

5-11-2021

# **Mental Imagery in the Regulation of Differential Fear Conditioning: A Multimodal Investigation Involving Self-Report, Psychophysiology, and Brain Imaging**

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**MENTAL IMAGERY IN THE REGULATION OF  
DIFFERENTIAL FEAR CONDITIONING:  
A MULTIMODAL INVESTIGATION INVOLVING SELF-  
REPORT, PSYCHOPHYSIOLOGY, AND BRAIN IMAGING**

A Dissertation

Submitted to the Graduate Faculty of the  
Louisiana State University and  
Agricultural and Mechanical College  
in partial fulfillment of the  
requirements for the degree of  
Doctor of Philosophy

in

The Department of Psychology

by  
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August 2021

At school, new ideas are thrust at you every day. Out in the world, you'll have to find your inner motivation to seek for new ideas on your own.

—Bill Watterson, *Calvin and Hobbes*, 1-10-1990 4:1

## **ACKNOWLEDGEMENTS**

My heartfelt thanks go out to everyone in the LSU Psychology department who has helped me along the way to graduation, especially the members of my committee, Dr. Beck, Dr. Elliott, and Dr. Cox. I have been met with nothing but support and patience from the department, and it has been a pleasure to work with you all. I would also like to thank Dr. Cherry, as she and her seminars were influential in the direction my future research has taken.

I would not be where I am now without my advisor, Dr. Greening, and all the guidance he has given me over the years. It is thanks to his mentorship that I have grown as a researcher and will be able to take on future challenges with confidence. For that, I will always be grateful.

Finally, I don't have enough words to thank my parents for the overwhelming support they have given me throughout my life and my career. It has been a joy to be your son. Thank you also to my Grandmother for your constant encouragement, and to my sister Lauren, who was also there.

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## **ABSTRACT**

Mental imagery is a common component in a range of emotion regulation techniques. However, the effectiveness and neural mechanisms of regulation via mental imagery are underexplored due to a lack of studies targeting mental imagery specifically. This discrepancy results in uncertainty regarding the mechanism of regulation in existing paradigms. Biased competition for attentional resources presents a plausible model by which a mental imagery-based distracter can downregulate response to an emotional stimulus. If visualizing an imagined distracter effectively regulates emotional response, the inclusion of mental imagery components in other techniques represents a potential confound. To address this discrepancy, this dissertation investigates the effectiveness and neural correlates of mental imagery in the regulation of differentially conditioned fear. Results of this investigation indicate that mental imagery-based regulation is comparably effective to object-based distraction, but requires a greater investment of cognitive resources to perform. Furthermore, while neural mechanisms of this regulation are consistent with biased competition, mental imagery-based distraction demonstrates notable differences in neural correlates from those identified in object-based distraction. In conclusion, mental imagery represents both a distinct and effective technique in emotion regulation.



## INTRODUCTION

We do not typically choose to experience an emotion. Regulation, distraction, distancing, and mindfulness all allow us to manipulate our emotional experience voluntarily, but the initial appraisal of an emotional stimulus occurs as soon as the stimulus is attended (Ochsner & Gross, 2005). Emotional stimuli include those that are inherently aversive or conducive, as well as stimuli that have become associated with aversive or conducive outcomes. This leaves the experience of emotion in the complex position of relying on both subjective and automatic processes (Knight, Waters, & Bandettini, 2009; Mechias, Etkin, & Kalisch, 2010; Phillips, Ladouceur, & Drevets, 2008; Todd, Cunningham, Anderson, & Thompson, 2012). Interaction between these subjective and associative influences results in ongoing modulation of our emotional experience (Todd et al., 2012). The functional and anatomical bases of these interactions are still being explored. This investigation seeks to clarify the cognitive and neural mechanisms underlying voluntary regulation of conditioned fear response, with a focus on visual imagery as a regulation tactic.

Visual imagery was chosen as the target of our investigation due to its common inclusion in emotion regulation techniques, particularly those using distraction (Kanske, Schönfelder, Forneck, & Wessa, 2015; Ochsner, Silvers, & Buhle, 2012; Scheibe, Sheppes, & Staudinger, 2015; Strauss, Ossenfort, & Whearty, 2016). The biased competition model of attention selection offers a framework from which we can predict how object-based and mental imagery-based regulation will affect fear processing (Bishop, 2008; Blair & Mitchell, 2009). Differential fear conditioning was chosen as our method of establishing a fear response throughout the investigation. This approach allowed high experimental control over our stimuli and explored an under-represented approach to fear regulation research (Delgado, Nearing, LeDoux, & Phelps,

2008; Greening et al., 2021). By measuring self-reported fear and skin conductance (SCR) in addition to fMRI, we could address both subjective and autonomic changes across regulation. Meanwhile, fMRI allowed us to investigate the neural mechanisms underlying these changes.

Our investigation began with a study using self-report and physiological measures to test the prediction that mental imagery can regulate differential fear conditioning with similar effectiveness to visual distracters (STUDY 1). This was followed by an fMRI study that sought to determine the neural basis of visual imagery as a regulation technique, with a focus on activity in the anterior insula (aIn) and regions associated with visual processing of faces and places (STUDY 2). In the final study, we attempted to distinguish between processes in the anterior insula related to subjective appraisal with those related to associative learning in the amygdala (STUDY 3). This experiment used a repeated shock/no-shock paradigm with reported threat expectancy in addition to fMRI measures of blood-oxygen-level-dependent (BOLD) activity.

## **FEAR CONDITIONING IN EMOTION RESEARCH**

In emotion research, differential fear conditioning refers to the repeated pairing of an aversive stimulus with a neutral stimulus to build a learned association between the originally neutral stimulus and feelings of aversion. For example, an initially neutral image of an object or animal could be paired with a mild aversive shock to produce a fearful association between seeing the image and feeling the painful outcome. In conditioning paradigms, these two stimuli are referred to as the conditioned stimulus (CS), in the case of the original image, and the unconditioned stimulus (US), in the case of the aversive shock. Following conditioning, the trained CS is referred to as the CS+, while a control stimulus without aversive association is referred to as the CS-. The use of fear conditioning in studies of emotion offers a way to reduce

the impact of participants' idiosyncratic reactions to a picture or scene and ensure internal validity in studying emotion (Delgado et al., 2008; Greening et al., 2021). Additionally, fear conditioning can be performed with simple images to minimize potential confounds. Currently, the majority of studies addressing fear utilize standardized visual stimuli such as the ubiquitous IAPS set (Buhle et al., 2014; Lang, Bradley, & Cuthbert, 1997; Ochsner & Gross, 2005). Standardized affective image sets rely on emotionally graded scenes that can often be visually distinct from neutral or positive scenes (Redies, Grebenkina, Mohseni, Kaduhm, & Dobel, 2020), and may introduce unplanned differences between conditions that can be avoided in differential conditioning paradigms. A wide range of individual differences in response to emotional scenes has also been noted for affective image sets (Barke, Stahl, & Kröner-Herwig, 2012; Ito & Cacioppo, 2005). This is of particular concern for smaller within-subjects designs such as those used in many fMRI studies.

Comparison between unconditioned fear-evoking stimuli such as the IAPS set and conditioned fear stimuli indicates differences in the neural pathways involved in these responses (Knight et al., 2009). Existing research has drawn strong associations between amygdala activity and fear (Pessoa & Adolphs, 2010). However, studies investigating conditioned fear response have shown reactivity in both the amygdala and anterior insula with varying degrees of consistency (Dunsmoor et al., 2011; Fullana et al., 2016; Knight et al., 2009; McRae et al., 2010). Meta-analysis of conditioned fear studies shows that amygdala activation has not been universally identified across fear paradigms, despite its association with fear learning and experience (Fullana et al., 2016). Mechanical differences between unconditioned and conditioned fear raise the concern that studies targeting one form of fear may not reliably apply to the other.

## **SUBJECTIVE FEAR AND AUTONOMIC RESPONSE**

Basic emotions such as fear can be described as both autonomic drives and appraisal of subjective emotional experience (Berridge, 2018; Flannelly, Koenig, Galek, & Ellison, 2007; Hofmann, 2008; Riskind, 1997). In appraising our fear response, we are integrating external information with interception of our internal emotional and physiological state (Hofmann, 2008; Ochsner & Gross, 2005). How we describe, operationalize, and measure “fear” in this context requires careful consideration. Autonomic reactivity such as skin conductance response (SCR) may reflect a component of the fear experience, but may not fully measure subjective fear as an emotional state (LeDoux & Pine, 2016). Understanding this distinction becomes critical in the case of emotion regulation, where failing to measure the impact of regulation on the subjective experience of fear may misrepresent the effects of regulation. We argue that both autonomic response and subjective fear must be measured to accurately model cognitive-affective interactions such as emotion regulation via distraction. Existing evidence supports autonomic response as a measure of conditioned associative fear (Esteves, Parra, Dimberg, & Öhman, 1994; Hodes, Cook, & Lang, 1985). However, the relationship between associative fear and subjective awareness of fear is complex, with conflicting reports of neural correlates for subjective appraisal (Mechias et al., 2010), and growing evidence that autonomic response does not map one-to-one with subjective experience of fear (Taschereau-Dumouchel, Kawato, & Lau, 2020). If associative fear response and inherently fearful stimuli rely on different functional pathways for their effectiveness, how these different pathways vary in their interaction with subjective appraisal is uncertain.

In conditioning models, we find a case in which predictions by models of subjective appraisal and those of associative learning may lead to contradictions. As a conditioned response is acquired, the associative strength model predicts that the strength of the learned response increases with more frequent pairings of the CS and US (Perruchet, 2015; Rescorla & Solomon, 1967). This follows the classic Pavlovian interpretation of fear conditioning. In contrast to the associative strength model, the expectancy model posits that fear conditioning is the result of a conscious expectation of the US following the CS (Boddez, Moors, Mertens, & De Houwer, 2020; Mitchell, De Houwer, & Lovibond, 2009). This implies a subjective appraisal of threat when presented with the CS and propositional knowledge of its relationship to the aversive US. In the expectancy model, sequential un-reinforced presentations of the CS bias participants towards higher expectation of the US (Burns & Corpus, 2004), in direct contradiction to the predictions of the associative strength model.

From these models, we demonstrate that approaching conditioned fear as subjective appraisal or associative response exclusively can result in different predicted outcomes. A third approach is to treat both components as parts of an integrated two-systems model (LeDoux & Pine, 2016). However, the two-systems model is underexplored. One paradigm that attempts to compare subjective expectation and associative strength behaviorally has shown that number of sequential un-reinforced CS presentations predicted subjective threat expectancy, in support of the expectancy model (Perruchet, Grégoire, Aerts, & Poulin-Charronnat, 2016). However, prior to this investigation, the neural correlates of this paradigm had not been explored for comparison with previous research in fear acquisition and regulation.

## **VISUAL STIMULI IN EMOTION REGULATION**

A core focus of this investigation is the role of visual processing in the regulation of conditioned fear. Emotion regulation literature relies heavily on visual stimuli, such as the aforementioned IAPS set, as well as visual distraction paradigms. mental imagery-based or imagined distractors, however, are underrepresented in the literature. Visual distraction is assumed to operate via goal-directed attention selection (Desimone & Duncan, 1995), in which top-down attentional control can bias the processing of attended stimuli over that of unattended stimuli. As attentional capacity is limited, unattended stimuli are represented less clearly in the brain and their associated impact is diminished. This process is described by the biased competition model (Bishop, 2008; Blair & Mitchell, 2009). In the context of emotion regulation, biased competition comprises both the top-down influence of attention selection and bottom-up influences from stimulus features such as complexity and emotional valence. Existing literature supports attention selection as a mechanism of emotion regulation, consistent with the predictions of this model (Bishop, 2008; Blair & Mitchell, 2009; Desimone & Duncan, 1995). For example, despite the bottom-up influence of a negative emotional scene, directing attention to non-emotional parts of the scene, or away from the scene entirely, can result in downregulation of the negative stimulus. Competition for attentional resources is assumed to have similar effects on emotion processing whether the target is object-based or mental imagery-based. Unlike object-oriented attention, mental imagery is internally directed. However, similar regions of the brain are activated by mental imagery as are found during visual perception, albeit to a weaker extent (Ganis, Thompson, & Kosslyn, 2004; Pearson, Naselaris, Holmes, & Kosslyn, 2015). If so, mental imagery should represent a target for attention selection under the biased competition model. Evidence suggests that mental imagery can downregulate differential fear

conditioning by disrupting prefrontal representation of the emotional stimulus (Greening et al., 2021). However, this effect has not been directly compared to object-based distraction, and has only been demonstrated using low-level visual stimuli, rather than objects, faces, or scenes. This limits our ability to compare these findings to other distraction and emotion regulation techniques. As a result, it is unknown whether mental imagery is able to downregulate a conditioned stimulus as effectively as object-based distraction.

Visual imagery components can also be found in other emotion regulation techniques. Tasks in emotion regulation research regularly describe imagining outcomes or context changes (McRae et al., 2012; Opitz, Cavanagh, & Urry, 2015), but the degree to which these processes depend on visual imagery is unclear. If visual imagery is a significant part of the mechanism of these techniques, it calls into question our understanding of how this regulation takes place in the brain. Biased competition models suggest that competition between an imagined distracter and a visual fear stimulus could result in limited availability of perceptual processing resources and reduction in the representation of the fear stimulus even before amygdala activation, should both stimuli rely on visual processing centers (Bishop, 2008; Greening, Lee, & Mather, 2014). However, the process model of emotion regulation describes attention-based regulation and cognitive reappraisal as sequential steps, in which reappraisal can only be performed when attending to an emotional stimulus (Gross, 1998). Competition for visual processing resources in many regulation paradigms, such as reappraisal, would suggest that these techniques are more mechanically similar to distraction than the cognitive manipulations described by regulation literature (Buhle, et al., 2014; Gross, 1998; Ochsner & Gross, 2005) and are misrepresented in existing research.

## **NEURAL CORRELATES OF VISUAL EMOTION REGULATION**

Clarifying the mechanisms of interaction between visual imagery and conditioned fear requires targeted investigation of the neural pathways associated with fear and emotion regulation. The neural basis of emotion is distributed across a number of regions, including the amygdala, hypothalamus, insula, and areas of the prefrontal cortex associated with the subjective emotional experience (Etkin, Egner, & Kalisch, 2011; LeDoux, 2003; McRae, Ciesielski, & Gross, 2012; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008). As previously noted, the amygdala has been a central focus in emotion research (LeDoux, 2003). Studies have also demonstrated the anterior insula to be another predictor of fear experience in fear conditioning paradigms (Etkin et al., 2015; Kanske et al., 2011; Otto, Misra, Prasad, & McRae, 2014). Meta-analyses indicate a relationship between elevated activity in the anterior insula and decreases in amygdala response, suggesting that the anterior insula plays a role in the regulation of emotion (Delgado, Nearing, LeDoux, & Phelps, 2008; Etkin, Büchel, & Gross, 2015; Ochsner, Silvers, & Buhle, 2012). Given the insula's involvement in interoception and awareness of emotional states (Craig, 2009), these patterns fit the hypothesis that activity the anterior insula reflects subjective appraisal of fear more so than associative learning.

Furthermore, frontoparietal regions associated with cognitive control processes, such as those implied by directed visual attention, have demonstrated top-down modulation of the activity in the anterior insula and amygdala (Teckentrup, et al., 2019, Wager, et al., 2008). Connectivity analysis of the insula and the dorsolateral prefrontal cortex during visual search tasks shows elevated functional connectivity when resisting emotional distraction (Pedale, Macaluso, & Santangelo, 2019). Functional overlap between visual perception and mental imagery in working memory (Pearson, Naselaris, Holmes, & Kosslyn, 2015) suggests that a



regulatory task utilizing visual imagery could interact similarly to an external visual distractor with regards to emotional regulation. In summary, if the insula receives top-down influences from prefrontal regions associated with working memory and visual attention during subjective appraisal of emotion, competition for resources between a visual emotional stimulus and an imagined distracter could result in decreased subjective fear without changes to associative learning. This would separate regulatory techniques that use visual imagery from forms of fear regulation shown to alter long-term associations (Ahn, et al., 2015).

## **GOALS AND CENTRAL HYPOTHESIS**

The primary goal of this investigation is to assess the regulation of fear using mental imagery as measured by self-report, physiological, and BOLD intensity. The secondary aim is to dissociate the neural correlates of subjective fear experience and autonomic fear response. This additional aim was formed following results from the first two studies. The central hypothesis of our research is that using visual imagery to regulate conditioned fear will effectively down-regulate fear as measured via self-report and physiological response, and that this regulation will be detectable via corresponding BOLD activity in the anterior insula. Activity in the amygdala is predicted to reflect fear learning, but not subjective fear appraisal, with elevated activity in the dlPFC present during subjective appraisal. These hypotheses are based on existing literature on the distinct roles of the anterior insula and amygdala as parts of the network responsible for fear learning and regulation (Alves et al., 2013; Etkin et al., 2015; Dunsmoore et al., 2011; Kanske et al., 2011), and evidence that the anterior insula (aIn) may represent a metric for subjective fear intensity in regulation paradigms (Buhle et al., 2014; Kanske et al., 2011). Current literature supports the presence of a functional network between the prefrontal cortex, insula, and

amygdala during fear regulation of unconditioned stimuli (Deen et al., 2011; Zou et al., 2016), in support of the secondary aim of our investigation.

## **CHAPTER 1. OBJECT-BASED ATTENTION VERSUS MENTAL IMAGERY**

Just as when a physician instructs a patient to imagine the coming weekend before sticking them with the needle, distraction is a ubiquitous strategy for emotion regulation. While attentional processes such as distraction are a central component in many theoretical models of emotion control (Gross, 1998, 2015; Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner & Gross, 2005), most research into distraction has relied on external distraction tasks. For example, ignoring an aversive stimulus and instead attending to externally presented visual, verbal, or mathematical reasoning tasks can significantly reduce measures of negative affect (Kanske, Heissler, Schönfelder, Bongers, & Wessa, 2011; Lim, Padmala, & Pessoa, 2009; McRae, 2016; Pessoa, Kastner, & Ungerleider, 2002). However, as the opening example demonstrates, emotion control can also be carried out via internal distraction, for example using mental imagery (Delgado, Nearing, LeDoux, & Phelps, 2008; Greening et al., 2021; Martins, Ponzio, Velasco, Kaplan, & Mather, 2015; Opitz, Cavanagh, & Urry, 2015). The purpose of the present study is to compare the impact of external versus internal distraction (i.e., visual imagery) on differential fear conditioning as measured by self-reported fear and skin conductance response (SCR).

The majority of emotion regulation studies involving external distraction rely on the use of visual scenes as the emotion elicitor (Kanske et al., 2011; McRae et al., 2010; Ochsner et al., 2012; Scheibe et al., 2015; Strauss et al., 2016), such as the ubiquitous IAPS (Lang et al., 1997). However, such emotional scenes can produce highly varied and idiosyncratic responses across participants (Barke et al., 2012; Ito & Cacioppo, 2005). Moreover, the inclusion of a neutral condition requires the use of neutral scenes which can be quite visually distinct from the emotional scenes (Redies et al., 2020). On the other hand, differential fear conditioning offers a robust tool for studying the cognitive control of fear with a high degree of experimental control

(Delgado, Nearing, LeDoux, & Phelps, 2008; Greening et al., 2021). In differential fear conditioning, an initially neutral conditioned stimulus (CS+) is paired with an unconditioned aversive stimulus (US; e.g., mild shock) while a second conditioned stimulus (CS-) is never paired with the US. Successfully fear conditioning has occurred if the CS+ without the US elicits a greater conditioned response than the CS-. The conditioned response can include self-reported fear, or autonomic reactivity such as the SCR (Fullana et al., 2015; Kim & Jung, 2006; Lovibond & Shanks, 2002).

