.e. "How afraid are you of this woman?") was collected during preconditioning, after conditioning, and after extinction.

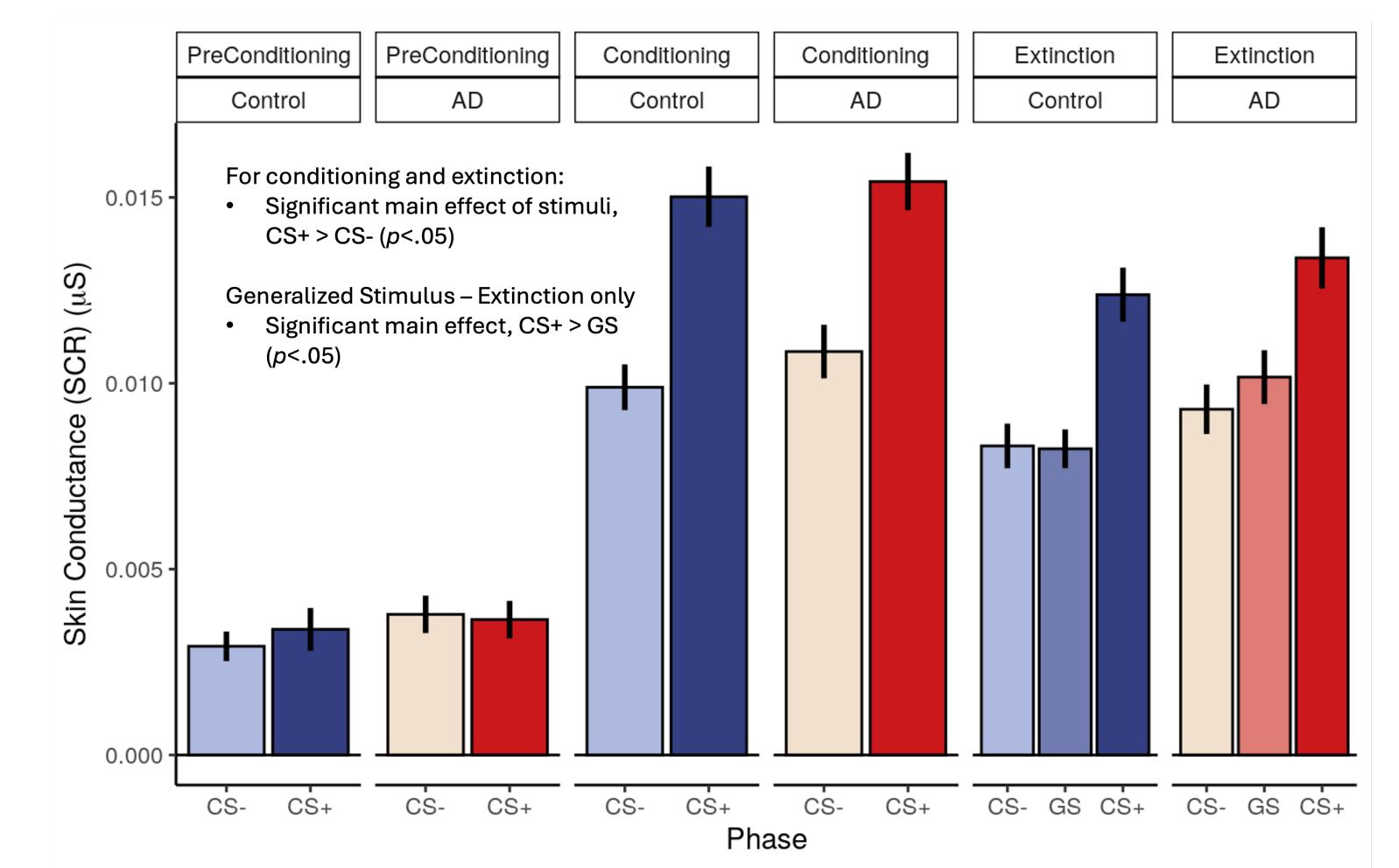


ANALYSES

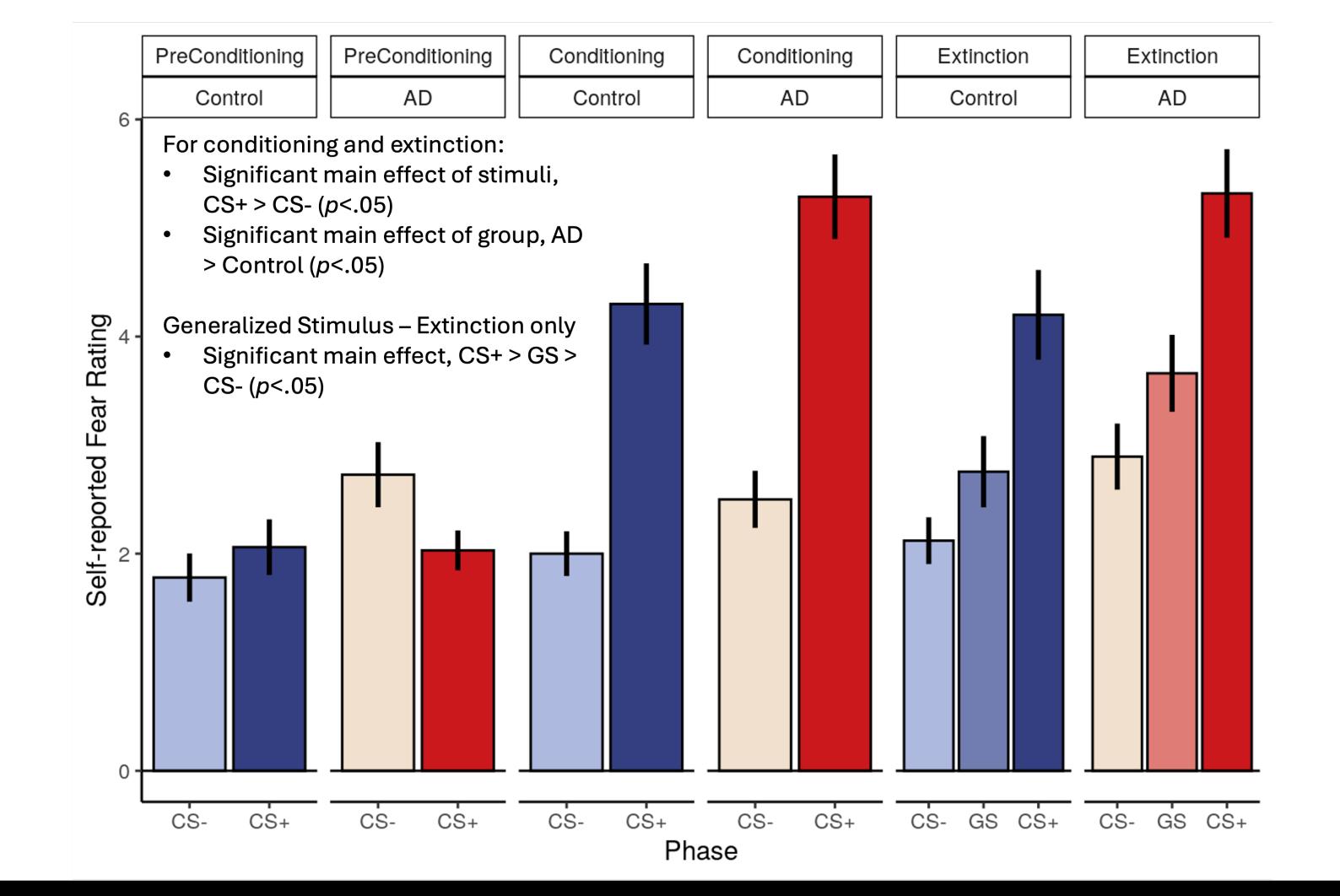
- Separate linear mixed effect models for each experimental phase (preconditioning, conditioning, and extinction) were used to test effects of group (AD, control), stimuli (CS+, CS-), and their interaction for SCR and self-reported fear.^{4,5}
- A linear mixed effect model was also used to test the effects of group on SCR to the UCS.^{4,5}
- All models controlled for site of data collection and participant sex.

