# Learning to feel safe: A translational study of the influence of safety learning on anxiety-related overgeneralized fear

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## BACKGROUND

- Anxiety disorders are among the most common, debilitating mental disorders affecting approximately a third of the population in their lifetime (Kessler et al., 2012).
- However, a third of the patients with anxiety do not respond to current gold-standard treatments (Bystritsky, 2006), demonstrating significant gaps in our understanding of the underlying mechanisms in the etiology and remediation of anxiety.
- One such mechanism is overgeneralized fear (OGF), which is the tendency to respond to non-threat as if it were threatening.
- OGF has been examined using fear learning, and it is reflected in reduced discriminative learning about threat-safety signals.
- While research has focused on maladaptive fear learning in the emergence of OGF, recent evidence suggests that impaired safety learning may play a unique role (Kong et al., 2010), and that safety learning may reduce behavioral indices of anxiety (Pollak et al., 2009).
- Yet, the independent influence of safety learning on anxiety-related OGF is still unclear.

## HYPOTHESES

Using methods that are directly translated from rodent research, we hypothesized that safety, versus fear learning will

1. *Reduce* anxiety-related response towards a conditioned stimulus (i.e., the conditioned cue operates as an explicit safety signal)
2. *Enhance* discriminative learning about threat-nonthreat signals, indicating less OGF.
3. Further, we will explore whether the saliency and timing in safety cues influences these effects.

## METHODS

**Participants**

Participants were 21 adults, aged 18-45 ($M$ = 21.86, $SD$ = 4.39). There were 10 males (47.6%) and 11 females (52.4%). Participants were assigned to one of the four tasks: 1) Fear Learning ($n$ = 7), 2) Safety Learning 1 ($n$ = 5), 3) Safety Learning 2 ($n$ = 5), and 4) Safety Learning 3 ($n$ = 4).

**Fear and Safety Learning Task**

Skin conductance response (SCR) was collected on the BIOPAC MP 150 system (BioPac Systems Inc., Goleta, CA). Recording was filtered with a 2 Hz low-pass filter before analysis. Mean skin conductance level was calculated for each CS ("CS-On") and ITI ("CS-Off"), and scores were generated by computing the mean across all trials.