External distraction appears to operate via the mechanisms of goal-directed attention selection (Desimone & Duncan, 1995), and is a reliable form of emotion regulation (Gross, 1998; Ochsner & Gross, 2005; Pessoa & Ungerleider, 2004). This has been demonstrated using a variety of attentional manipulations, such as covert spatial attention (Pessoa, McKenna, Gutierrez, & Ungerleider, 2002), feature-based attention (Fusar-Poli et al., 2009), and object-based attention (Lim, Padmala, & Pessoa, 2008; Mitchell et al., 2007). In general, goal-directed attention prioritizes the processing of the distracter, thereby suppressing the perceptual processing of the emotional stimulus (Bishop, 2008; Blair & Mitchell, 2009). In the case of visual emotional stimuli, this suppression of processing has been observed throughout aspects of the ventral visual pathway, including occipital and temporal regions (Amting, Miller, Chow, & Mitchell, 2009; Pessoa & Ungerleider, 2004). Regarding differential conditioning, the suppression of perceptual processing has been shown to produce subsequent down-regulation of amygdala activity or SCR (Delgado et al., 2008; Lim et al., 2008), though its effect on self-reported fear is unknown.

In addition to the processes of externally directed attention selection, attention can also be directed internally in order to prioritize information already stored in mind (Chun, Golomb, &

Turk-Browne, 2011). Visual mental imagery is an example of internally directed attention, which activates similar regions of visual processing as those engaged during visual perception, though to a weaker extent (Ganis et al., 2004; Pearson et al., 2015). This suggests that mental imagery could be employed as a form of internal distraction in the context of emotion regulation that operates via similar goal-directed attention selection mechanisms as an external distracter. Recent evidence suggests that mental imagery can modulate differential fear conditioning via goal-directed internal attention by disrupting the representation of the emotion elicitor in early visual cortices (Greening et al., 2021). However, Greening et al. (2021) relied on a basic low-level visual stimulus (a Gabor patch) and did not compare their manipulation of internal distraction to external distraction. Thus, it is unknown how effective mental imagery is as an internal distraction for more complex objects commonly associated with emotion, such as faces, or how internal distraction compares to external distraction as an emotion regulation strategy.

The present study tested the hypothesis that both external (object-based attention) and internal (i.e., mental imagery) distraction can effectively down-regulate differential fear conditioning. A novel paradigm was developed that presents CS+ and CS- face images along with intact or scrambled distracter place images (i.e., a building or a house) in the form of composite images. Participants were instructed to attend to the face stimulus (i.e., the CS+ or CS-), or to either attend to or imagine the place image. Alternatively, as mental imagery is more analogous to a weaker form of perception (Pearson et al., 2015), we would predict that either the magnitude of down-regulation produced by mental imagery would be less than that produced by external distraction, or the effort required to produce the same magnitude of down-regulation would be greater for internal compared to external distraction.

## **METHODS**

### **Participants**

Forty-three undergraduate participants (32 female, 11 male), aged 18-24 were recruited through Louisiana State University's SONA system. Participants reported no presence or history of psychological or neurological disorders. As no sufficiently similar research has been published on the topic of external and internal distraction, the target sample size was based on prior studies in distraction and fear conditioning using visual imagery or external distraction. With previous samples in the range of 9-26 participants (Delgado et al., 2008; Greening et al., 2021; Lim & Pessoa, 2008; Yates, Ashwin, & Fox, 2010), we aimed for a final sample size greater than 30-35. All participants gave written informed consent and the protocol was approved by the Louisiana State University institutional review board.

### **Materials**

Participants completed three phases over the course of the experiment: Habituation, Fear Conditioning, and Regulation. The Regulation phase was comprised of two distinct alternating blocks of trials: The External Distracter blocks (Ext. blocks) and the Internal Distracter blocks (Int. blocks). Experimental Ext. and Int. blocks were always interleaved, and their order was counterbalanced order across participants. These phases consisted of series of presented visual stimuli, paired with audio instructions and, in the case of the Fear Conditioning and Regulation phases, a calibrated shock stimulus. The visual conditioned stimuli used were two standardized greyscale face images drawn from the Cohn-Kanade emotional faces database. Both images depict white males with neutral emotional affect. The face images were cropped to show only the face from hairline to chin and had the background replaced with a flat grey tone. One face image served as the CS+, the other the CS-. The image selected as the CS+ was counterbalanced across

participants. The images used as distracters were two greyscale place images depicting a house and a building. As with the face images, the background was replaced with a flat grey tone. Face and Place images were then combined to produce composite (see Figure 1.1) images (O’Craven, Downing, & Kanwisher, 1999; Serences, 2004), with a critical difference between the two distraction blocks. In External Distraction blocks, both the face and place images were both visually intact in the generated composites. On the other hand, in the Internal Distraction blocks, another set of composite images was generated in which the face images were visually intact and the place images were scrambled along a 10x10 grid (each element was made up of 40x40 pixels) before being layering with a face image (Figure 1.1).

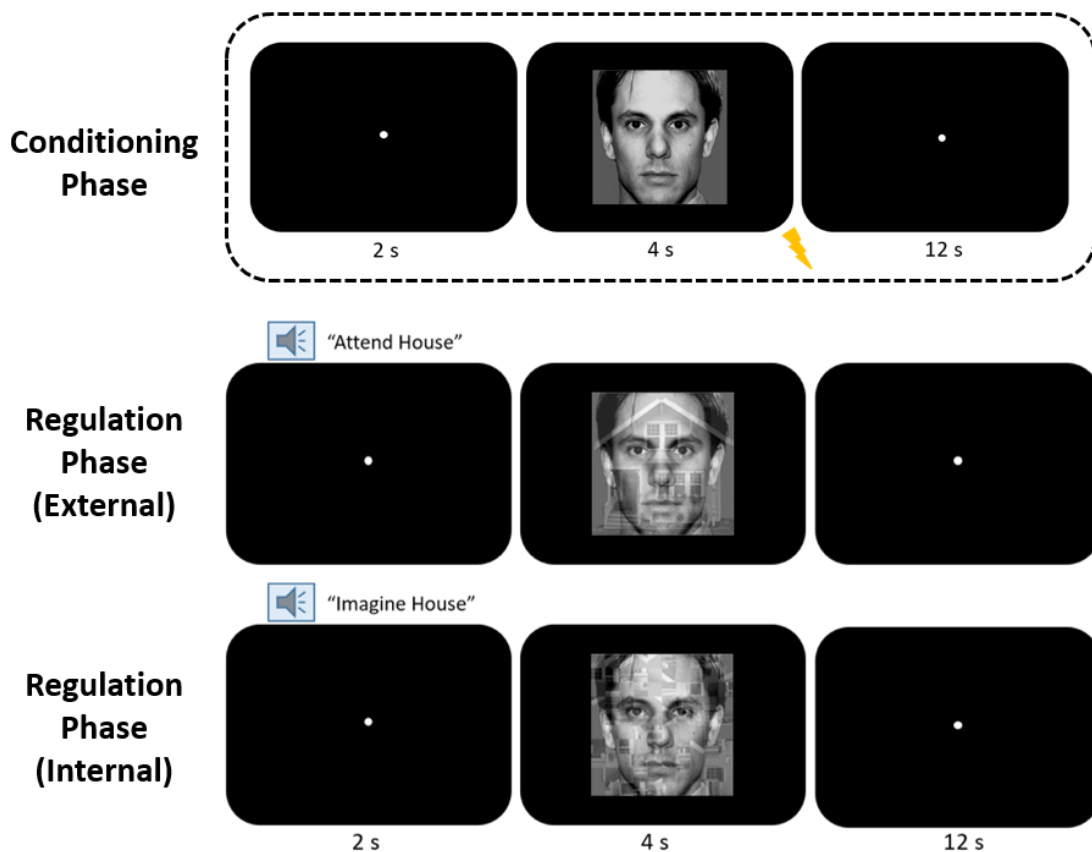


Figure 1.1 Experiment structure and example stimuli for Conditioning and Regulation Phases.

The purpose of using scrambled images during Internal distraction trials was to ensure that the same degree of visual complexity and low-level visual features were present during both the External and Internal blocks of the Regulation Phase. Additionally, this ensured that the face stimuli were visually salient to the same extent during both external and internal distraction.

The audio instructions used in the Regulation phases were generated using TextAloud text-to-speech software (Language: British English, Voice: Emma, Speed: Medium). Two-second sound clips were produced that instructed participants to either “Attend Face,” “Attend House,” “Attend Building,” “Imagine House,” or “Imagine Building.”

A mild electrical shock to the distal phalanges of the pointer and middle fingers of the dominant hand served as the unconditioned stimulus (US). Shocks were delivered using a BIOPAC STMISOC module for a duration of 5ms at 50Hz and co-terminated with the CS+. Shock intensity was calibrated independently for each participant to highest intensity described as “uncomfortable, but not yet painful” (Range: 2.00-50.00 mA). Shock intensity was calibrated in a single session prior to the conditioning phase.

## **Design and Procedure**

### **Habituation Phase**

Prior to fear acquisition, participants were habituated to the two face and two place images to ensure neutral baseline reactivity to all images, as well as to expose participants to the distracter images they would later be instructed to visualize. Composite images were not included in the Habituation phase, and no audio instructions or shocks were delivered at this stage. The Habituation phase consisted of 2 presentations per face or place image, for a total of 8 trials. Each trial included an initial two-second fixation dot, a 4-second image presentation, and a 14-second inter-trial interval (ITI) with a fixation dot. Participants were instructed at the



beginning of the phase to keep their eyes on the central fixation dot and to pay attention as they would need to visualize some of the images later.

### **Fear Conditioning Acquisition Phase**

In the conditioning phase, participants completed a single block of the fear-conditioning task. During this phase the CS+ and was paired with a co-terminating shock on 60% of presentations. The CS- was never paired with the US. Each face image was presented 10 times for 20 total trials. Trials in the conditioning phase consisted of an initial 2-second fixation dot, a 4-second image presentation, and a 14-second ITI with fixation dot. No audio instructions were delivered during this phase following the initial instruction to focus on the fixation point and maintain attention on the presented images.

### **Emotion Regulation Phase**

The Regulation phase consisted of alternating External (Ext.) and Internal (Int.) Distraction blocks. In both Ext. and Int. blocks, trials began with a two 2-second audio instruction with fixation dot. The auditory instruction was followed by a 4-second image presentation of either a face alone, a place alone, or a composite image. Each trial ended with a 12-second ITI with fixation dot. Blocks included 2 CS+ alone, 2 CS- alone, 2 House alone, 2 Building alone, 1 CS+ alone with reinforcing shock, and 8 trials with composite images producing our 4 key conditions of interest, each of which comprised 2 trials per block: The CS+ Attend Face condition [i.e., CS+ face w/ house (“attend face”) and CS+ face w/ building (“attend face”)]; the CS+ Attend Place condition [i.e. CS+ face w/ house (“attend house”) and CS+ face w/ building (“attend building”)]; the CS- Attend Face condition [i.e. CS- face w/ house (“attend face”) and CS- face w/ building (“attend face”)]; and the CS- Attend Place condition [i.e. CS- face w/ house (“attend house”) and CS- face w/ building (“attend building”)]. There were 17

trials per block in total. On External Distraction blocks, the composite images consisted of a face (CS+ or CS-) and a visually intact distracter (House or Building). Participants were instructed to “attend face,” “attend house,” or “attend building,” prior to each image presentation. In the Internal Distraction blocks, the composite images consisted of a visually presented face and a scrambled distracter image, with participants instructed to “attend face,” “imagine house,” or “imagine building,” prior to each image.

### **Self-report Methods and Analysis**

Self-report data was gathered via a questionnaire presented after the completion of the experiment. Participants were instructed to report their level of fear when viewing each of the face, place, and composite images shown throughout the study. Participants also reported their perceived difficulty performing the distracter tasks for each condition involving composite images and the vividness of imagery during the imagined distracter task (i.e., the Internal blocks).

Participants’ self-reported fear and task difficulty were independently analyzed using a 2x2x2 within-subjects ANOVA to compare conditions across CS type (CS+, CS-), target (face, distracter), and distracter type (visual, imagined). Three participants were excluded from analysis of self-report fear and difficulty data due to unreadable responses to one or more questions. Self-reported vividness was only reported for the two Internal Distraction conditions. Vividness ratings were analyzed by paired-samples t-test.

### **Physiological Methods and Analysis**

Skin conductance (SCR) values were recorded throughout the conditioning and experimental phases using a BIOPAC MP-150 data acquisition system sampling at 2000Hz. Electrodes for SCR measurement were attached to second and third digit of the non-dominant

hand, opposite the shock electrodes on the second and third digit of the dominant hand. SCR acquisition and processing were performing using AcqKnowledge (BIOPAC systems, Goleta, CA, USA) and Matlab R2019b (version 9.7.0) software.

SCR data analysis followed steps derived from previous research (Grégoire & Greening, 2019; Jiang, Burleigh, & Greening, 2021). Preprocessing applied a first-order Butterworth bandpass filter with a frequency range of .05 to 5 Hz. Data were then detrended and down-sampled to 100Hz. A time window from 1.0-6.5 seconds after onset was extracted for each SCR epoch and baseline-corrected against the mean signal from one second before the epoch onset. Trials within this window with peak SCR values .02 $\mu$ S above baseline were extracted and all other trials were zeroed. Peak SCR values by condition were then analyzed using a 2x2x2 (CS type (CS+, CS-), target (face, distracter), and distracter type (visual, imagined)) within-subjects ANOVA. SCR data for eleven participants were discarded as non-responders such that there was no reliable SCR response to the US (i.e., the mild shock), due to excessive noise in the time series such that reliable SCRs could not be extracted, or due to a technical failure in acquisition.

## **RESULTS**

### **SCR Results**

#### **Conditioning Phase**

SCR was the only measure gathered during the conditioning phase. Importantly, analysis using paired-samples t-test confirmed that there was significant group-level differential fear conditioning (Figure 1.2a). SCR values during presentation of the CS+ ( $M = 0.69$ ,  $SD = 0.53$ ) were significantly higher than during presentation of the CS- ( $M = 0.31$ ,  $SD = 0.27$ ),  $t(31) = 5.605$ ,  $p < .001$ ,  $d = 0.92$ .

## Regulation Phase

SCR effects during face-alone trials in the regulation blocks were first analyzed to determine whether the effects of conditioning persisted through the experimental trials (Figure 1.2b). A 1-way within-subjects ANOVA comparing CS+ face-alone, CS- face-alone, and place-alone conditions showed a main effect of CS-type [ $F(1,31) = 6.37, p = .017, \eta^2 = .17$ ]. Paired-samples t-tests identified significant differences in response between CS+ and CS- face-alone images,  $t(31) = 2.062, p = .048, d = 0.25$ , supporting the presence of differential conditioning. SCR was also significantly lower in the presence of place-alone images than either CS+,  $t(31) = 2.524, p = .017, d = 0.50$ , or CS-,  $t(31) = 2.736, p = .010, d = 0.26$ , images.

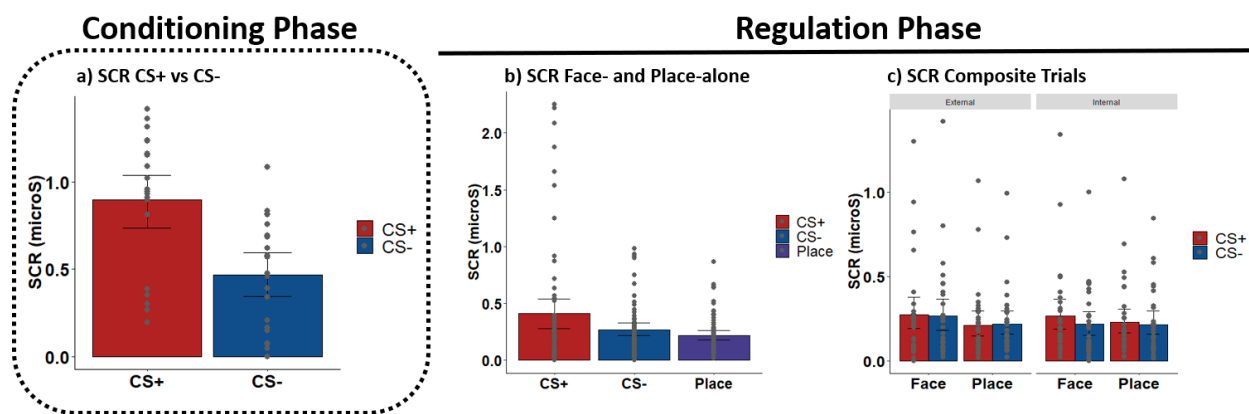


Figure 1.2. Effects of CS-type on SCR during Conditioning Phase (a); stimulus type on SCR during Regulation Phase (b); and CS-type, attentional target, and block-type on SCR during Regulation Phase (c). Error bars show 95% confidence interval. Each dot represents one participant.

Next, we inspected participant SCR during the composite image presentations (Figure 1.2c). A repeated-measures 2x2x2 ANOVA, with CS-type (CS+, CS-), attentional target (attend face, attend/imagine place), and block type (External, Internal) as within-subject variables identified a main effect of attentional target (attend face vs attend/imagine place) [ $F(1,31) = 5.317, p = .028, \eta^2 = .006$ ], such that irrespective of CS-type and block-type there was higher

recorded SCR when attending to the face stimuli compared to attending to or imagining the place stimuli.

Table 1.1. Study 1 ANOVA Results, GSR Values in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta^2_g$
(Intercept)	1	31	14.64	8.81	51.53	.000	.52
CS	1	31	0.02	0.94	0.51	.482	.00
Target	1	31	0.08	0.49	5.32	.028	.01
Block	1	31	0.01	1.63	0.13	.721	.00
CS x Target	1	31	0.01	0.12	2.67	.112	.00
CS x Block	1	31	0.01	0.32	1.40	.245	.00
Target x Block	1	31	0.02	1.01	0.63	.434	.00
CS x Target x Block	1	31	0.00	0.36	0.10	.753	.00

*Note.*  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta^2_g$  indicates generalized eta-squared.

No main effects were identified for either CS-type [ $F(1,31) = 0.506$ ,  $p = .482$ ,  $\eta^2 = .001$ ], or block-type [ $F(1,31) = 0.130$ ,  $p = .721$ ,  $\eta^2 = .0004$ ] and no interaction effects were identified for CS-type by attentional target [ $F(1,39) = 2.67$ ,  $p = .112$ ,  $\eta^2 = .0007$ ], CS-type by block-type [ $F(1,39) = 1.40$ ,  $p = 0.24$ ,  $\eta^2 = .001$ ], or attentional target by block-type [ $F(1,39) = 0.63$ ,  $p = .434$ ,  $\eta^2 = .001$ ]. No three-way interactions were found in SCR [ $F(1,39) = 0.10$ ,  $p = .752$ ,  $\eta^2 = .00009$ ].

Two post-hoc planned comparisons were evaluated to test the prediction that distraction reduces the SCR response to the CS+, one for the External Distraction blocks and the other for the Internal Distraction blocks. We observed a significant reduction in SCR during the External Distraction blocks during the CS+ attend place condition compared to the CS+ attend face condition,  $t(31) = -2.501$ ,  $p = .018$ ,  $d = 0.42$ . However, during the Internal Distraction blocks

CS+ imagine place did not produce a significant reduction in SCR versus the CS+ attend face condition,  $t(31) = 1.373$ ,  $p = .180$ ,  $d = 0.15$ .