RESULTS - SCR and Self-Reported Fear to Potential Threat (CS+ and CS-)

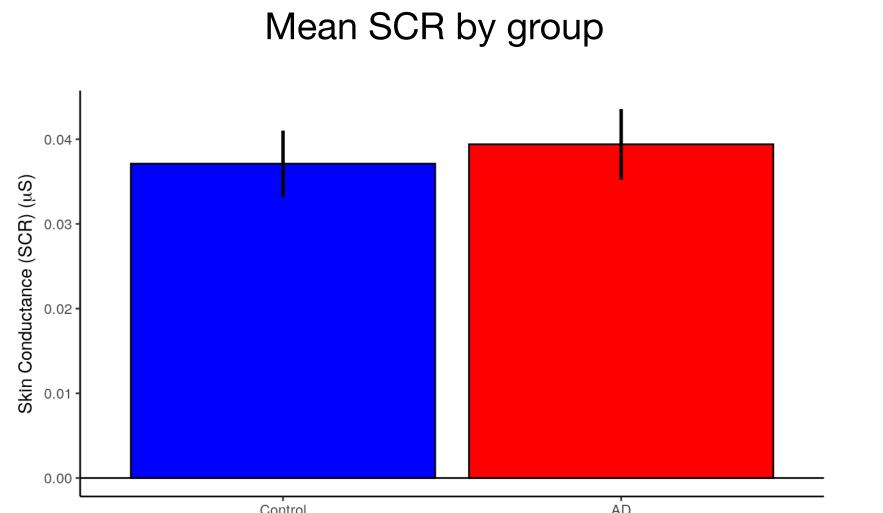
Mean SCR by stimuli, group, and phase



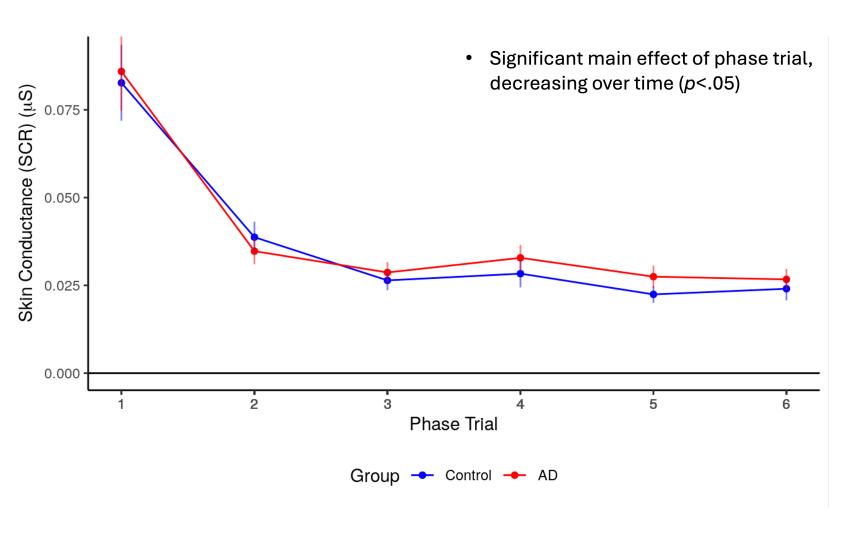
Mean self-reported fear rating by group, stimuli, and phase



RESULTS - SCR to Immediate Threat (UCS)



SCR by group over time



CONCLUSIONS

- Results demonstrate that ADs are not associated with higher physiological responses to threat or safety cues, or differential fear generalization.
- Conversely, AD youth reported higher self-reported fear levels to threat and safety cues after fear learning and extinction.
- Taken together, results suggest that youth with and without ADs have similar physiological responses to threat and safety cues, but they interpret these physiological responses differently, as shown by a significant difference in subjective responses.
- Youth with and without ADs have similar physiological responses to threats, and they also habituate to threats at a similar rate.

REFERENCES

- 1. 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*, 103431. https://doi.org/10.1016/j.brat.2019.103431
- . Abend, R., Gold, A. L., Britton, J. C., Michalska, K. J., Shechner, T., Sachs, J. F., Winkler, A. M., Leibenluft, E., Averbeck, B. B., Pine, D. S. (2020). Anticipatory threat responding: Associations with anxiety, development, and brain structure. *Biological Psychiatry*, 87(10). https://doi.org/10.1016/j.biopsych.2019.11.006
- Jenness, J., Ernst, M., Grillon, C., & Pine, D. S. (2008). Fear conditioning in adolescents with anxiety disorders: results from a novel experimental paradigm. *Journal of the American Academy of Child and Adolescent Psychiatry*, 47(1), 94–102. https://doi.org/10.1097/chi.0b01e31815a5f01
- 4. R Core Team (2020). R: A language and environment for statistical computing.
- 5. Douglas Bates, Martin Maechler, Ben Bolker, Steve Walker (2015). Fitting Linear Mixed-Effects Models Using Ime4. *Journal of Statistical Software, 67*(1), 1-48. doi:10.18637/jss.v067.i01.