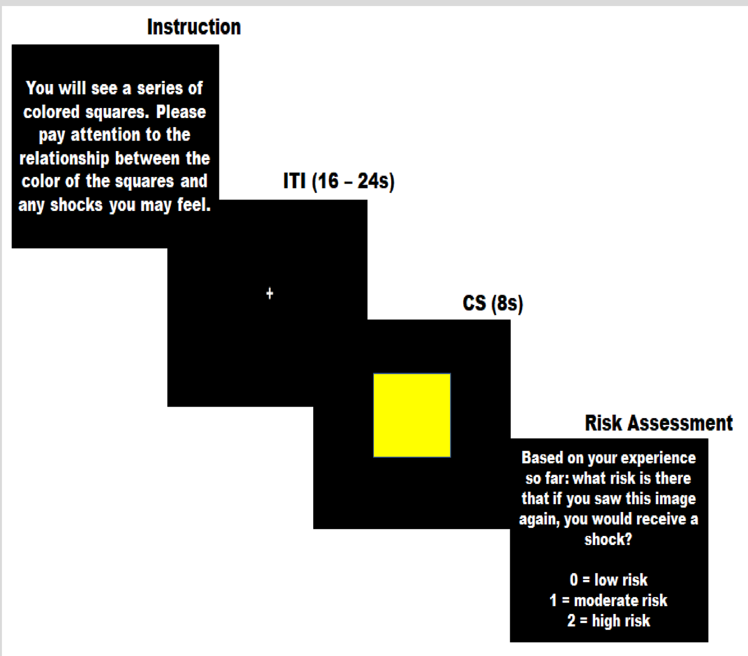


*Figure 1. Temporal Sequence of a Typical Trial.*

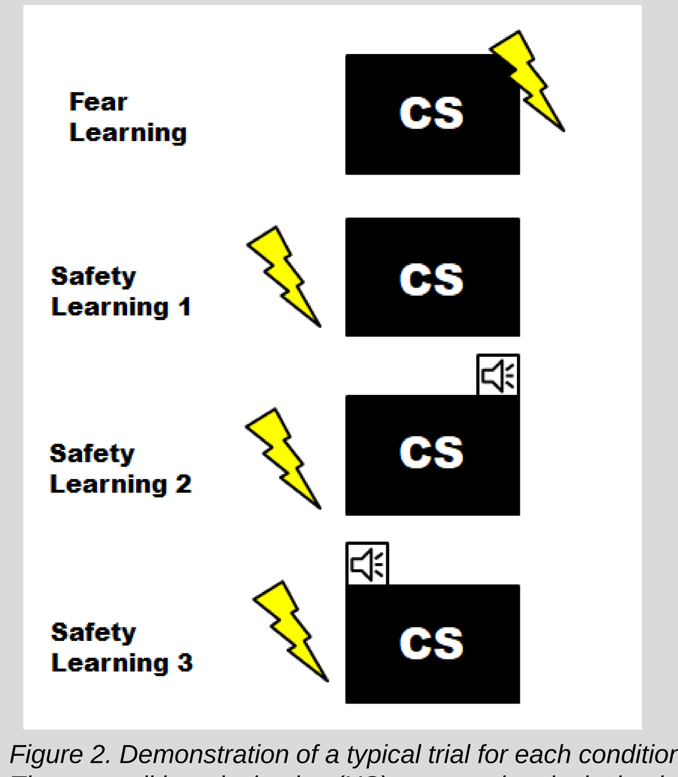


*Figure 2. Demonstration of a typical trial for each condition. The unconditioned stimulus (US) was an electrical stimulation on the left forearm. An auditory cue co-terminated (Safety Learning 2) or co-occurred (Safety Learning 3) to add more saliency to the CS.*

## Fear Generalization Task

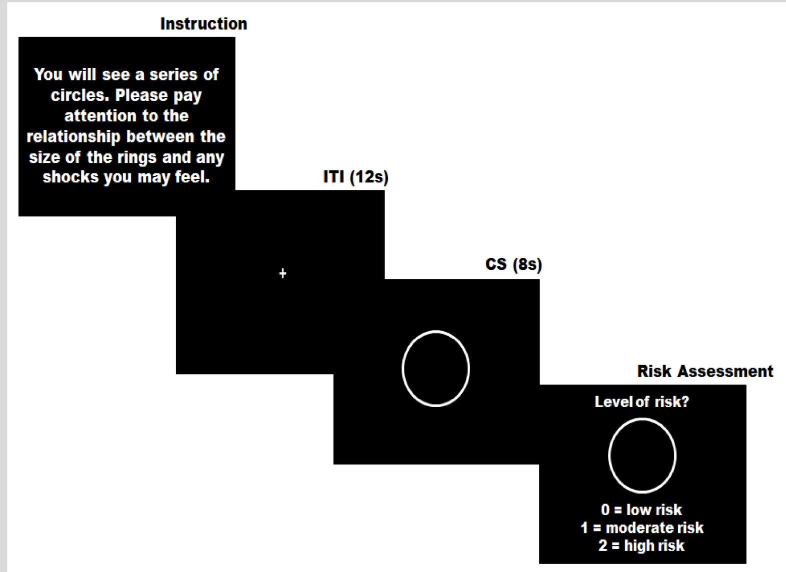


*Figure 3. Temporal Sequence of a Typical Trial. After presentation of each stimulus, participants rated the risk associated with the stimulus on a 3-point scale (0 = low risk, 1 = moderate risk, and 2 = high risk).*