## **Likert Results**

### **Self-Reported Fear**

An initial comparison of CS+ face-alone, CS- face-alone, and place-alone images using a 1-way within-subjects ANOVA demonstrated the presence of the differential conditioning (Figure 1.3a) into the experimental phase [ $F(2,39) = 130.34$ ,  $p < .001$ ,  $\eta^2 = .77$ ]. Specifically, pairwise comparisons showed that the CS+ ( $M = 5.4$ ,  $SD = 1.56$ ) elicited significantly higher self-reported fear than either the CS- ( $M = 1.7$ ,  $SD = 1.20$ ),  $t(39) = 11.56$ ,  $p < .001$ ,  $d = 2.60$ , or the place-alone images ( $M = 1.6$ ,  $SD = 0.88$ ),  $t(39) = 11.56$ ,  $p < .001$ ,  $d = 2.95$ . No significant difference in reported fear were found between CS- and place-alone images,  $t(39) = 0.514$ ,  $p = .610$ ,  $d = 0.095$ .

Critically, the analysis of self-reported fear during the presentation of the composite images found that the use of both visual and imagined distracters successfully down-regulated the conditioned fear response (Figure 1.3b). Likert responses during composite image presentation were analyzed using a repeated-measures 2x2x2 ANOVA, with CS-type (CS+, CS-), attentional target (Attend Face, Attend/Imagine Place), and block-type (External, Internal) as within-subject variables. This revealed a significant three-way interaction [ $F(1,39) = 4.15$ ,  $p = .048$ ,  $\eta^2 = .002$ ]. Follow-up pairwise comparisons revealed significantly higher self-reported fear for the CS+ compared to the CS- in the following instruction-specific pairs: External Distraction Attend Face:  $t(39) = 6.17$ ,  $p < .001$ ,  $d = 1.07$ ; External Distraction Attend Place:  $t(39) = 6.44$ ,  $p < .001$ ,  $d = 1.16$ ; Internal Distraction Attend Face:  $t(39) = 7.74$ ,  $p < .001$ ,  $d = 1.45$ ; and Internal Distraction Attend Place:  $t(39) = 5.81$ ,  $p < .001$ ,  $d = 1.07$ .

## Regulation Phase

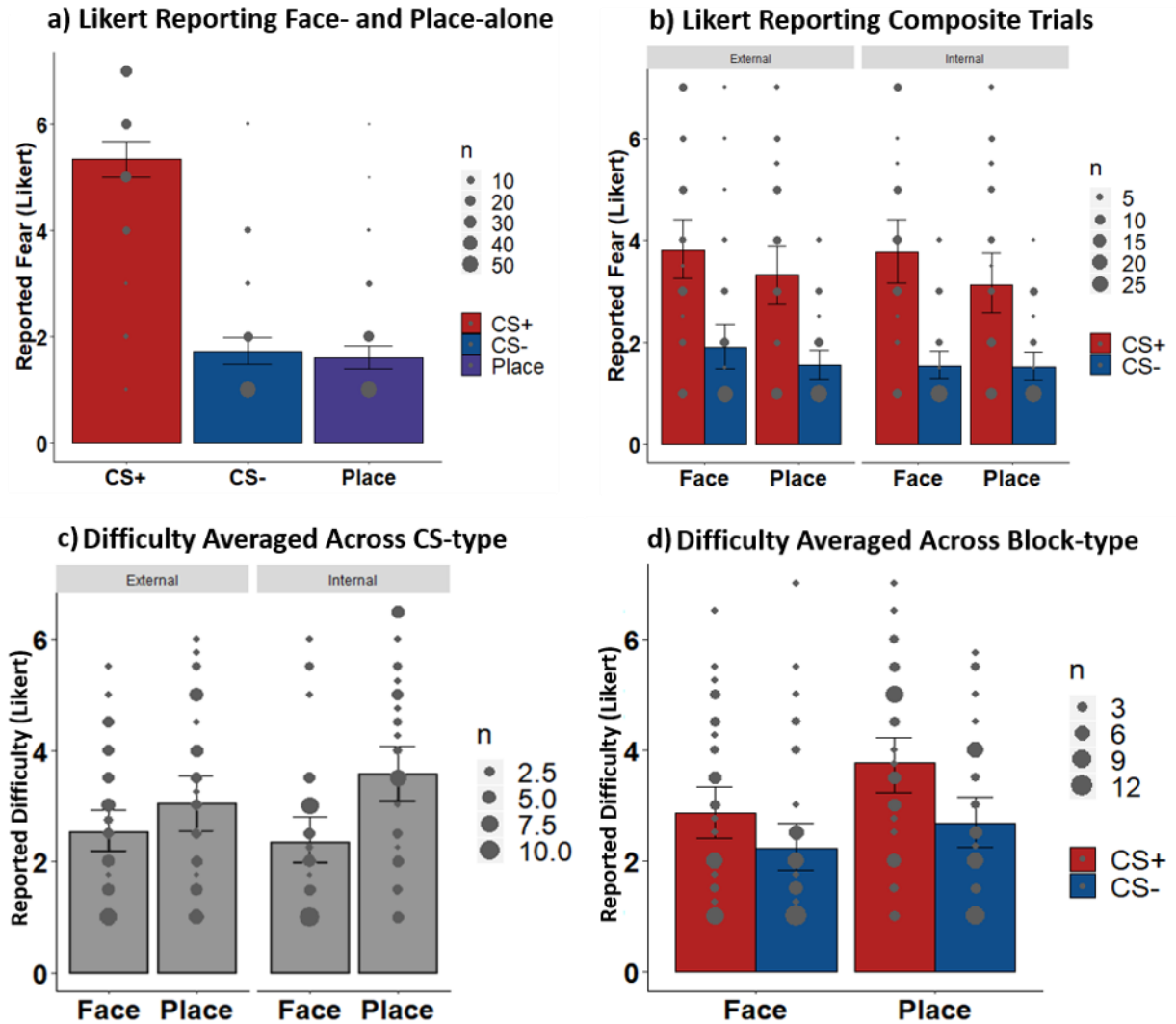


Figure 1.3. Effects of stimulus type on self-reported fear (a); CS-type, attentional target, and block-type on self-reported fear (b); attentional target and block-type on self-reported task difficulty (c); and CS-type and attentional target on self-reported task difficulty (d) in the Regulation Phase. Error bars show 95% confidence interval. Dots represent number of participants reporting a given value.

We observed evidence of significant down-regulation of self-reported fear in both the External Distraction and Internal Distraction blocks. Specifically, pairwise comparisons revealed that self-reported fear was significantly greater in the CS+ Attend Face compared to the CS+ Attend Place trials in both the External,  $t(39) = 2.42, p = .020, d = 0.24$ , and the Internal,  $t(39) =$

3.09,  $p = .004$ ,  $d = 0.32$ , block types. No significant differences were found between CS-conditions. We also observed main effects of CS-type [ $F(1,39) = 61.84$ ,  $p < .001$ ,  $\eta^2 = .26$ ] and attentional target [ $F(1,39) = 14.76$ ,  $p < .001$ ,  $\eta^2 = .01$ ]. No main effect of block-type [ $F(1,39) = 1.77$ ,  $p = .191$ ,  $\eta^2 = .002$ ], CS-type by attentional target interaction [ $F(1,39) = 3.29$ ,  $p = .077$ ,  $\eta^2 = .004$ ], CS-type by block-type interaction [ $F(1,39) = 0.23$ ,  $p = .637$ ,  $\eta^2 = .0003$ ], or attentional target by block-type interaction [ $F(1,39) = 0.31$ ,  $p = .582$ ,  $\eta^2 = .0002$ ] was observed.

Table 1.2. Study 1 ANOVA Results, Self-Reported Fear in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta^2_g$
(Intercept)	1	39	2116.65	438.22	188.37	.000	.73
CS	1	39	281.25	177.38	61.84	.000	.26
Target	1	39	10.88	28.75	14.76	.000	.01
Block	1	39	1.95	43.05	1.77	.191	.00
CS x Target	1	39	2.81	33.31	3.29	.077	.00
CS x Block	1	39	0.20	34.55	0.23	.637	.00
Target x Block	1	39	0.15	19.35	0.31	.582	.00
CS x Target x Block	1	39	1.25	11.75	4.15	.048	.00

*Note.*  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta^2_g$  indicates generalized eta-squared.

### Self-Reported Difficulty.

A second repeated-measures 2x2x2 ANOVA, with CS-type (CS+, CS-), attentional target (face, place), and block-type (External, Internal) as within-subject variables was conducted to compare reported difficulty of attending/imagining the target in each condition. Notably, this revealed two significant interaction effects, an attentional target by block-type interaction [ $F(1,39) = 6.27$ ,  $p = .017$ ,  $\eta^2 = .01$ ] and a CS-type by attentional target interaction [ $F(1,39) = 4.37$ ,  $p = .004$ ,  $\eta^2 = .004$ ].



Table 1.3 Study 1 ANOVA Results, Self-Reported Task Difficulty in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta^2_g$
(Intercept)	1	39	2653.63	389.46	265.73	.000	.74
CS	1	39	36.79	127.43	11.26	.002	.04
Target	1	39	59.08	168.64	13.66	.001	.06
Block	1	39	2.36	71.86	1.28	.264	.00
CS x Target	1	39	4.16	37.18	4.37	.043	.00
CS x Block	1	39	0.09	34.75	0.11	.746	.00
Target x Block	1	39	10.33	64.26	6.27	.017	.01
CS x Target x Block	1	39	0.41	35.31	0.46	.503	.00

Note.  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta^2_g$  indicates generalized eta-squared.

Regarding the first, collapsing across CS-type, imagining the place versus attending to the faces was proportionately more difficult (i.e., during the Internal Distraction blocks) than attending to the place versus attending to the face during the External Distraction blocks (Figure 1.3c). Specifically, during the Internal Distraction blocks, difficulty was greater for the Imagine Place versus the Attend Face condition,  $t(39) = -4.19, p < .001, d = 0.79$ . During the External Distraction blocks, no difference in difficulty between the Attend Place versus Attend Face condition was found,  $t(39) = -1.99, p = .054, d = 0.35$ . Additionally, attending to the face stimuli was not significantly more difficult between block-types,  $t(39) = 1.17, p = .249, d = 0.14$ , while attending/imagining the place stimuli was more difficult in the Internal block,  $t(39) = -2.14, p = .039, d = 0.33$ .

Regarding the second interaction, collapsing across block-type, attending/imagining the place was harder than attending to the face in the presence of the CS+, but not in the presence of the CS- (Figure 1.3d). Specifically, paired-samples t-tests showed significantly higher difficulty for attending/imagining the distracter in the presence of CS+,  $t(39) = -4.31, p < .001, d = 0.56$ ,

but no significant differences in difficulty were observed between attentional targets in the presence of the CS-,  $t(39) = -1.82, p = .077, d = 0.31$ . Additionally, task difficulty was higher in the presence of the CS+ than the CS- when attending to either the face,  $t(39) = 2.84, p = .007, d = 0.42$ , or place stimuli,  $t(39) = 3.78, p < .001, d = 0.70$ . We also observed main effects of CS-type [ $F(1,39) = 11.26, p = .002, \eta^2 = .04$ ], and attentional target [ $F(1,39) = 13.66, p < .001, \eta^2 = .06$ ]. No main effect of block-type was identified [ $F(1,39) = 1.28, p = .264, \eta^2 = .003$ ], nor was there a CS-type by block-type [ $F(1,39) = .106, p = .75, \eta^2 = .0001$ ] or three-way interactions in reported difficulty [ $F(1,39) = 0.46, p = .503, \eta^2 = .0004$ ].

### **Self-Reported Imagery Vividness**

Reported vividness of visual imagery was compared via paired-samples t-test. Participants reported higher vividness while visualizing the distracter in the presence of the CS+ than in the presence of the CS-,  $t(42) = 2.158, p = .037, d = 0.23$ .

## **DISCUSSION**

The goal of this study was to determine the effectiveness of external (object-based) attention and internal distraction (i.e., mental imagery) as distraction-based emotion regulation strategies for differential fear conditioning. Consistent with our primary prediction, we found evidence that both external distraction and mental imagery-based distraction can successfully down-regulate differential fear conditioning as measured with self-report. The SCR results were less clear overall, though provided independent confirmation of the acquisition of differential fear conditioning and provided partial support for the effectiveness of external distraction in the down-regulation of the SCR response. Additionally, we also observed that distraction by mental

imagery required greater effort to perform generally, which is consistent with our secondary prediction

The self-reported fear ratings supported the primary hypothesis that differential fear conditioning can be down-regulated using both external and internal distraction. First, the self-reported fear towards the faces and places alone indicated that differential conditioning persisted into the regulation phase. Second, during the regulation phase, we observed significantly lower fear in response to CS+ composite images when attending to or imagining the places versus to attending to the CS+ face compared to compositive images that included the CS-. This indicates that both object-based and mental imagery-based distracters effectively lower subjective differential fear. This is consistent with previous work demonstrating that object-based, external, distraction can suppress the impact of a fear conditioning image on perceptual processing and behavior (Yates et al., 2010). Furthermore, the internal distraction findings are consistent with Greening et al. (2021), which observed that mental imagery of a CS- while viewing a CS+ could down-regulate self-reported fear. Our self-reported fear findings indicate that an imagined distractor can reduce fear comparably to an object-based distracter. However, the self-reported fear findings do not rule out the possibility that, all else being equal, internal distraction requires greater effort to obtain similar outcomes.

Compared to visual perception, mental imagery is associated with increased frontoparietal activity (Dijkstra, Bosch, & van Gerven, 2019; Ganis et al., 2004; Greening et al., 2021) in regions associated with mental effort or cognitive demand (Duncan, 2010). This greater degree of frontoparietal activity associated with imagery is consistent with the pattern of reported difficulty found by our study. Specifically, the observed attentional target by block-type interaction suggests that internal distraction is generally more difficult than external distraction

compared to attending to faces, irrespective of CS-type (i.e., either the CS+ or CS- face). Specifically, higher self-reported task difficulty was observed for imagined distraction compared to attending to either the CS+ and CS- face, while external distraction trials only found this difference in the presence of the CS+. We also observed a CS-type by attentional target interaction such that the presence of the CS+ resulted in greater distraction task difficulty. As emotional stimuli are highly attentionally engaging, the increased difficulty of the task may reflect the higher effort necessary to disengage from the CS+ face than the emotionally neutral CS- (Eippert, Gamer, & Buchel, 2012; Grégoire, Kim, & Anderson, 2020). In addition to the previous literature on distraction, our results indicate that distraction using mental imagery is more difficult than object-based distraction, while distracting in the presence of a fearful stimulus was found to be more difficult generally.

Regarding the SCR data, the effects of successful differential conditioning were observed in both the conditioning phase and the face-alone trials of the regulation phases. This is consistent with the similar to the conditioning phases of previous studies of fear conditioning and object-based distraction (Lim & Pessoa, 2008; Yates et al., 2010). The SCR results, however, were less clear during the composite image trials. We did observe a main effect of attentional target such that SCR levels were generally lower while attending to or imagining the distracter than attending to the face stimuli, irrespective of CS-type. We did not observe the predicted two-way, CS-type by attentional target, interaction. Neither Yates et al. (2010), nor Lim et al. (2008) reported in their studies of external object-based distraction whether or not SCR was modulated as a function of attentional load. Thus, it is unclear whether or not our lack of an interaction is consistent with previous research. Nevertheless, we did observe in our planned comparisons that in the External Distraction blocks, attention to the place image in the presence of the CS+ could

significantly reduce the SCR compared to attend face CS+ trials. This down-regulation of SCR is similar to that observed by Delgado et al. (2008) and Greening et al. (2021), both of which used forms of internal distraction. Conversely, we did not observe the same evidence of SCR down-regulation in our Internal Distraction blocks. One possibility in the present study is that the layered compositive images reduced the saliency of the face stimuli thereby reducing the CS discriminability to some degree. Future research is required to determine whether salience in this composite image paradigm represents a meaningful confound. This could be addressed by using more visually distinct stimuli, such as a male versus female face as in Lim et al. (2008), or using objects and animals (Dunsmoor, Kroes, Braren, & Phelps, 2017).

Our findings are broadly consistent with the biased-competition model and the role for attention selection in the regulation of emotion (Bishop, 2008; Blair & Mitchell, 2009). Moreover, the self-reported findings in particular are consistent with Greening et al. (2021), which found that mental imagery can disrupt differential condition by inhibiting the representation of the CS+ in early regions of the ventral visual stream. However, given the use of complex objects (i.e., faces and places) and the lack of brain imaging measures in the current study, future research is required to determine if our observed results of down-regulation can be attributed to inhibition of the representation of the CS+ in the ventral visual stream (Cohen & Tong, 2015).

While our findings regarding mental imagery as an internal distracter are relevant to the impact of distraction on emotional reactivity, they may also have implications for other areas of emotion regulation. Existing assumptions regarding cognitive reappraisal assert that the mechanism of reappraisal involves adjusting one's interpretation of a scene by modifying the meaning of the scene (McRae et al., 2012). For example, imagining either a celebration or a

funeral to change the emotion depicted in an image of crying people. However, there are some findings indicate that mental imagery could play a role in cognitive reappraisal and the adjustments of meaning (Ochsner, Silvers, & Buhle, 2012; Opitz, Cavanagh, & Urry, 2015), just as the example above suggests. For example, in their meta-analysis of cognitive reappraisal, Ochsner et al. (2012) observed greater activation during reappraisal in aspects of the temporal and occipital cortices. Other research with cognitive reappraisal has observed the modulation of regions associated with visual processing, which might reflect processes of goal-directed attention (Greening, Lee, & Mather, 2014), though the existing literature does not disentangle the potential contributions of external attention from internal attention in the reappraisal process. Together with the current findings, we speculate that imagined scenes or the addition of novel imagined elements to a scene contributes to emotional down-regulation via mechanisms of goal-directed attentional selection in the occipitotemporal lobes. Future research using brain imaging methods will be necessary to identify the neural correlates of both internal and external distraction, as well as where and how they contribute to various emotion regulation strategies ranging from distraction to forms of cognitive reappraisal.

## **CHAPTER 2. EFFICACY AND NEURAL BASIS OF IMAGINED DISTRACTERS**

Attention control has an established history as an effective means of modulating emotion (Greening, Lee, & Mather, 2014; Ochsner & Gross, 2005; Ochsner et al., 2012). Top-down attention selection can deprioritize processing of an emotional stimulus in favor of an attended distracter, reducing the impact of the emotional stimulus (Pessoa et al., 2002). While distraction tasks commonly rely on visual distractors to redirect attentional resources (Buhle et al., 2014; Ochsner et al., 2012), distraction using mental imagery is poorly specified in comparison to visual distraction (Martins et al., 2015; Oliver & Page, 2008; Strauss et al., 2016). This study aims to compare the efficacy and neural correlates of object-based (external) and mental imagery-based (internal) distraction in emotion regulation.

Fear research commonly relies on standardized affective images, such as the IAPS set by Lang, Bradley, and Cuthbert (2008). While broadly effective, emotion-inducing scenes are limited by the range of idiosyncratic responses they elicit (Barke et al., 2012; Ito & Cacioppo, 2005). Differential fear conditioning offers an alternative method for establishing a reliable fear response. By pairing a neutral conditioned stimulus (CS+) with an aversive unconditioned stimulus (US) such as a mild shock. If successful, the resulting negative stimulus can be compared to a neutral control (CS-). Meta-analysis of previous research on the neural correlates of fear acquisition and processing has shown largest effect sizes in the bilateral anterior insula, but does not identify significant involvement by the amygdala (Fullana et al., 2016).

Affective image stimuli have been shown to induce elevated BOLD activity in the amygdala associated with fear processing (Anders, Lotze, Erb, Grodd, & Birbaumer, 2004; Sabatinelli, Bradley, Fitzsimmons, & Lang, 2005). However, emotion processing and regulation in the case of conditioned stimuli has been shown to correlate with elevated BOLD activity in the

left anterior insula (Buhle et al., 2014; Delgado et al., 2008; M A Fullana et al., 2015). As this study focuses on regulation of conditioned fear, we anticipate that regulatory effects will correlate with activity in the anterior insula. While object-based stimuli (External) and mental imagery-based stimuli (Internal) originate from different sources, research indicates that both form similar mental representations (Etkin et al., 2015; Romero-Rebollar, Jiménez-Ángeles, Dragustinovis-Ruiz, & Medina-Bañuelos, 2016). We hypothesize that both types of distracter will influence emotion processing similarly.

Existing models of interaction between cognitive emotion regulation tasks and the experience of emotion suggest that activity in the dorsolateral prefrontal cortex introduces a down-regulatory effect on emotion processing in the amygdala and insula by way of inhibitory influence through the ventromedial prefrontal cortex (Delgado et al., 2008). Maintenance of visually presented fear stimuli should require the continued engagement of visual processing and associative networks. The biased competition model suggests that top-down attentional control can bias visual processing of an attended stimulus over that of an unattended stimulus, despite the unattended stimulus having a higher emotional impact (Desimone & Duncan, 1995; Pessoa et al., 2002). We predict lower reported fear during both external and internal distraction tasks than when attending to conditioned fear images. We expect this effect to be reflected by accompanying changes in BOLD activity in the aIn.

## **METHODS**

### **Participants**

Twenty-nine undergraduate and graduate participants (22 female), aged 18-30, were recruited from pre-screened volunteer lists gathered at Louisiana State University. Participants



reported no presence or history of psychological or neurological disorders. One participant withdrew from the study partway through the MRI procedure and was excluded from analysis. An additional three participants were excluded from analysis due to failure to complete more than two thirds of the planned experimental trials, resulting in a final sample of 25 participants. All participants gave written informed consent and the protocol was approved by the Louisiana State University institutional review board.

## **Materials**

Each participant completed four phases of the experiment (Habituation, Fear Conditioning, Regulation (External/Internal Distractor), and Functional Localizer). Each phase presented combinations of object-based and mental imagery-based stimuli. Two face images were used for the conditioned stimuli. Greyscale images of two males with neutral expressions were taken from the Cohn-Kanade emotional faces database. The face images had the background removed and were cropped to show only the head from hairline to chin. Two place images (one house and one building) were used as distractors. The place images were also greyscale and had the backgrounds removed such that only a building or house was visible. Faces were selected as the conditioning stimuli due to their reliable representation in the fusiform face area (FFA) (Ghuman et al., 2014; Kanwisher, McDermott, & Chun, 1997), while place images were used as distractors due to the ease of identifying place processing in the parahippocampal place area (PPA) (Epstein, Harris, Stanley, & Kanwisher, 1999). From these base images, an additional set of composite face-place images were generated from all possible face/place pairings. For the purposes of the Internal Distraction blocks, the composite images contained one of the two faces along with a scrambled place image. Scrambled images were generated in Matlab by dividing place images into a grid of 40x40px and scrambling grid blocks.

The purpose of including the scrambled place rather than simply having the face alone was to produce a resulting composite image with the same visual complexity as those used in the External Distraction blocks.

In our fear conditioning procedure, one face served as the conditioned stimulus (CS+) and was paired with the unconditioned stimulus (US; a mild shock to the distal phalanges of the pointer and middle fingers of the left hand), while the second face was never paired with shock (CS-). Which face image served as CS+ was counterbalanced across participants. The mild ( $M_{intensity} = 6$  mA,  $SD = 11.03$ , range: 1.00-50.00 mA) shock was delivered using a BIOPAC STMISOC module with MR-compatible leads and electrodes. Shock duration was 500ms at 50Hz. During the Internal Distraction Task participants were cued to imagine either a house or place using an auditory instruction. These auditory instructions were created using TextAloud text-to-speech software (Language: British English, Voice: Emma, Speed: Medium) to produce 2-second spoken clip and delivered during scanning using MRI-compatible insert earphones.

## **Design and Procedure**

### **Habituation**

Once in the scanner, participants underwent a habituation run comprising the selected face and place images. Composite images were not included in habituation. This phase was necessary to both ensure a neutral baseline for the images to be used in conditioning, and to expose participants to the distractor images that they would later be instructed to mentally image. Habituation included 2 presentations of each image, for a total of 8 trials. After an initial two-second fixation dot, each trial consisted of a 4-second image presentation followed by a 14-second inter-trial interval (ITI) with fixation dot. The total duration of the habituation run was 144 seconds.

## Fear Conditioning Acquisition

After habituation, participants performed a brief threshold task in which their shock level was determined for the remainder of the study. Participants were instructed to report a shock's intensity as "not uncomfortable", "uncomfortable", or "painful." A participant's shock level was established at the highest intensity rated "uncomfortable" but not painful.

Having established an aversive shock threshold, participants underwent one run of fear conditioning acquisition (Figure 2.1a).

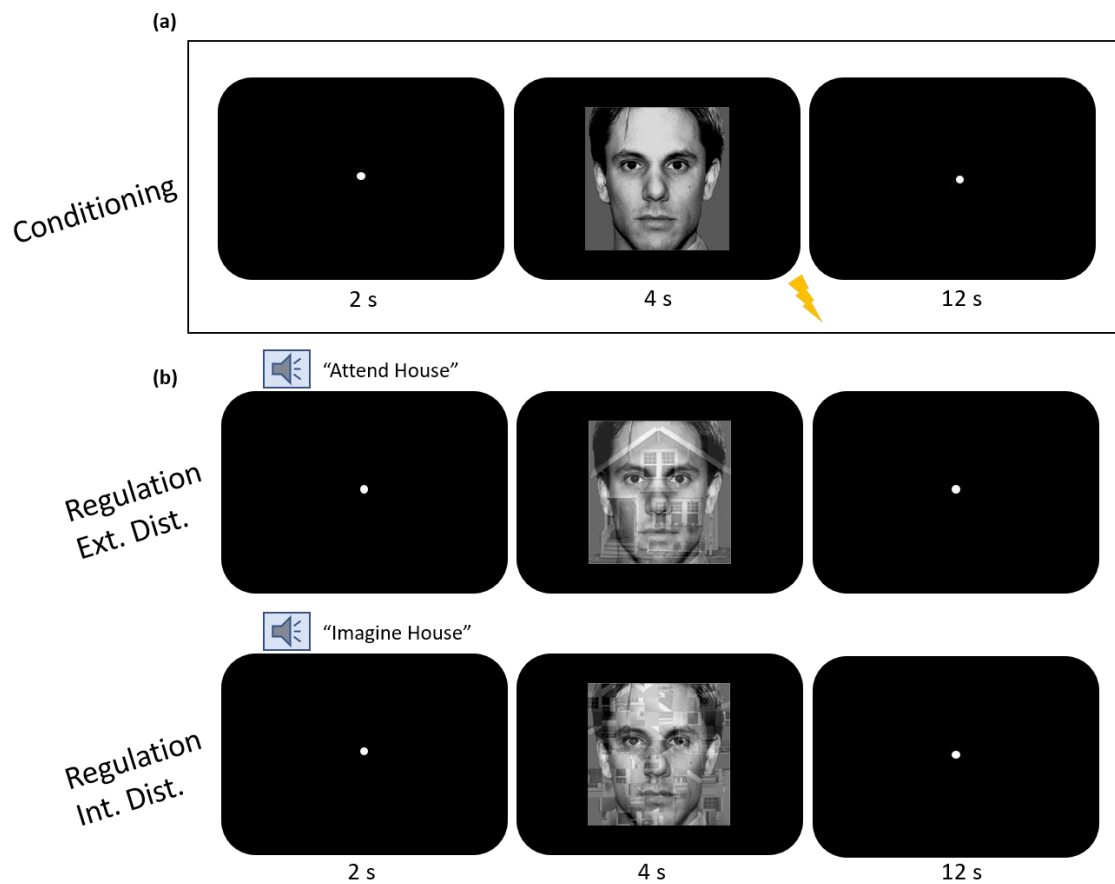


Figure 2.1. Experiment structure and example stimuli for Conditioning and Regulation Phases.

One of the two face images was chosen at random to be the CS+, while the remaining face image was designated as the CS-. As with habituation, the conditioning phase contained no instructions on a per-trial basis, only the direction to keep their eyes on the fixation point at the center of the screen and to pay attention. In this phase, participants viewed both CS+ and CS- in a randomized series. 60% of CS+ presentations were paired with the shock stimulus, while the CS- face was never accompanied by a shock. Each face image was presented 10 times for 20 total presentations, 4 CS+ without shock, 6 CS+ with shock, and 10 CS-. Following the initial 2-second fixation dot, each trial comprised a 4-second image presentation, followed by a 14-second ITI with fixation dot. In shock trials, a 500ms shock was coterminous with the end of the image presentation. The full duration of the conditioning task was 360 seconds.

### **Emotion Regulation Task**

After conditioning, participants began the primary experimental phase (Figure 2.1b). This phase comprised two independent block types, External Distraction Task blocks and Internal Distraction Task blocks (Figure 2.1). Block types were presented in alternating order with a random starting type, meaning a participant could start with either an External or Internal Distraction block. In both External and Internal Distraction Task block types, participants viewed series of faces, places, and composite face-place images paired with audio instructions.

In the External Distraction Task, each trial began with the auditory instruction (2 seconds) to either “Attend House,” “Attend Building,” or “Attend Face.” A fixation dot was present during this section. The auditory instruction was followed by the presentation of either a face alone, a place alone, or a composite image (4 seconds). Each trial ended in a 12-second ITI with fixation dot. Blocks comprised 2 CS+ alone, 2 CS- alone, 2 House alone, 2 Building alone, 1 CS+ alone with reinforcing shock, and 8 composite trials (1 for each possible combination of

CS, Distractor, and Instruction) for a total of 17 trials per block. The duration of each block was 308 seconds.

The Internal Distraction Task was similar to the External Distraction Task, with the only difference being the specific auditory instructions and the nature of the composite images. The auditory instructions in the Internal Distraction Task direct the participant to either “Attend Face,” “Imagine House,” or “Imagine Building.” The composite images comprised one face and one scrambled-place image and the instructions became either “attend face,” “imagine house,” or “imagine building.” In “attend” conditions, participants viewed the presented image and instructed to direct attention only to the visible face or place, while ignoring other elements. In the “imagine” conditions, participants were instructed to imagine the House or Building portion while still viewing the scrambled composite image. Image distribution consisted of 2 of each CS+ and CS- alone images, 2 of each place distractor, and 8 composite images for each combination of CS/Distractor/Instruction. An additional CS+ with shock was included as a conditioning reinforcement in each block for a total of 17 trials per block. Each experimental block was 306 seconds in length.

### **Functional Localizer**

To independently localize the FFA and PPA for analysis, a single functional localizer run was conducted. Unlike the previous phases, a new set of 20 face and 20 place images was drawn from the same face and place stimulus sets as those used throughout the study. Faces and places were divided into type-specific blocks of rapidly presented images. Each image was visible for 0.75 seconds with a 0.25 second ISI. Each block was presented five times in alternating order with a 15 second ITI between face and place blocks for a total runtime of 356 seconds

### **Self-report measures**

At the end of the experiment, participants were given a set of 7-point Likert scales recording self-reported ratings on fear response to each condition, difficulty of regulation by condition, and the vividness of the imagined distractors in the Internal Distraction Task. This set of data were analyzed in R to compare self-reported fear response and task difficulty.

### **SCR Method and Analysis**

Additional Skin Conductance Response (SCR) measures were recorded during the fear conditioning phase and all External and Internal Regulation phases. SCR was not recorded during either Habituation or the Functional Localizer. SCR measures were recorded using a BIOPAC MP-150 data acquisition system sampling at 2000Hz from MR-compatible electrodes placed on the fourth and fifth digit of the non-dominant hand. SCR data were processed in AcqKnowledge and Matlab software. In all phases, with the exception of the Functional Localizer, image presentations lasted for four seconds, following a two second audio cue and followed by a twelve second ITI. This timing allowed for a return to baseline BOLD response following the onset of a shock stimulus. Shock trials (both conditioning and reinforcement) were excluded from SCR analysis.

Gathered SCR data were detrended and smoothed with a median filter over 50 samples to reduce noise generated by the MRI, then down-sampled to 100Hz. A time window from 1.0-6.5 seconds after onset was extracted for each SCR epoch and baseline-corrected against the mean signal from one second before the epoch onset. Within this window, trials with peak SCR values above baseline were extracted and all other trials were zeroed. Three participants experienced SCR malfunctions that resulted in incomplete SCR recordings during the experimental phases

and could not be included in analysis. As fMRI data and Likert reports for these participants were unaffected, they were subsequently included in those analyses.

## **fMRI Acquisition and Analysis**

### **MRI Acquisition**

Data for fMRI analyses were gathered using a 3T GE Discovery MR750w research scanner and 36-channel head coil at Pennington Biomedical Research Center. Anatomical imaging used a 256x256 T1-weighted protocol with 1mm slice thickness at 1.0x1.0 in-plane voxel resolution for 176 sagittal slices at a 10° flip angle. Functional image acquisition used a single-shot gradient echo EPI sequence (TR = 2000ms, TE = 20ms, FOV = 22.4cm, flip angle = 90°, bandwidth = 7812.5 Hz/px, echo spacing = .578ms for 38 slices). Functional trials used an in-plane voxel resolution of 3.0x3.0mm with a 3mm slice thickness in interleaved ascending order. For both the Internal and External Distraction Task, each block had 154 volumes. Blocks for the Fear Conditioning phase ran for 181 volumes, while the Functional Localizer phase ran for 179 volumes. Each block included an initial three-volume set of dummy volumes that were not included in the analysis.

### **Preprocessing and Whole-brain Univariate Analysis**

fMRI Expert Analysis Tool (FEAT) version 6.00 within the FSL software package was used to perform analysis of the gathered fMRI data. Prior to analysis, pre-statistical processing was conducted on the functional and structural data. Brain extraction was performed on anatomical trials using BET. Functional trials underwent motion correction using MCFLIRT, slice-timing correction using Fourier-space time-series phase-shifting, 7mm FWHM spatial smoothing, and 100s high-pass temporal filtering (Gaussian-weighted least-squares straight line

fitting). FSL's motion outliers function was used to generate motion correction parameters for nuisance regressors in any volume with  $>0.9\text{mm}$  framewise displacement.

At the block-wise level (lvl 1), the study used a double-gamma hemodynamic response function (HRF) to convolve each condition of interest. A model was generated for the temporal derivatives of each condition from onset to offset of the image presentation. This model included the previously noted nuisance regressors for motion and a shock regressor for the reinforcement trial present in each External and Internal Distraction block. These lower-level contrasts were combined into subsequent participant level (lvl 2) fixed-effects analyses. Group-level (lvl 3) analyses were performed using FLAME 1+2 mixed effects modeling with automatic outlier detection. Z-scores obtained from this analysis were thresholded at values of  $Z > 2.3$ , reflecting a cluster significance of  $p > 0.05$ . BOLD data from the Functional Localizer and Conditioning phase sets were analyzed separately using the same pre-processing but phase specific modelling of relevant conditions. These phases underwent lvl 1 FEAT analysis, then level 3 fixed effects modeling due to the presence of only one run per participant. In the functional localizer, conditions were modeled at the run level by image presentation set (face or place), rather than on an image-by-image basis due to the rapid speed of image presentation.

### **Region-of-Interest (ROI) Derivation and Analyses**

ROIs were produced from both the Fear Conditioning Acquisition run (Left/Right Amygdala, Left/Right Anterior Insula) and the Face/Place Functional Localizer run (Fusiform Face Area (FFA), Parahippocampal Place Area (PPA), Occipital Face Area (OFA)). Masks for the left and right aIn were generated from the clusters of highest activity in the bilateral insula for ROI analyses of data from the regulation phase of the experiment. Single subject ROIs were produced by first performing a group-level analysis to locate regions of elevated activity. The



threshold for the group group-level data was then elevated to isolate discrete clusters of activity. A mask was generated for each identified region using FLIRT and all voxels outside said mask zeroed. The remaining voxel of highest activity for each experimental phase was then located. A 3mm sphere was masked around each identified peak voxel, and the mean value from this spherical mask recorded for analysis. Mean BOLD values from the recorded peak spheres were analyzed in R to determine changes in regional activity by condition.

## **RESULTS**

### **Fear Conditioning**

#### **Self-report Measures**

In order to test the success of differential fear conditioning to the CS+ versus the CS- and the distractor stimuli (i.e., the house and building), we first evaluated the trials in which the faces and places were viewed alone. Results indicated significantly higher reported fear ratings for the CS+ conditioned face image ( $M = 4.81$ ,  $SD = 1.72$ ) than the CS- unconditioned face ( $M = 1.81$ ,  $SD = 1.33$ ),  $t(25) = 7.36$ ,  $p < .001$ ,  $d = 1.95$ , or either House ( $M = 1.38$ ,  $SD = 0.75$ ) or Building ( $M = 1.50$ ,  $SD = 0.99$ ) place images,  $t(25) = 8.38$ ,  $p < .001$ ,  $d = 2.58$ ,  $t(25) = 7.59$ ,  $p < .001$ ,  $d = 2.36$ . No significant differences were found in fear ratings between the CS- and the place images,  $t(25) = 1.96$ ,  $p = 0.06$ ,  $t(25) = 1.25$ ,  $p = 0.22$ , or between the place images themselves,  $t(25) = -1.00$ ,  $p = 0.33$  (Figure 2.2).

#### **SCR Results**

The initial acquisition of a fear response to the CS+ face image was tested by comparing peak SCR values during presentation of the CS+ and CS- faces in the conditioning phase. Trials ending in a shock stimulus were excluded from this analysis. When viewing a CS+ face,

participants exhibited significantly higher SCR levels than while viewing a CS- face,  $t(25) = 3.14$ ,  $p < 0.01$ ,  $d = 0.53$ , indicating successful acquisition of a conditioned fear response (Figure 2.2c).