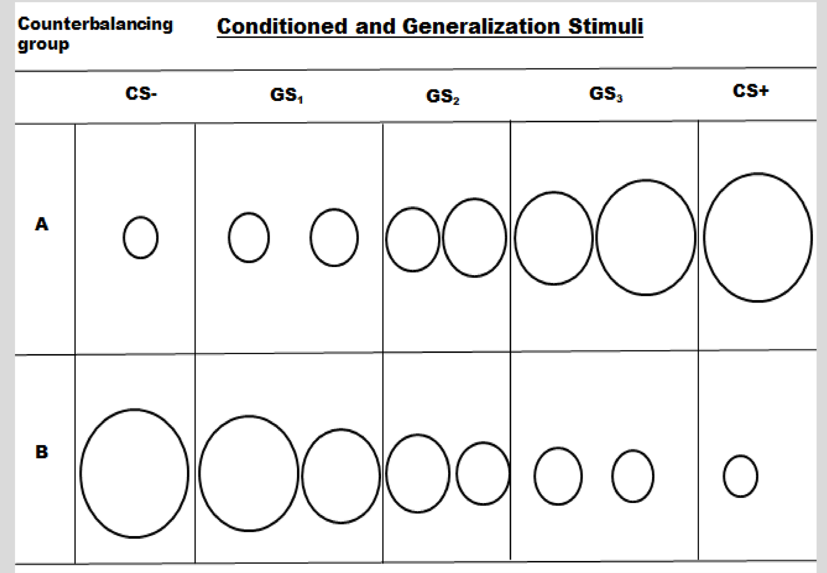


*Figure 4. Conditioned and generalization stimuli were adopted from Lissek et al. (2008) and modified for the study. Each GS class contains two rings that are similar in size. The diameter of the rings was progressively increased/decreased by 20%.*

## RESULTS

### Hypothesis 1: Fear and Safety Learning

*Figure 5. An example of participant in the Fear Learning Condition. The first row represents skin conductance response, in which fluctuations indicate changes of the response during CS presentation (second row). Higher in value and peaks indicate greater response.*

*Figure 6. An example of participant in the Safety Learning Condition. The first row represents skin conductance response, in which fluctuations indicate changes of the response during CS presentation (second row). Lower in values and drop in the graph indicate smaller response.*

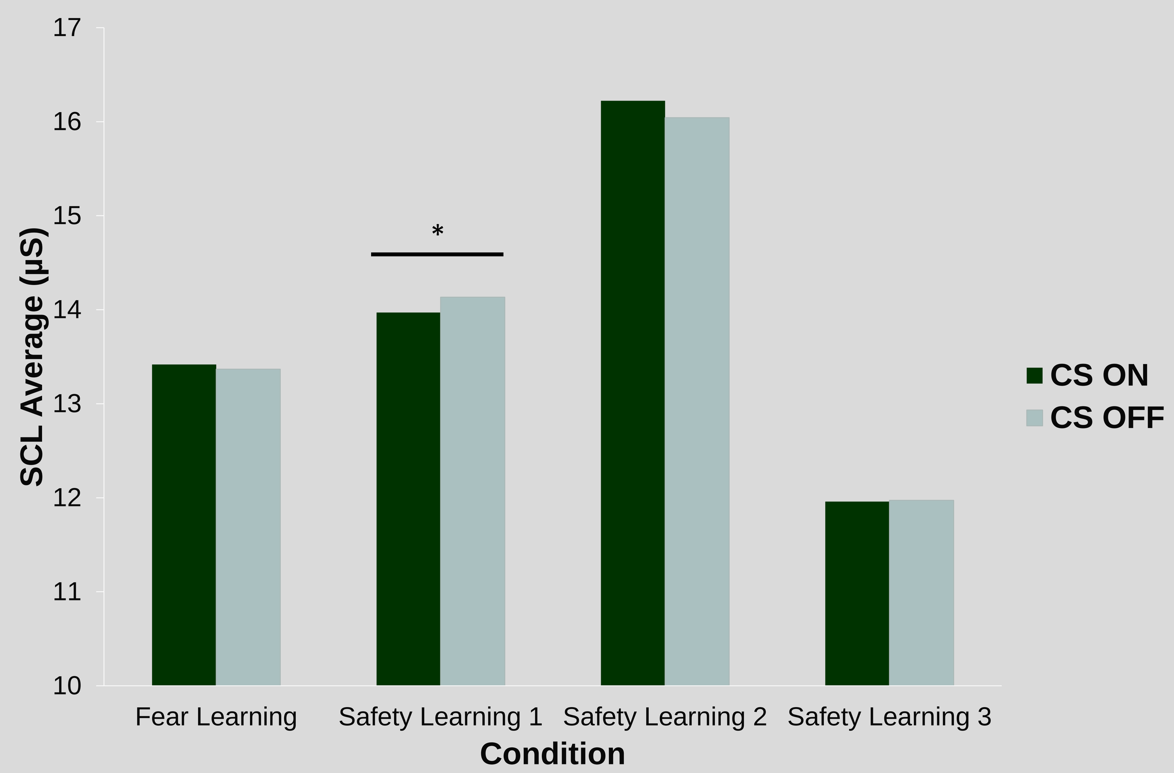


*Figure 7. SCL mean (µS) comparison for CS-On and CS-Off periods for each condition. *p < .05*