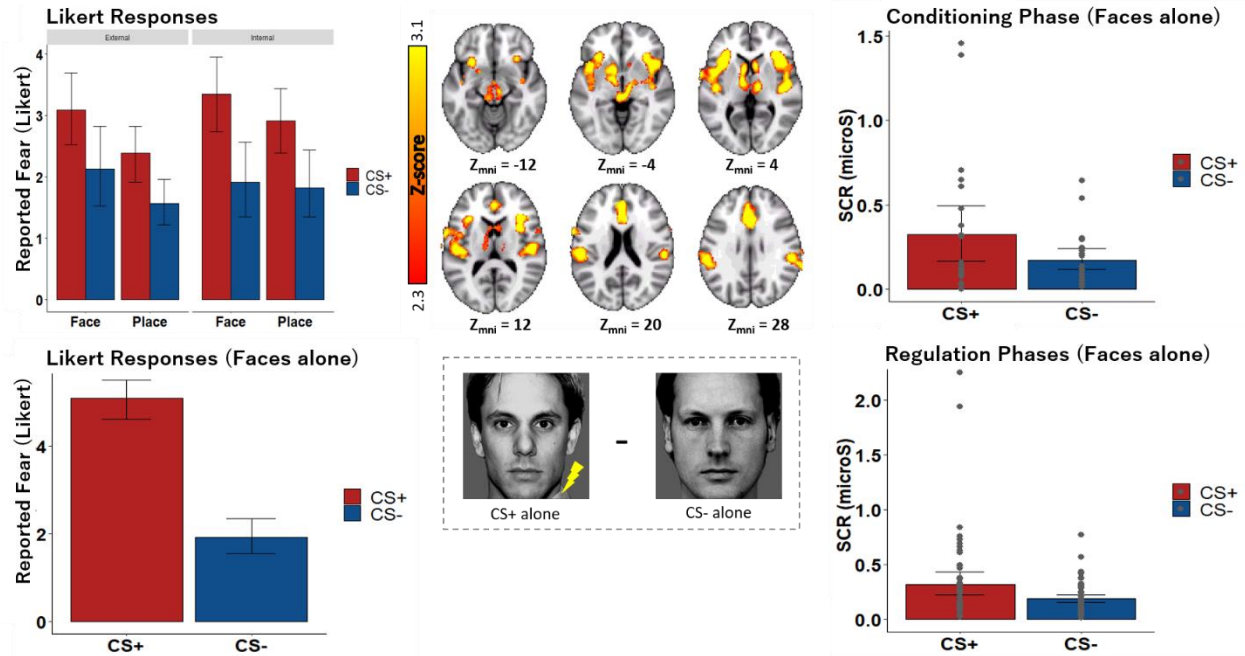


Figure 2.2. Evidence of conditioned fear response persistent throughout regulation phase. a) Self-reported fear across experimental conditions. Likert reports show a consistent effect by conditioning, with higher reported fear in the presence of the CS+ face across conditions, and lower reported fear during both internal and external distraction tasks. b) BOLD activity of during CS+ > CS- face alone images during regulation phase, collapsed across session types. Patterns of BOLD response indicate activation in networks associated with fear learning. c) GSR measures of CS+ and CS- alone images during conditioning phase. d) GSR measures of CS+ and CS- alone images during regulation phase. GSR recordings in the presence of only the CS+ and CS- images indicate the continued presence of the conditioning effect into the regulation phase.

## fMRI Results

Whole-brain univariate analysis during fear acquisition identified a canonical network of elevated activity in the bilateral anterior insula, bilateral thalamus, bilateral caudate, left dACC, and bilateral midbrain (Fullana et al., 2015). Activity in these regions was significantly greater during viewing of the CS+ face than while viewing the CS- face. No regions were identified with

significantly higher activity during viewing of the CS- face than the CS+ face.

## Emotion Regulation Phase

### Self-report Measures

In order to test our main prediction regarding the role of external versus internal distraction in the regulation of differentially conditioned fear response we ran a 2x2x2 repeated-measures ANOVA on self-reported fear for the composite images, with CS-type (CS+, CS-), attentional target (face, distractor), and block-type (External, Internal) as within-subject variables. Results show a main effect of CS, with CS+ faces rated significantly higher than CS- faces across conditions [ $F(1,22) = 13.15, p = .001, \eta_g^2 = 0.13$ ] (Figure 2.2a). This supports the continued efficacy of the conditioning paradigm throughout the experiment. Another main effect of attentional target was also identified, with participants reporting lower fear when attending to a distractor [ $F(1,22) = 4.99, p = .036, \eta_g^2 = 0.026$ ], supporting the hypothesis that both Internal and External Distraction conditions would regulate the fear response.

Table 2.1. Study 2 ANOVA Results, Self-Reported Fear in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta_g^2$
(Intercept)	1	22	1056.96	142.91	162.71	.000	.76
CS	1	22	53.27	89.11	13.15	.001	.13
Target	1	22	9.14	40.24	4.99	.036	.03
Block	1	22	1.96	18.91	2.28	.145	.01
CS x Target	1	22	0.66	14.22	1.02	.324	.00
CS x Block	1	22	1.57	15.80	2.19	.153	.00
Target x Block	1	22	1.57	12.80	2.70	.115	.00
CS x Target x Block	1	22	0.14	7.74	0.39	.541	.00

*Note.*  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta_g^2$  indicates generalized eta-squared.

An additional 2(CS-type)x2(attentional target)x2(block-type) ANOVA on self-reported difficulty for the composite images was conducted to compare difficulty ratings across conditions.

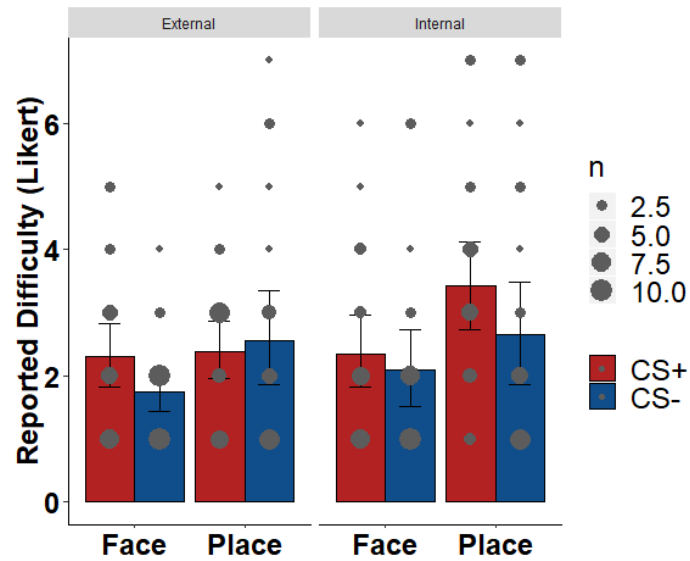


Figure 2.3. Self-reported difficulty across conditions. A main effect of target of attention was identified, with significantly higher difficulty reported in the Internal than the External “attend place” condition.

Table 2.2. Study 2 ANOVA Results, Self-Reported Task Difficulty in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta^2_g$
(Intercept)	1	22	1095.66	113.22	212.90	.000	.73
CS	1	22	5.92	77.96	1.67	.210	.01
Target	1	22	18.92	71.96	5.78	.025	.04
Block	1	22	6.66	37.22	3.94	.060	.02
CS x Target	1	22	0.14	18.74	0.16	.693	.00
CS x Block	1	22	1.22	9.65	2.79	.109	.00
Target x Block	1	22	1.57	50.30	0.69	.416	.00
CS x Target x Block	1	22	4.57	25.30	3.97	.059	.01

Note.  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta^2_g$  indicates generalized eta-squared.

A main effect of attentional target was identified [ $F(1,22) = 5.78$ ,  $p = .025$ ,  $\eta^2_g = 0.45$ ]. Pairwise comparisons also indicated significantly higher reported difficulty in attending to the internal distracter in the presence of the CS+ ( $M = 3.43$ ,  $SD = 1.73$ ) than attending to the external distracter in the presence of the CS+ ( $M = 3.52$ ,  $SD = 1.86$ ),  $t(22) = -2.41$ ,  $p = 0.025$ ,  $d = 0.71$ .

### SCR Results

A planned comparison between CS+ and CS- alone images from this phase indicates that the CS+ and CS- faces did retain the effects of fear conditioning in the absence of a distraction image,  $t(24) = 2.11$ ,  $p = .046$ ,  $d = 0.46$  (Figure 2.2d). SCR data during the Internal and External Distraction conditions were also analyzed using the previous 2(CS-type)x2(attentional target)x2(block-type) ANOVA. An interaction effect of target of attention by block-type was identified [ $F(1,22) = 7.87$ ,  $p = .010$ ,  $\eta^2_g = 0.010$ ].

Table 2.3. Study 2 ANOVA Results, GSR Values in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta^2_g$
(Intercept)	1	24	5.19	2.48	50.26	.000	.59
CS	1	24	0.01	0.34	1.07	.312	.00
Target	1	24	0.02	0.17	2.97	.097	.01
Block	1	24	0.00	0.15	0.07	.789	.00
CS x Target	1	24	0.00	0.10	0.21	.652	.00
CS x Block	1	24	0.01	0.11	1.91	.180	.00
Target x Block	1	24	0.04	0.12	7.87	.010	.01
CS x Target x Block	1	24	0.00	0.11	0.28	.604	.00

*Note.*  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta^2_g$  indicates generalized eta-squared.

Paired t-tests revealed that, collapsed across CS-type, SCR was significantly higher while attending the face image ( $M = 0.19$ ,  $SD = 0.18$ ) than while attending the place image ( $M = 0.14$ ,

SD = 0.11) in External trials,  $t(49) = 2.77, p = .008, d = 0.33$ , but not significantly different between Internal face (M = 0.16, SD = 0.12) and place (M = 0.16, SD = 0.12) trials,  $t(49) = -0.76, p = .453$ .

### **fMRI Results, ROI Analyses**

Similar to the self-report and SCR data, we first evaluated the neural response the face and place alone trials, followed by independent analyses for the trials involving the composite images. Regions were targeted based on their theoretical involvement in fear intensity or regulation. Given the involvement of the right and left aIn as the regions with the largest differential fear conditioning effects identified in the meta-analysis of Fullana et al (2016), we interrogated the regions to evaluate the impact of external and internal attention on the neural representation of differential fear conditioning. The PPA and FFA were targeted due to their assumed involvement in place and face representation during the distraction paradigm (Epstein et al., 1999; Ghuman et al., 2014).

**Anterior Insula.** Prior to analyzing composite trials, face and place alone images were compared to confirm the persistence of differential conditioning. Comparison between CS+ (M = 2.71, SD = 2.73), CS- (M = 0.88, SD = 1.26), and place alone (M = 1.38, SD = 1.56) “view” conditions in the left aIn showed that BOLD activity during the CS+ condition was higher than when during either the CS-,  $t(47) = 4.56, p < .001, d = 0.86$ , or place alone,  $t(47) = 4.03, p < .001, d = 0.58$ , conditions. There was also a difference identified between CS- and place alone images,  $t(47) = -2.11, p = .041, d = 0.35$ , with CS- showing lower left aIn activity than the place alone condition.

A 2(CS-type)x2(attentional target)x2(block-type) ANOVA found critical interaction effects of CS by attentional target [ $F(1,23) = 5.85, p = .024, \eta^2 = 0.008$ ] and target of attention

by block-type [ $F(1,23) = 11.23, p = .003, \eta^2 = 0.023$ ]. Regarding the first interaction, paired t-tests showed significantly higher BOLD activity collapsed across External and Internal sessions while viewing the CS+ compared to the CS- during attend face conditions,  $t(47) = 3.62, p = .001, d = 0.52$ , but not during attend place conditions,  $t(47) = 0.30, p = 0.768$  (Figure 2.3c).

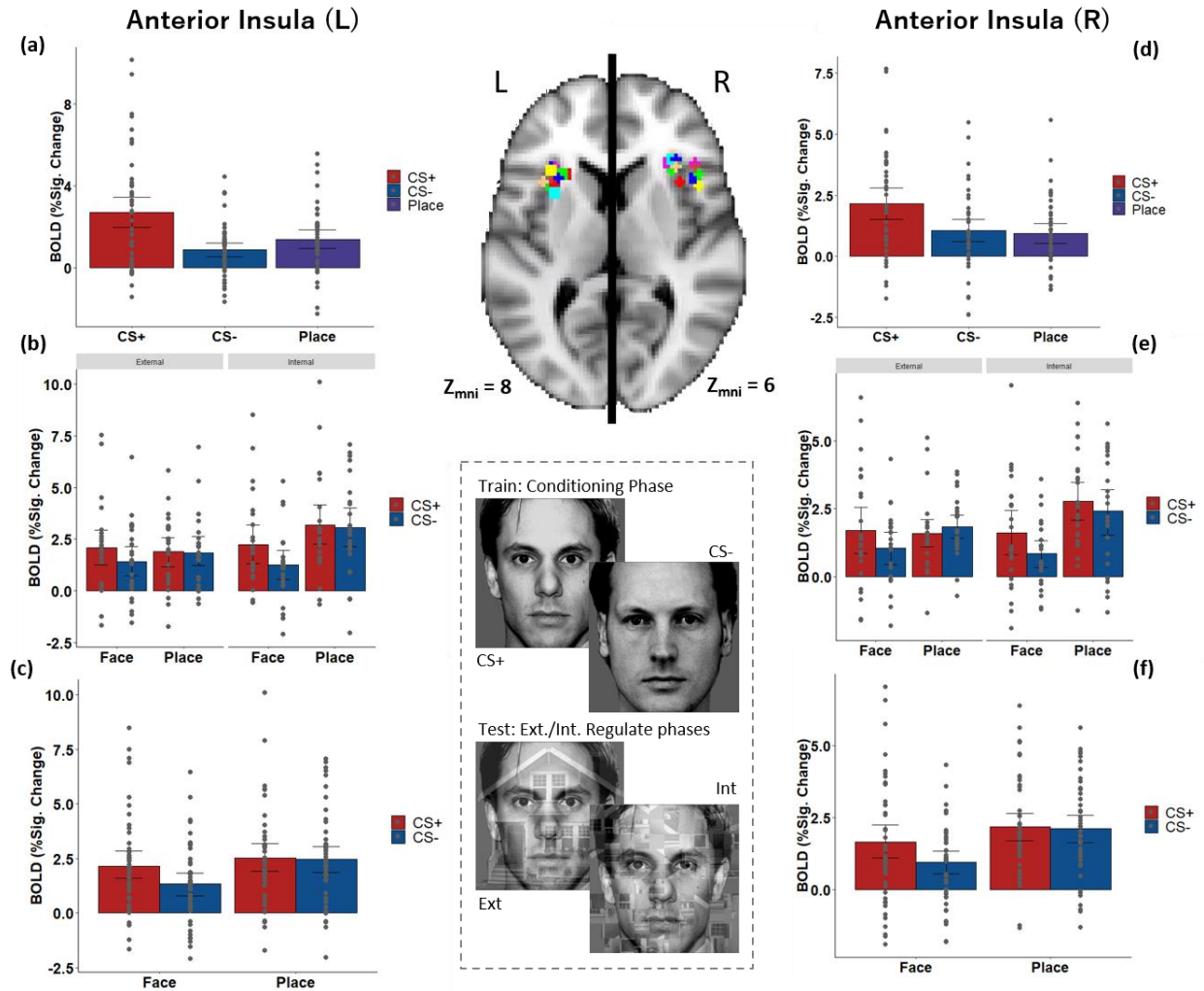


Figure 2.4. Left and Right anterior insula BOLD activity. Graphs a(Left) and d(Right) display average peak sphere BOLD during attend CS+, CS- and Place alone conditions in the left and right hemispheres, while Graphs b(Left) and e(Right) display average peak sphere BOLD activation in the left insula during each composite attention condition. Notable is the elevated activity during the presence of the CS+, both in the CS+ alone condition, and in composite conditions when the participant is instructed to attend to the CS+ stimulus. Graphs c(Left) and f(Right) displays BOLD activity collapsed across External/Internal trials. Mean peak BOLD values localized in the left anterior insula collapsed across internal and external sessions. The presence of the conditioning effect is discernable when attending to the face stimulus, but absent when attending to the distracter.

This supports that the conditioning effect is present when the face is the attentional target, but is no longer discernable when attention is directed toward the distractor.

Table 2.4. Study 2 ANOVA results, Left aIns BOLD Activity in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta^2_g$
(Intercept)	1	23	863.88	539.46	36.83	.000	.52
CS	1	23	9.60	23.83	9.27	.006	.01
Target	1	23	27.44	48.48	13.02	.001	.03
Block	1	23	19.11	49.33	8.91	.007	.02
CS x Target	1	23	6.61	25.97	5.85	.024	.01
CS x Block	1	23	0.42	30.99	0.31	.583	.00
Target x Block	1	23	18.87	38.64	11.23	.003	.02
CS x Target x Block	1	23	0.14	50.55	0.06	.801	.00

*Note.*  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta^2_g$  indicates generalized eta-squared.

Regarding the second interaction, paired t-tests showed significantly higher BOLD activity collapsed across CS-type in the Internal trials while attending to the place ( $M = 3.13$ ,  $SD = 2.42$ ) than while attending to the face ( $M = 1.75$ ,  $SD = 2.13$ ),  $t(47) = 4.74$ ,  $p < .001$ ,  $d = 0.61$ . No significant differences were found between attending to External face ( $M = 1.74$ ,  $SD = 2.02$ ) and place ( $M = 1.87$ ,  $SD = 1.74$ ) stimuli,  $t(47) = 0.50$ ,  $p = .618$ . Main effects of attentional target [ $F(1,23) = 13.02$ ,  $p = .001$ ,  $\eta_g^2 = 0.033$ ] and CS-type [ $F(1,23) = 9.27$ ,  $p = .006$ ,  $\eta_g^2 = 0.012$ ], matching findings from the behavioral data. An additional main effect of block-type was found [ $F(1,23) = 8.909$ ,  $p = .007$ ,  $\eta_g^2 = 0.023$ ], indicating differences between Internal and External distractors not identified in the subjective responses.

In the right aIn, analysis of the CS+ ( $M = 2.15$ ,  $SD = 2.19$ ), CS- ( $M = 1.05$ ,  $SD = 1.59$ ), and place alone ( $M = 0.93$ ,  $SD = 1.40$ ) conditions showed significantly higher activation during



the CS+ condition than either CS-,  $t(47) = 3.56, p = .001, d = 0.57$ , or place alone,  $t(47) = 4.32, p < .001, d = 0.66$ , trials. There was no significant difference in activation between viewing the CS- and the place alone images,  $t(47) = 0.55, p = .583$ . This indicates that differential conditioning persisted into the regulation phase.

Applying the 2(CS-type)x2(attentional target)x2(block-type) ANOVA identified a critical interaction effect of attentional target by block-type [ $F(1,23) = 6.35, p = .019, \eta^2_G = 0.023$ ]. As with the analysis of the left aIn, subsequent paired-subjects t-tests indicated significantly higher peak activation while attending to the CS+ face compared to the CS- face collapsed across block type,  $t(47) = 2.74, p = .009, d = 0.40$ , but no significant differences by CS-type when attending to the distractor across session type,  $t(47)=0.26, p=0.796$  (Figure 2.3f). A main effect of attentional target was also identified [ $F(1,23) = 14.38, p < .001, \eta^2_G = 0.059$ ].

Table 2.5. Study 2 ANOVA results, Right aIns BOLD Activity in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta^2_g$
(Intercept)	1	23	571.33	258.72	50.79	.000	.51
CS	1	23	7.09	58.24	2.80	.108	.01
Target	1	23	34.71	55.54	14.38	.001	.06
Block	1	23	6.68	58.96	2.61	.120	.01
CS x Target	1	23	5.09	29.80	3.93	.060	.01
CS x Block	1	23	1.45	22.42	1.49	.235	.00
Target x Block	1	23	12.91	46.76	6.35	.019	.02
CS x Target x Block	1	23	0.78	20.43	0.88	.357	.00

*Note.*  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta^2_g$  indicates generalized eta-squared.

**PPA, Single Image Conditions.** In the left PPA, attend place alone trials ( $M = 4.93, SD = 3.00$ ) exhibited significantly higher BOLD activity than either attend CS+ ( $M = -1.73, SD =$

1.39),  $t(47) = -13.41$ ,  $p < .001$ ,  $d = 2.85$ , or CS- ( $M = -0.95$ ,  $SD = 1.31$ ),  $t(47) = -12.49$ ,  $p < .001$ ,  $d = 2.54$ , alone trials. BOLD activity while attending to the CS+ alone condition was also bilaterally lower than when attending to the CS- condition,  $t(47) = -3.234$ ,  $p = .002$ ,  $d = 0.58$ .

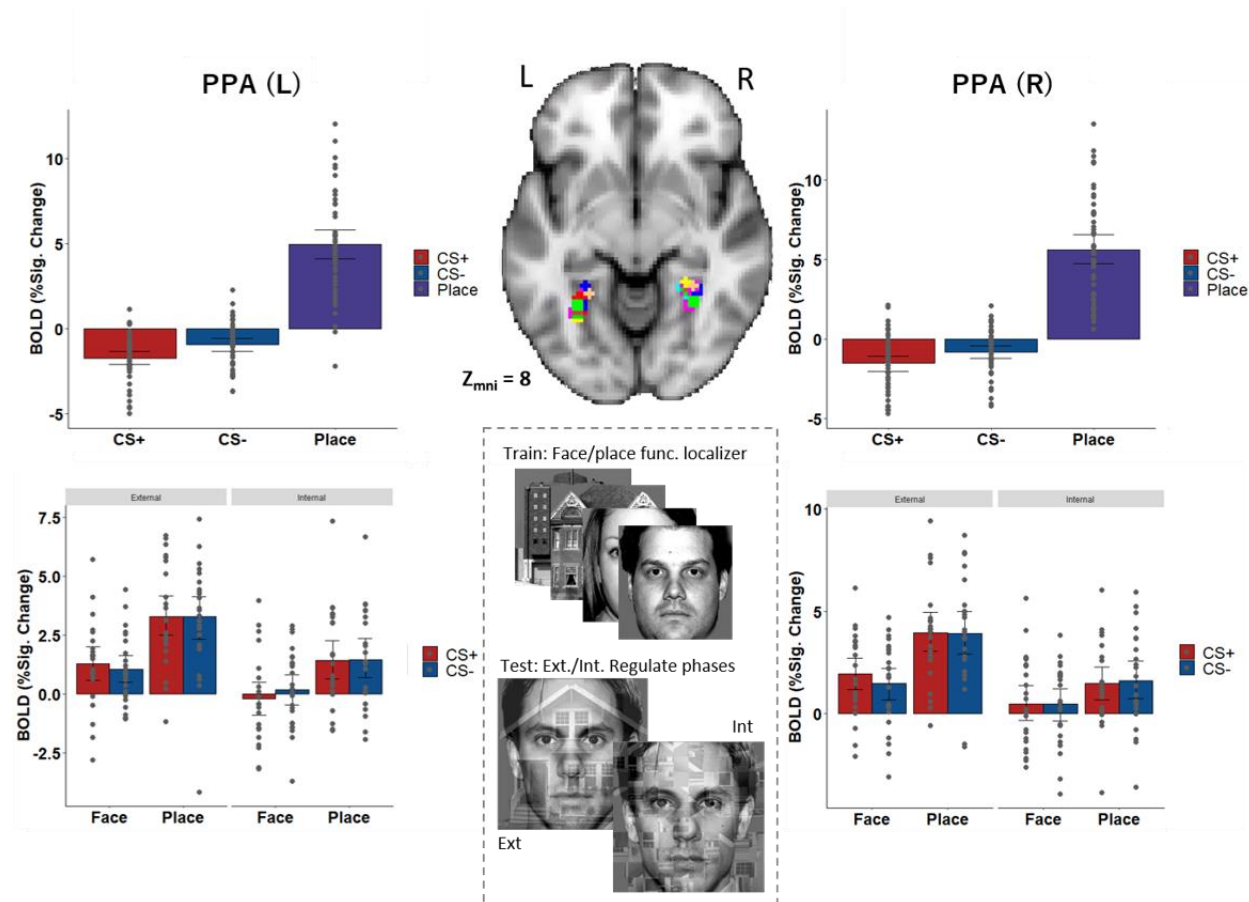


Figure 2.5. Bilateral PPA activity during single image and composite image conditions. a,c) Average peak sphere BOLD during attend CS+, CS- and Place alone conditions. b,d) Average peak sphere BOLD activation in the left insula during each composite attention condition. Participants attending to a place image showed elevated BOLD activity in the PPA while attending to place images in both External and Internal conditions. The FFA did not show differentiation in activity between CS+ and CS- faces.

In the right PPA, attend place alone trials ( $M = 5.61$ ,  $SD = 3.26$ ) exhibited significantly higher activity than either attend CS+ ( $M = -1.52$ ,  $SD = 1.72$ ),  $t(47) = -13.27$ ,  $p < .001$ ,  $d = 2.74$ , or attend CS- ( $M = -0.81$ ,  $SD = 1.47$ ),  $t(47) = -13.69$ ,  $p < .001$ ,  $d = 2.54$ , alone trials. BOLD

activity while attending to the CS+ alone condition was again lower than when attending to the CS- condition,  $t(47) = -2.97, p = .005, d = 0.44$ .

**PPA, Composite Conditions.** PPA activity during composite trials was analyzed using the same 2(CS-type)x2(attentional target)x2(block-type) ANOVA as previous regions. In the left PPA, main effects of attentional target [ $F(1,23) = 33.26, p < .001, \eta_g^2 = 0.18$ ] and block-type [ $F(1,23) = 32.69, p < .001, \eta_g^2 = 0.14$ ] were identified. A planned t-test showed significantly higher levels of BOLD activity during the CS+ Internal attend distractor condition ( $M = 1.43, SD = 2.09$ ) than during the CS+ Internal attend face condition ( $M = -0.20, SD = 1.86$ ),  $t(23) = -3.074, p = .005, d = 0.82$ .

Table 2.6. Study 2 ANOVA results, Left PPA BOLD Activity in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta_g^2$
(Intercept)	1	23	412.53	366.41	25.90	.000	.37
CS	1	23	0.04	30.57	0.03	.857	.00
Target	1	23	153.70	106.28	33.26	.000	.18
Block	1	23	109.99	77.38	32.69	.000	.14
CS x Target	1	23	0.03	18.99	0.04	.851	.00
CS x Block	1	23	1.18	27.71	0.98	.332	.00
Target x Block	1	23	5.38	29.53	4.19	.052	.01
CS x Target x Block	1	23	1.02	41.52	0.56	.460	.00

*Note.*  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta_g^2$  indicates generalized eta-squared.

In the right PPA, an interaction effect of attentional target by block-type was identified [ $F(1,23) = 7.34, p = .012, \eta_g^2 = 0.017$ ] (Figure 2.4b). Main effects of attentional target [ $F(1,23) = 60.92, p < .001, \eta_g^2 = 0.13$ ] and block-type [ $F(1,23) = 40.64, p < .001, \eta_g^2 = 0.15$ ] were also identified. A planned t-test again showed significantly higher levels of BOLD activity during the

CS+ Internal attend distractor condition ( $M = 1.47$ ,  $SD = 2.04$ ) than during the CS+ Internal attend face condition ( $M = 0.47$ ,  $SD = 2.22$ ),  $t(23) = -2.94$ ,  $p = .007$ ,  $d = 0.47$ .

Table 2.7. Study 2 ANOVA results, Right PPA BOLD Activity in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta^2_g$
(Intercept)	1	23	705.17	611.84	26.51	.000	.44
CS	1	23	0.34	35.67	0.22	.644	.00
Target	1	23	131.54	49.66	60.92	.000	.13
Block	1	23	158.13	89.48	40.64	.000	.15
CS x Target	1	23	1.13	22.76	1.14	.297	.00
CS x Block	1	23	1.33	32.49	0.94	.342	.00
Target x Block	1	23	15.95	49.96	7.34	.012	.02
CS x Target x Block	1	23	0.29	21.59	0.31	.586	.00

*Note.*  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta^2_g$  indicates generalized eta-squared.

**Fusiform Face Area.** BOLD activity in the FFA showed greater elevation during the “view face” alone conditions for both CS+ ( $M = 3.96$ ,  $SD = 2.51$ ),  $t(47) = 6.35$ ,  $p < .001$ ,  $d = 0.68$ , and CS- ( $M = 4.08$ ,  $SD = 2.43$ ),  $t(47) = 7.57$ ,  $p < .001$ ,  $d = 0.74$ , when compared to the “view place” alone ( $M = 2.33$ ,  $SD = 2.30$ ) condition. No significant differences were noted between CS+ and CS- “attend face” conditions,  $t(47) = -1.35$ ,  $p = .184$ . In the FFA, the same 2(CS-type)x2(attentional target)x2(block-type) repeated-measures ANOVA revealed an interaction effect of attentional target by block-type [ $F(1,23) = 4.49$ ,  $p = .045$ ,  $\eta^2_g = 0.002$ ]. Paired t-tests revealed that, collapsed across CS-type, BOLD activity was significantly higher when attending to face ( $M = 4.41$ ,  $SD = 2.74$ ) images than place images ( $M = 3.57$ ,  $SD = 2.51$ ) in Internal trials,  $t(47) = 3.46$ ,  $p = .001$ ,  $d = 0.32$ , but not significantly different between face ( $M = 4.87$ ,  $SD = 2.85$ ) and place ( $M = 4.51$ ,  $SD = 2.63$ ) images in External trials,  $t(47) = 1.45$ ,  $p = .153$ .

Main effects were identified for attentional target [ $F(1,23) = 6.80, p = .016, \eta^2_G = 0.012$ ] and block-type [ $F(1,23) = 9.16, p = .006, \eta^2_G = 0.017$ ]

Table 2.8. Study 2 ANOVA results, FFA BOLD Activity in Regulation Phases

Predictor	$df_{Num}$	$df_{Den}$	$SS_{Num}$	$SS_{Den}$	$F$	$p$	$\eta^2_g$
(Intercept)	1	23	3614.80	1086.38	76.53	.000	.73
CS	1	23	0.40	30.21	0.31	.586	.00
Target	1	23	17.08	57.80	6.80	.016	.01
Block	1	23	23.63	59.35	9.16	.006	.02
CS x Target	1	23	1.98	40.55	1.12	.300	.00
CS x Block	1	23	0.66	44.59	0.34	.565	.00
Target x Block	1	23	2.79	14.29	4.49	.045	.00
CS x Target x Block	1	23	0.01	18.91	0.02	.897	.00

*Note.*  $df_{Num}$  indicates degrees of freedom numerator.  $df_{Den}$  indicates degrees of freedom denominator.  $SS_{Num}$  indicates sum of squares numerator.  $SS_{Den}$  indicates sum of squares denominator.  $\eta^2_g$  indicates generalized eta-squared.

## fMRI Results, Whole-brain Univariate Analyses

**Conditioning Effects.** In order to evaluate the persistence of differential fear conditioning throughout the experimental phases of the experiment, a whole-brain univariate analysis compared patterns of activity between “attend” CS+ alone and “attend” CS- alone conditions (Figure 2.2). Greater elevated activity was observed during the CS+ condition compared to the CS- condition in the bilateral anterior Insula, ACC, left Caudate, and bilateral midbrain. Additionally, elevated activity in this contrast was noted in the bilateral central operculum, extending into the parietal operculum. In the CS- > CS+ contrast, regions of greater activity during viewing of the CS- than while viewing the CS+ included the bilateral superior frontal gyrus, dorsomedial precentral gyrus, and left anterior hippocampus.

**Internal Regulation Effects.** A second whole-brain analysis was performed to explore the BOLD activity specific to the External and Internal regulation of the CS+. Individual contrasts defining the effect of distraction as a difference in differences between BOLD values while attending to the distractor (CS+ vs CS-) and BOLD values while attending to the face (CS+ vs CS-) were generated at the first level. A mixed-effects FLAME 1+2 analysis contrasted this effect of distraction between External and Internal blocks.

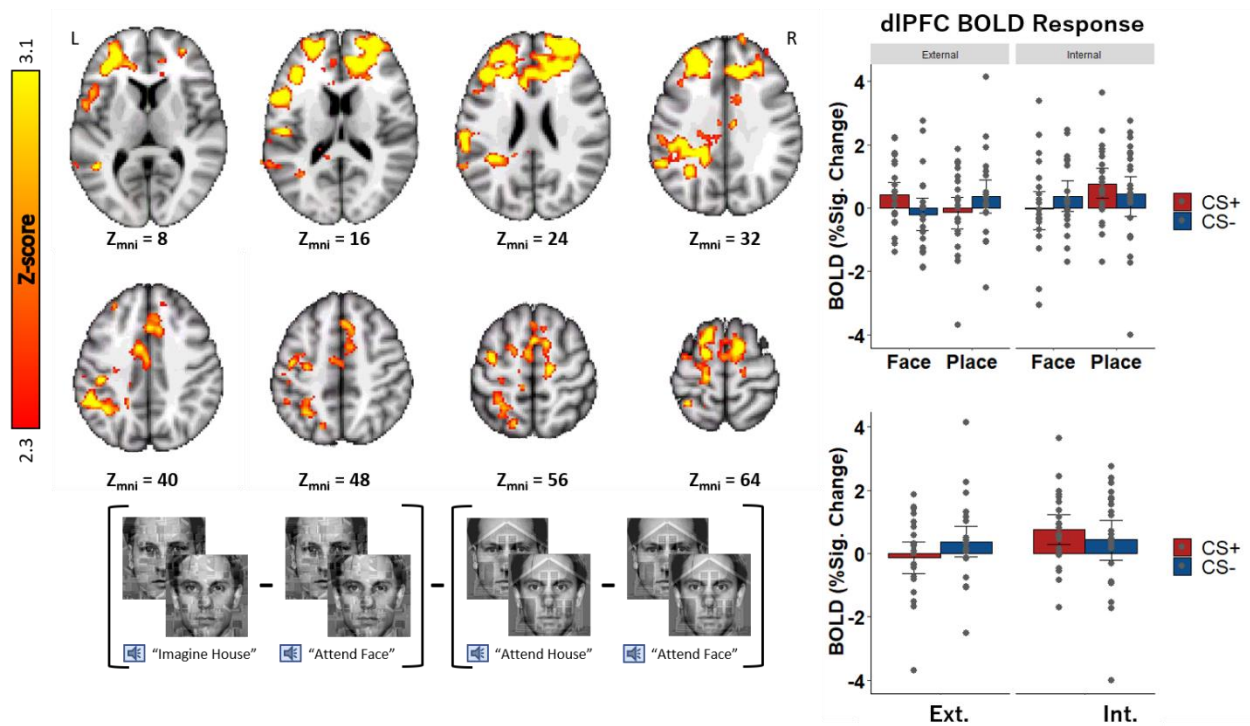


Figure 2.6. BOLD activity of regulation of the CS+ by distraction, Int > Ext. A first-level contrast was created to isolate the effects of distraction on the CS+ face  $x = ((CS_{plusDistract} - CS_{minusDistract}) - (CS_{plusFace} - CS_{minusFace}))$  across trials and then compared at the group level by contrasting the External and Internal blocks ( $Int(x) - Ext(x)$ ). a) BOLD activity in the DIPFC across conditions. A mask for the DIPFC was generated using the univariate interaction analysis and applied to all conditions. Activity in the DIPFC was significantly elevated in the Internal distraction condition. b) DIPFC BOLD activity during distraction tasks only.

Regions of significantly higher activity in the Internal “attend place” > Internal “attend face” contrast over the External contrast were identified (Figure 2.5). These regions indicate a

prefrontal network that includes the bilateral dorsolateral prefrontal cortex, the right anterior cingulate gyrus, and areas of the left inferior frontal gyrus. These results suggest that this network shows significantly greater activity during an Internal Distraction task than during an External Distraction task.

Table 2.9. Internal and External Distraction Effects

#	k	Brain Region	H	Z	MNI		
					<i>x</i>	<i>y</i>	<i>z</i>
<b>Internal Distraction &gt; External Distraction</b>							
1	12699	Middle Frontal Gyrus, Superior and Inferior Frontal Gyrus, Frontal Pole, Orbitofrontal Gyrus, Angular Gyrus, Cingulate Gyrus, Paracingulate Gyrus, Precentral Gyrus, Middle Temporal Gyrus, Superior Parietal Cortex, Supramarginal Gyrus	R/L	4.86	12	42	18
<b>External Distraction &gt; Internal Distraction</b>							
n.s.							

# = the number of a cluster, ordered by size; k = the number of contiguous voxels in the cluster; Brain region = regions of local maxima included in the broader cluster. The region names are taken generally from the Harvard Oxford atlas in FSL; H = principal hemisphere of the cluster, right (R) or left (L); Z = maximum z-value from the cluster within the given brain region; MNI(X,Y,Z) = coordinates of the voxel with the maximum effect in the standardized space of the Montreal Neurological Institute (MNI), represented in units of millimeters (mm).

### fMRI Results, PPA/Insula Correlation Analysis

Calculating differences in BOLD activity between attend face and attend distractor conditions generated a “distraction effect” value for each ROI. Correlational analysis between distraction effect in the PPA and Insula yielded a bilateral correlation between distraction effect in the PPA and distraction effect in the insula in the Internal condition [ $r(24) = 0.43, p = .037$ ]. This relationship was not significant in the external condition.

## DISCUSSION

Across both behavioral and fMRI data, results from this study indicated that both object-based and mental imagery-based distractors effectively down-regulated differentially conditioned fear. The internal distraction task was similarly effective to the external task for reducing the effects of a conditioned fear stimulus. These findings are broadly consistent with the biased-competition model regarding attention and emotion regulation (Bishop, 2008; Blair & Mitchell, 2009). The internal distractor also resulted in significantly elevated activity in regions associated with emotional and cognitive processing (anterior insular cortex and prefrontal cortex respectively). This pattern of activity suggests that while the Internal distractor is as effective as the External distractor in regulating fear, it requires considerably more cognitive resources to deploy than distraction via a visual object-based stimulus.

Our initial hypothesis posited that directing attention to a distractor would result in a reduction in both reported fear response and a corresponding decrease in BOLD activity in the anterior Insula compared to attending to the CS+. Our prior behavioral study (Study 1) supported the theory that fear responses decreased during both distraction tasks, as measured by self-report ratings. Behaviorally, that pattern was supported by the results of this study. Results from the SCR measures showed that the conditioning effect in CS+ vs CS- image alone trials was significant, but this difference was not distinguishable in the composite image trials. This lack of SCR modulation despite downregulation in subjective reports has been noted in previous research using cognitive regulation tasks (Wiemer, Rauner, Stegmann, & Pauli, 2021). Results from the behavioral Likert reports supported the assertion that fear was successfully conditioned in the participant sample, and that both Internal and External distraction tasks reduced fear ratings.



Of particular interest to this study was how these findings were reflected in the fMRI results and whether the theorized mechanism of this effect can be supported by evidence from other regions. Elevated activity from the right anterior insula can be considered indicative of the successfully conditioned emotional response. BOLD activity in attend face conditions matched the conditioned response seen in Likert reports. In both Internal and External distract conditions, insular response did not differentiate between CS+ and CS-. This lack of differentiation can be taken as support for the hypothesis that both forms of distraction effectively moderated the conditioning effect. However, BOLD activity in the anterior insula was significantly elevated in the internal distraction condition, even above that recorded during the CS+ alone condition. It seems likely that there is an additional effect on BOLD activity in the insula during the internal distraction task that is elevating activity independent of the controlled conditioning or distraction effects initially predicted by the study. This does not contradict the support for our hypothesis, as in both conditions, the effect of conditioning was diminished. However, it encourages further investigation into how the mechanisms behind generating mental imagery could produce these effects.

To confirm that participants were performing the imagine-place distractor task, the left and right PPA were identified and masked using BOLD data from the initial habituation scans. Analysis of the PPA revealed elevated activity during attend-place trials in both External and Internal composite conditions. From this, we can infer that the participants were imagining the distractors during the Internal task. While this supports the PPA's involvement in our noted down-regulatory effects, it does not explain the elevated activity noted during the Internal Distraction task. Earlier analyses identified patterns of activation supporting the presence of fear conditioning, but did not draw a direct comparison between internal and external distraction

effects at the whole brain level. Comparison between External and Internal Distraction effects produced a whole-brain analysis indicating differential activity between block types unique to the internal distraction task. Elevated BOLD activity in the dorsolateral and medial prefrontal cortex suggests a higher degree of cognitive processing involved in the internal distraction task. This indicates that the internal distraction task required a greater degree of cognitive resources to produce the same fear reduction effect, offering a potential explanation for the elevated activity noted in the aIn.