### Hypothesis 2: Fear Generalization

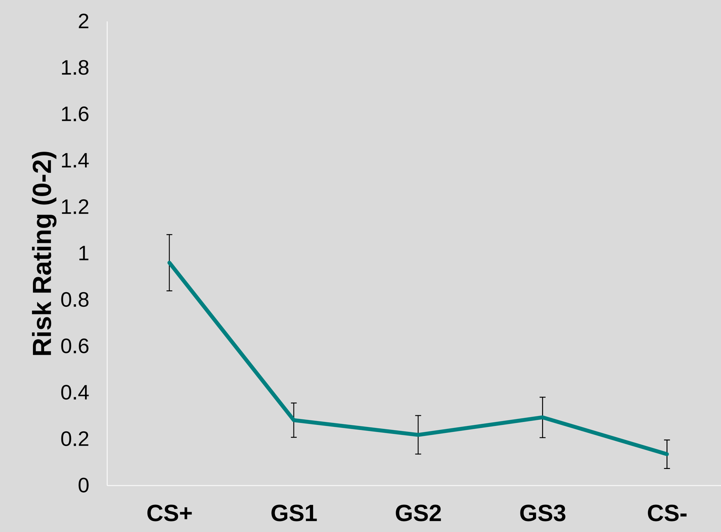


*Figure 8. Overall mean risk ratings (level of risk) of each stimulus type compared to CS+ were significantly different, ps < .05.*

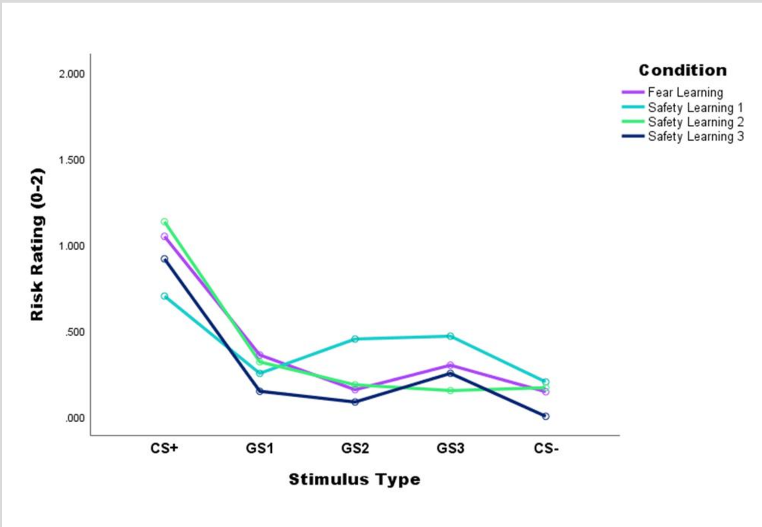


*Figure 9. Mean risk ratings (level of risk) separated by condition, ps < .05.*

## DISCUSSION

- Preliminary findings of this ongoing investigation of anxiety-related OGF in humans points to potentially unique roles of fear and safety learning.
- As hypothesized, the Safety Learning1 condition elicited reduced SCL responses when the CS was on versus off, suggesting that the CS was recognized as a safety cue.
- Across conditions, participants discriminated threat from all non-threat cues including GS 1 which is the most perceptually similar, based on behavioral ratings. This is consistent with the literature in non-clinical samples (Lissek et al., 2008).
- Hypothesis 2 was not supported. Interestingly, the Safety Learning 1 condition induced more OGF compared to other conditions although the differences were not statistically significant. This demonstrates the importance of developing safety learning methods focusing on the saliency and timing of safety cues (i.e., the Safety Learning 2 and Safety Learning 3).
- Findings may inform development of innovative treatment approaches.

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## ACKNOWLEDGEMENT

This research was funded by Professional Staff Congress of the City University of New York (PSC-CUNY) grant and the Doctoral Student Research Grant Round 13.