That mental imagery-based distraction requires significantly greater cognitive effort raises several questions when comparing our findings to the broader literature on distraction in emotion regulation. Mental imagery-based distraction tasks are not uncommon in regulation paradigms, but little direct comparison exists between object-based and mental imagery-based distractors. This discrepancy was one of the motivations for this study. Given our findings that mental imagery-based distraction was significantly more effortful than object-based distraction, we must consider what this implied for other forms of emotion regulation with mental imagery-based components. An internal distractor task may be effective due to the introduction of new cognitive demand, in addition to the established effects of attentional control. Whether this affects the practical applicability of mental imagery-based distractors as a regulatory technique remains to be seen. Both approaches were equally effective in this study, but existing paradigms may want to consider their stimuli and how their results may be interpreted in this context.

Regarding other emotion regulation techniques, cognitive reappraisal may benefit from closer inspection. Reappraisal models assert that the effectiveness of reappraisal as a regulatory technique is based on its manipulation of the meaning of the target stimulus without redirecting attention from the stimulus itself (McRae et al., 2012). Reappraisal is typically contrasted with

distraction, a technique in which regulatory effects are assumed to be based on intercepting direct engagement with the stimulus. Our results raise two possibilities: first, that this may not be the only mechanism by which a nominally distraction-based task may be effective, and second, that an internally generated distraction task can activate regions of cognitive processing that notably overlap with those found in cognitive reappraisal (Etkin et al., 2015). It seems prudent to address the possibility that some reappraisal paradigms may be relying on the same mechanisms as internal distraction, rather than representing a separate technique.

Cumulatively, our findings support mental imagery-based distraction as an effective technique for regulating conditioned fear, but indicate significant differences in how it is represented in the brain. The engagement of the PPA during both internal and external tasks indicates that both tasks share common mechanisms in visual imagery processing. However, the noted prefrontal activity, as well as the elevated  $\alpha$ 1n response during the internal distraction, suggest that the two approaches should not be considered equivalent. We feel that this calls for additional scrutiny on the design of distraction paradigms, and further investigation into the relationships between internal distraction and other forms of emotion regulation.

## **CHAPTER 3. ASSOCIATIVE STRENGTH AND SUBJECTIVE EXPECTANCY**

Fear is associated both with the conscious experience of feeling afraid and autonomic reactions, such as the skin conductance response (SCR) or heart rate, related to defensive behavior (Beckers, Krypotos, Boddez, Effting, & Kindt, 2013; Lang, Davis, & Öhman, 2000). While some research indicates that these aspects of fear are related (Jiang et al., 2021; Kron, Goldstein, Lee, Gardhouse, & Anderson, 2013), other research indicates that the conscious experience of fear is dissociable from the autonomic response to fearful stimuli (Lang et al., 2000; LeDoux & Pine, 2016).

Pavlovian conditioning is a prevalent procedure used to study fear in humans. This paradigm consists of repeated pairing of an initially neutral conditioned stimulus (CS+) with an aversive unconditioned stimulus (US; e.g., a mild shock). As a result, the presentation of the CS+ alone elicits a conditioned response (CR; e.g., self-reported fear or elevated SCR). Despite its apparent simplicity and extensive study (Lovibond & Shanks, 2002; Mertens & Engelhard, 2020; Sehlmeier et al., 2009), the cognitive and neural processes underlying fear conditioning, and Pavlovian conditioning more generally, are still the topic of much debate (Mertens & Engelhard, 2020; C. J. Mitchell et al., 2009).

One common interpretation is that CRs emerge as a function of the associative strength between a CS and an US (Perruchet, 2015; Rescorla & Solomon, 1967), encoded in the amygdala independent of declarative knowledge of the association (Bechara et al., 1995; Clark, 1998). This associative strength model posits that the magnitude of the CR changes as a function of the CS–US association history. For example, as the number of sequential CS+US (i.e., trials in which the CS and US are both presented) trials increases, the strength of the association increases, and conversely, the strength of the association decreases as the number of sequential

CS trials without the US (i.e., CS-alone) increases. Previous research in both humans and non-human primates indicates that the amygdala reflects the associative strength between the CS and US (Belova, Paton, & Salzman, 2008; Li, Schiller, Schoenbaum, Phelps, & Daw, 2011), as do sensory regions associated with the CS (Greening, Lee, & Mather, 2016; Miskovic & Keil, 2012; Moratti & Keil, 2009; Weinberger, 2004).

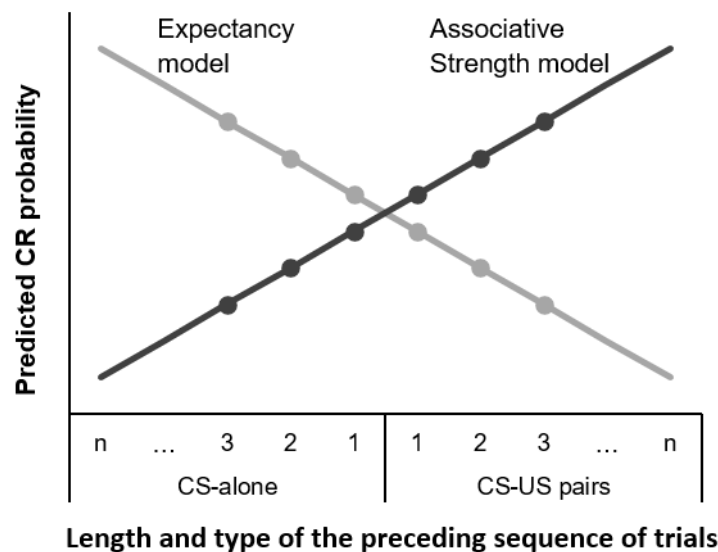


Figure 3.1. Visualization of the predicted self-reported CR probability by length of preceding trial sequence for the Expectancy versus Associative Strength model.

The expectancy model offers an alternative perspective predicting that human fear conditioning is the result of a conscious expectation of the US following the presentation of the CS. According to this model, propositional knowledge of the association is required for the generation of a CR (Boddez et al., 2020; C. J. Mitchell et al., 2009). One example is the so-called gambler's fallacy, in which sequential unreinforced CS+ trials increase participants' expectation of shock despite a fixed reinforcement rate of 50% (Burns & Corpus, 2004). Another example is instructed fear conditioning in which being told the CS–US relationship is sufficient to generate greater activity in the bilateral anterior insula (aIn) and dorsal anterior cingulate (dACC) but not

the amygdala for the CS+ versus CS- in differential conditioning (Mechias et al., 2010). This potentially reflects the role of the aIn and dmPFC in the conscious experience of fear and anxiety (Harrison et al., 2015; Uddin, Nomi, Hébert-Seropian, Ghaziri, & Boucher, 2017). Additionally, human (Kroes et al., 2019) and non-human animal (Shi & Davis, 1999) research suggests these regions are involved in the expression, though not the acquisition, of CRs.

In order to dissociate the predictions of the expectancy model from those of the associative strength model, the present study adopted a single-cue conditioning paradigm (Figure 3.1) combined with a pseudo-randomized trial sequence and a partial reinforcement schedule of 50% (Perruchet, 1985). The experiment comprised sequential CS+US or CS-alone trials of various lengths. This study is the first functional magnetic resonance imaging (fMRI) study to test the hypothesis that while activity supporting associative strength model would manifest in the amygdala and sensory cortices, support for expectancy model would be observed in the aIn and dACC. The identification of dissociable networks contributing to each model would be consistent with contemporary two-system models of fear conditioning (LeDoux & Pine, 2016).

## **METHODS**

### **Participants**

Twenty-three participants were recruited from the Louisiana State University community. All were English speakers and reported normal or corrected-to-normal visual acuity. No participant had neurological or psychiatric antecedents, and none were taking medication known to affect the central nervous system. One participant was excluded because of a technical issue. Data from one additional participant were discarded due to excessive head movements during the fMRI session. The final sample included 21 participants (11 females, mean age = 24.24 years,

$SD = 5.90$ ). This study was approved by the Institutional Review Board of the Louisiana State University. All participants provided written informed consent prior to testing, being fully aware of the nature of the stimuli to be presented. Subjects received a financial compensation of \$45 for their participation.

## **Apparatus**

The experimental paradigm was delivered using Matlab R2016b (Version 9.1; MathWorks, Natick, MA, USA) with the Psychtoolbox extension. Shock stimuli were administered using the STMISOC and STM100C modules of BIOPAC Systems and delivered by means of two MRI-safe electrodes placed on the distal phalanges of the fourth and fifth digits of the non-dominant hand. Participants reported by way of a two-response button box held in their dominant hand.

## **Stimuli**

The single face stimulus used in this study as the CS was a standardized 400x400px greyscale face image from the Cohn-Kanade emotional faces database. The image depicts a white male with neutral emotional affect. The image was cropped to show only the face from hairline to chin against a flat grey background. The US consisted of a mild 50-ms pulsed electric shock at 50Hz (10 pulses with a duration of 5-ms each). Shock intensity was calibrated independently for each participant (see below for details). Face (15 male, 15 female) and place (15 house, 15 building) images used in the functional localizer task following the experimental sessions were drawn from the same standardized image database. All were emotionally neutral 400x400 images in greyscale against flat grey backgrounds. The CS used in the experimental sessions was not included in the localizer set.

## Design

The experimental design was based on the one used by Perruchet (1985) and Moratti and Keil (2009). The main task consisted of three runs (i.e., functional runs in the scanner) of 45 trials per run for a total of 135 trials across all three runs. Half the trials were CS-alone trials in which the US was omitted.

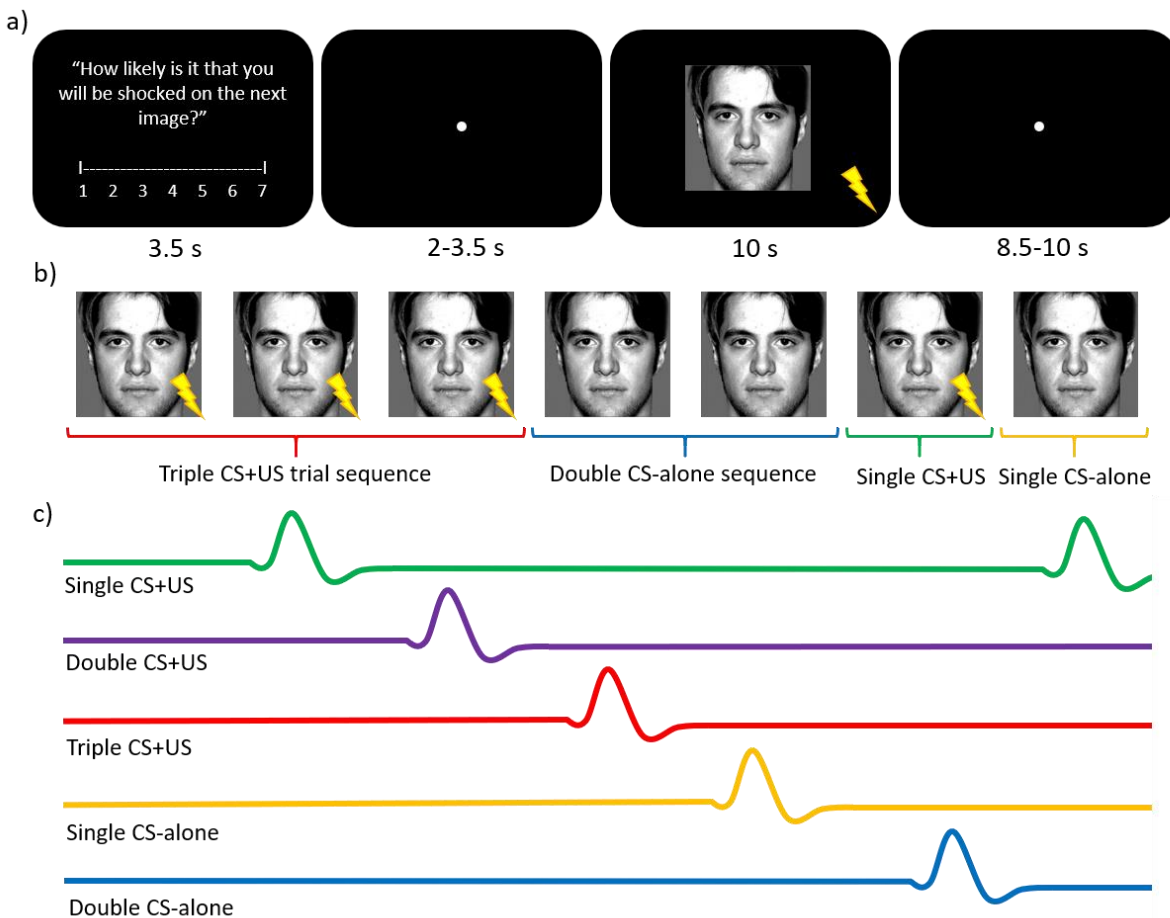


Figure 3.2. Sample trial structure (a) and a visualization of potential CS+US and CS-alone trial sequences. Note, in the trial sequences participants view the whole trial as exemplified above (b). Conditions are labeled and analyzed relative to the preceding trial sequence, including subsequences within longer sets. Peaks in (c) depict hypothetical modeling of BOLD signal by trial in order to separate sequence types, i.e., the trial following two CS+US images is labeled “double CS+US.”

In the other half of the trials (CS-US pairs), the CS co-terminated with the US. In each run, the



45 trials were presented as sequences of one-in-a-row (single), two-in-a-row (double), or three-in-a-row (triple) CS+US trials and as sequences of one-in-a-row (single), two-in-a-row (double), or three-in-a-row (triple) CS-alone trials (Figure 3.2b). The sequences were designed to conform to a binomial distribution of two equally probable events (CS-alone trials and CS+US trials). In a given run, the various sequences were randomly shuffled, following a method adopted from Nicks (1959). Additionally, a CS-alone trial was added at the end of each run to measure expectancy ratings and brain activity related to the last sequence of the run.

## **Procedure**

A graphical representation of the experimental procedure can be found in Figure 3.2a. Each trial began by presenting the Likert response task for 3.5s, followed by a variable ISI of 2s to 3.5s with a fixation dot before presenting the CS image for 10s. Each trial was followed by a variable ITI of 8.5s to 10s with fixation.

Before starting the main task, participants performed eight practice trials. They were instructed to pay attention to the face presented in each trial and to rate their expectancy for shock occurrence during the inter-trial interval. An explanation of the use of the rating device was provided prior to the practice session. Participants used a two-response button box to report their expectancy ratings. When they pressed on the left button, a marker on the screen moved toward the left side of a horizontal scale, and an opposite effect was obtained by pressing on the right button. The rating scale on the screen was divided into seven levels, from “1 = not at all” to “7 = very much so”. When the scale appeared on the screen, the cursor was always pointed at “4”, which meant that the subjective likelihood of receiving a shock on the next trial was 50 percent. The scale remained on the screen for 3.5 seconds (preliminary tests showed this time

was sufficient to properly perform the expectancy rating task). Participants were informed that no shock was delivered in the practice and the purpose was to become familiar with the task.

After the practice, electrodes for electrical stimulations were secured and the shock level was adjusted individually to be “unpleasant but not painful” ( $M_{\text{intensity}} = 5.91$  mA,  $SD = 3.64$ , range: 1.60-20.00 mA; (Grégoire & Greening, 2019, 2020; Murty, LaBar, & Adcock, 2012). Instructions included the information that the presentation of the face was randomly followed by an electrical stimulation on 50 percent of the trials. Timing was consistent between the practice and experimental sessions. Experimental sessions consisted of 45 trials, the final trial in each session being a dummy presentation to allow time for Likert reporting of the previous presentation.

To independently localize face processing in the amygdala, a single functional localizer run was conducted. Standardized sets of 20 neutral face and 20 place images were drawn from the same Kohn-Kanade database as the experimental face stimulus. Images were divided into category-specific blocks made up of rapid event-related trial sequences. Each trial sequence involved the presentation of an image for 0.75s with a 0.25s ISI. Each block was presented five times in alternating order with a 15s ITI between face and place blocks.

## **fMRI Acquisition and Analysis**

### **MRI Acquisition**

BOLD data for the fMRI analysis were acquired using a 3T GE Discovery MR750w research scanner with 36-channel head coil at Pennington Biomedical Research Center. Anatomical imaging acquired prior to functional trials used a 256x256 T1-weighted protocol with 1mm slice thickness at 1.0 x 1.0 in-plane voxel resolution at a 10° flip angle for 176 slices. Functional imaging was performed using a single-shot gradient echo EPI sequence (TR =

2000ms, TE = 20ms, FOV = 22.4cm, flip angle = 90°, bandwidth = 7812.5 Hz/px, echo spacing = .578ms for 38 slices) with an in-plane voxel resolution of 3.0mm x 3.0mm and 3mm slice thickness in interleaved ascending order. Functional trials were 582 volumes in length, while the functional localizer comprised 179 volumes. An initial three-volume set of dummy volumes from each run were excluded from the analysis.

### **Preprocessing and Whole-brain Univariate Analysis**

Analysis of acquired BOLD data was conducted within the FSL software package using the fMRI Expert Analysis Tool (FEAT) version 6.00. Anatomical data were first skull-stripped to isolate the brain from surrounding tissue using FSL's BET module, while functional data underwent motion correction using FSL's motion outliers function to identify and model out framewise displacement greater than 0.9mm. Functional data was then motion corrected using MCFLIRT, slice-time corrected using Fourier-space time-series phase-shifting, smoothed with a Gaussian kernel of FWHM 7mm, and ran through a 100s high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting).

The data were analyzed within the General Linear Model using a multi-level mixed-effects design. The first-level analysis was carried out at the single-subject level and each run was modelled separately. In the first-level analysis trial-by-trial data were model with 6 regressors of interest corresponding to each of our primary experimental conditions: single, double or triple CS+US trials, and single, double, or triple CS-alone trials. Importantly, the modeling of a given trial was based on what type of trial sequence had immediately preceded it (Figure 3.2c). For example, following two CS+US trials, the subsequent trial would be modelled as a double CS+US trial regardless of whether or not it was a CS+US or CS-alone trial itself. Additionally, in a triple CS+US sequence, the second trial in the sequence would be modelled as a single

CS+US trial and the third trial in the sequence would be modelled as a double CS+US trial in the GLM, in reference to the preceding CS+US trials. These contrasts were convolved using a double-gamma hemodynamic response function (HRF) to generate first level condition files from each run that modeled both the conditions of interest and nuisance regressors for motion and the shock stimulus. We included two important nuisance regressors to address the possibility that the US was a potential confound, one for the US delivery (i.e., to model out the impact of the physical shock) and one for US expectancy on non-shock trials (i.e., the same time period when shock would have occurred in a shock trial) to account for any confounding anticipatory US reactivity (Dunsmoor, Bandettini, & Knight, 2008; Wood, Kuykendall, Ver Hoef, & Knight, 2014). We also included regressors of no-interests relating to motion, including the 6 standard and 18 extended motion correction parameters, and motion censoring regressors from the framewise displacement evaluation at preprocessing. Each of the regressors of interest and the regressors relating to the US delivery and US expectancy were convolved using a double-gamma hemodynamic response function (HRF) including a model for the temporal derivative of each. Importantly, two first-level weighted contrasts were also created to weight trials based on the expectancy versus the associative strength models, respectively. To evaluate the regions associated with the expectancy model we assigned the highest weight (5) to triple CS-alone trials and the lowest weight (-5) to triple CS+US trials. The other weights were as follows: double CS-alone (3), double CS+US (-3), single CS-alone (1), and single CS+US (-1). Weighting conditions by +/- two was done to evaluate the presence of a linear effect by ensuring that the weighted difference was equal between adjacent trial types in the contrast model (i.e., a between conditions contrast of [-5 -3 -1 1 3 5]). Inverse weighting was applied to create a second linear weighted analysis that would evaluate the associative strength model, with positive weight

assigned to CS+US trials and negative weights assigned to CS-alone trials. First-level contrasts were then combined in second-level analyses at the single-subject level via fixed-effects analysis and transformed into MNI space. Finally, group-level analysis was performed using FLAME 1+2 mixed effects modeling. We applied a threshold of  $Z > 2.3$  and a (corrected) cluster size probability of  $p = 0.05$  (Worsley, 2001). A second set of univariate analyses contrasted BOLD activity during CS+US versus CS-alone sequences. Level 1 contrasts were generated for triple CS+US vs triple CS-alone, double CS+US vs double CS-alone, and single CS+US vs single CS-alone trials using the same parameters as the trend analyses. These three contrasts were also combined in second level analyses using fixed-effects analysis and analyzed at the group level using FLAME1+2 mixed effects modeling. As in the previous analysis, group level maps were thresholded to  $Z > 2.3$  with a (corrected) cluster size probability of  $p = 0.05$ .

### **Functional Localizer**

Preprocessing of the functional localizer applied the same parameters as used for the experimental sessions. Face and place blocks were modeled in FSL as separate contrasts at the first level before transformation to standard space at the second level. As this was a functional localizer to be used to define a group-specific functional region of interest (ROI) we performed a Fixed-effects group-level analysis of Face versus Place activity. A cluster defining the right amygdala was identified and used to generate a group-level functionally defined ROI. As the amygdala was an *a priori* region of interest with respect to the associative strength model, this was masked and the mask used to perform a small volume correction on the experimental data during a group level FLAME1+2 mixed effects analysis by limiting the search space to voxels responding to the experimental manipulation to those within the functional localizer-defined region.

## RESULTS

### Expectancy ratings

A repeated-measures analysis of variance (ANOVA) on expectancy ratings performed with trial sequence (6 levels) as a within-subject variable revealed a significant main effect of trial sequence [ $F(5, 100) = 57.98, p < 0.001, \eta_p^2 = 0.744$ ]. A significant linear trend was also identified, indicating that expectancy ratings decreased linearly with sequential shock [ $F(1, 20) = 71.88, p < 0.001, \eta_p^2 = 0.782$ ] (Figure 3.3).

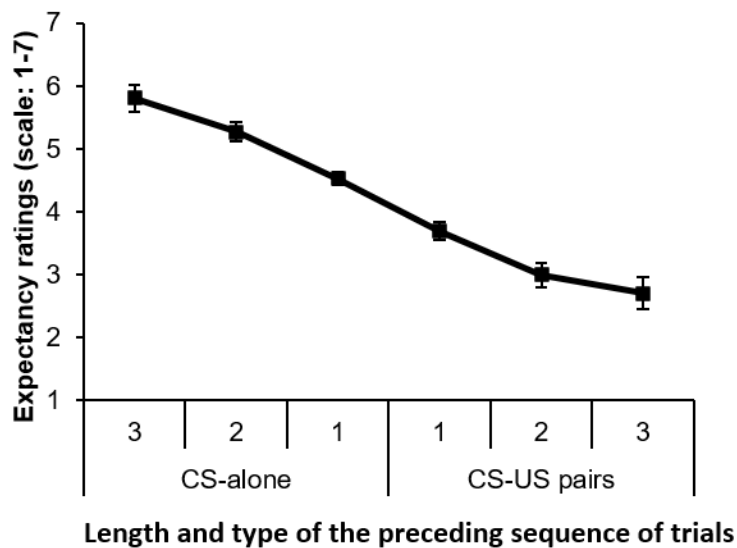


Figure 3.3. Self-reported expectancy ratings by preceding trial sequence. Error bars represent standard error of the mean.

### fMRI Univariate Results

(The unthresholded whole-brain maps used in these analyses can be found at <https://neurovault.org/collections/WMDOLFVB/>).

#### Associative Strength model

Patterns of BOLD activation from the mixed-effects Flame 1+2 analyses show a network

of regions responding to associative strength (Figure 3.4, Blue; Table 1). The contrast derived from the associative strength trend revealed significant activity in a network that includes the right lateral occipital cortex, right angular gyrus, as well as anterior-dorsal regions of the prefrontal cortex including bilateral superior and middle frontal gyri, and frontal pole. The ROI analysis using the functional localizer-derived amygdala mask revealed a significant cluster in the right amygdala consistent with the associative strength model (Figure 3.5).

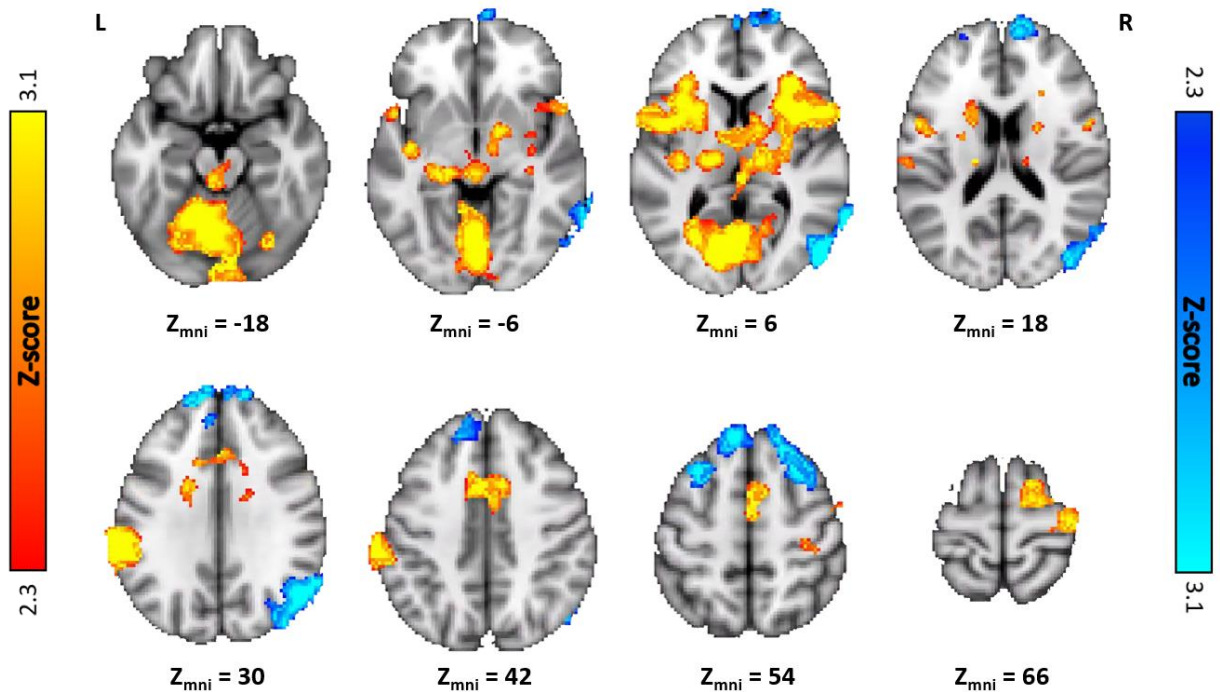


Figure 3.4. BOLD activity identified in the whole-brain corrected expectancy (orange) and associative strength (blue) trend analyses. Activity indicates results from CS-alone > CS+US (Expectancy) and CS+US > CA-alone (Associative Strength) weighted linear contrasts.

### Expectancy model

The expectancy trend analysis shows a second network of regions responding consistent with the expectancy model (Figure 3.4, Orange; Table 1). Longer sets of sequential CS-alone trials were followed by elevated activity in the bilateral aIn (Figure 3.5). Also identified were

regions of the dorsomedial prefrontal cortex that included the superior frontal gyrus, and the dorsal anterior cingulate cortex.

### **Contrasts of CS-alone and CS+US**

To further clarify the neural regions associated with sequences of CS-alone versus the CS+US an additional set of exploratory univariate whole-brain analyses were conducted.

**CS+US > CS-alone.** The single CS+US > single CS-alone contrast showed a wide network of elevated activity in the bilateral amygdala, hippocampus, medial prefrontal cortex, and frontal pole, as well as distributed regions in the intracalcarine, lateral occipital, and middle temporal cortices, and lingual gyrus, and posterior insula. (Figure 3.6, yellow).

The double CS+US > double CS-alone contrast showed a cluster of activity in the middle temporal and lateral occipital cortices (Figure 3.6, blue). The triple CS+US > triple CS-alone identified a dorsomedial prefrontal cluster extending into the superior frontal gyrus and frontal pole (Figure 3.6, green) similar to regions found in the single sequence contrast.

**CS-alone > CS+US.** Single CS-alone > single CS+US conditions showed no clusters of significantly elevated activity. In the double CS-alone > double CS+US trials we observed elevated activation in the intracalcarine cortex, lingual gyrus, and occipital pole (Figure 3.7, Blue).

In the triple CS-alone > triple CS+US contrast, significantly elevated activity was found in a number of regions, including the bilateral anterior insula (Figure 3.7, Green). This suggests higher activity in regions associated with subjective threat appraisal following CS-alone trials than was present following CS+US trials. Significant activity was also noted in the inferior and superior frontal gyrus, left hippocampus, and cingulate gyrus. Similar to the double trial contrast, the intracalcarine cortex, lingual gyrus, and thalamus were significantly active.



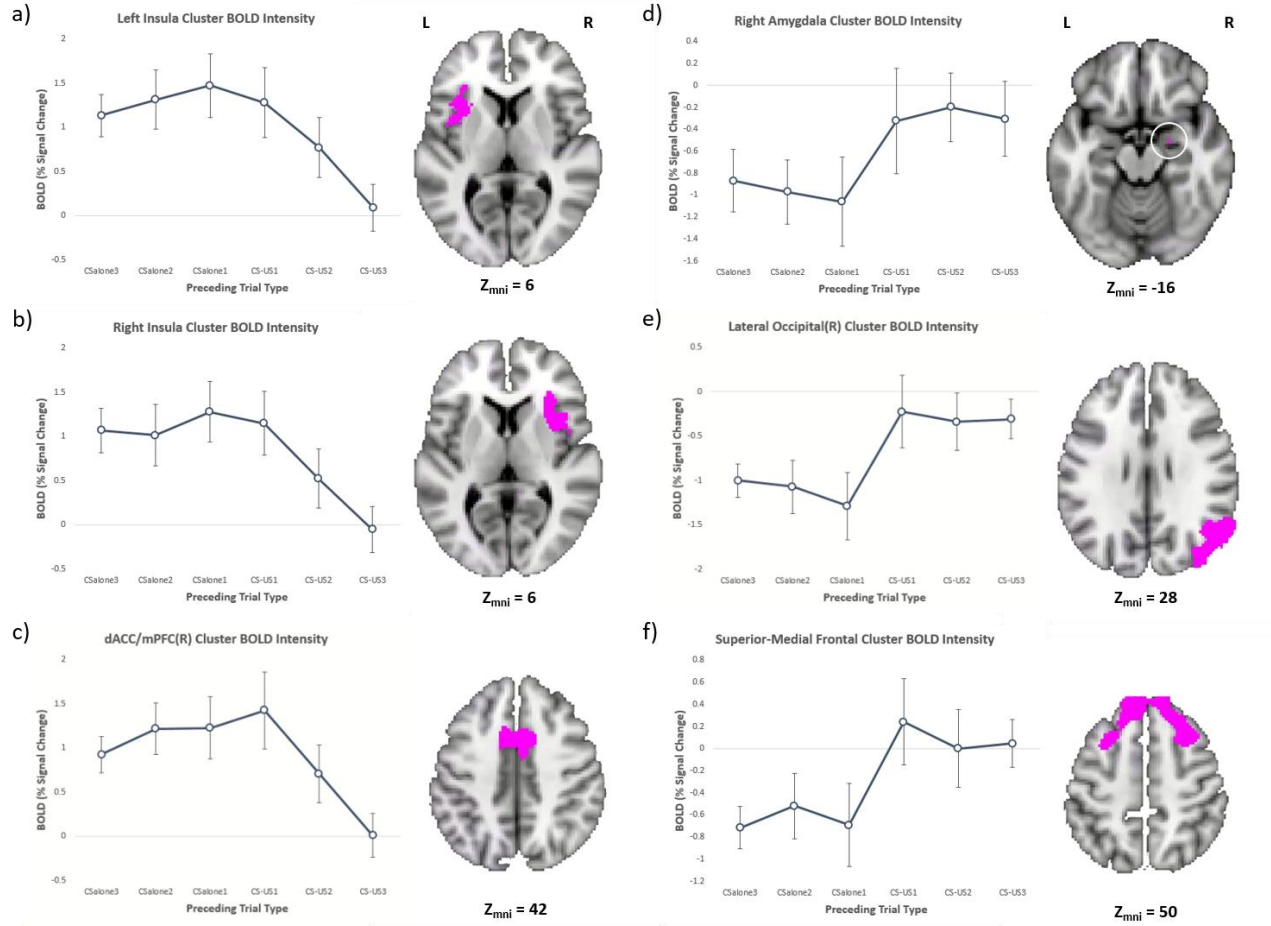


Figure 3.5. Graphical visualization of BOLD activity in notable regions from the trend analyses. Displayed regions were derived from expectancy (left anterior insula (a), right anterior insula (b), right dACC/mPFC (c)) and associative strength (right amygdala (d), right lateral occipital cortex (e), and superior-medial frontal cluster (f)) analyses respectively. For display purposes only, the left (a) and right (b) insula clusters are the result of thresholding the whole brain image at  $Z > 3.0$  and masking with the Harvard-Oxford Cortical Structural Atlas insula masks to isolate insula-related activity from a much larger cluster spanning several distinct brain regions. Error bars represent standard error of the mean.

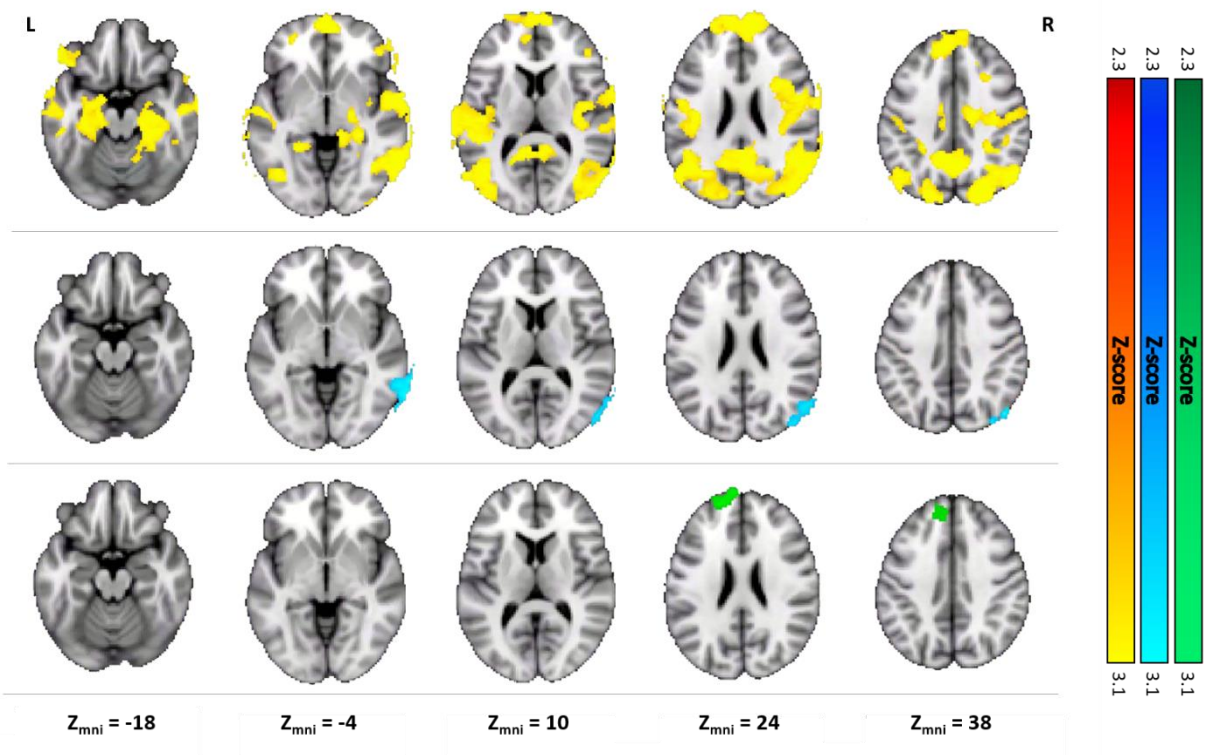


Figure 3.6. BOLD activity identified in whole-brain corrected CS+US > CS-alone contrasts. Yellow clusters represent single CS+US > single CS-alone results. Blue clusters represent double CS+US > double CS-alone results. Green clusters represent triple CS+US > triple CS-alone results.

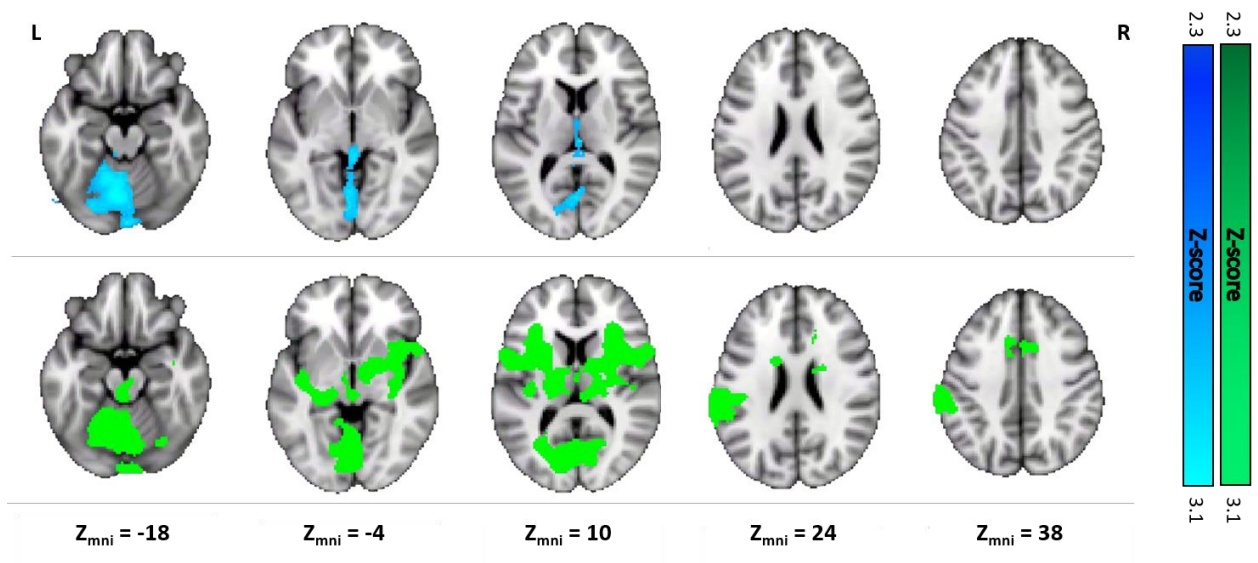


Figure 3.7. BOLD activity identified whole-brain corrected CS-alone > CS+US contrasts. Blue clusters represent double CS-alone > double CS+US results. Green clusters represent triple CS-alone > triple CS+US results.

Table 3.1. Associative Strength and Expectancy network BOLD clusters

#	k	Brain Region	H	Z	MNI		
					<i>x</i>	<i>y</i>	<i>z</i>
Associative Strength Trend							
1	2548	Inferior & Superior Lateral Occipital Cortex, Angular Gyrus, Middle Temporal Gyrus	R	4.44	54	-78	6
2	1914	Frontal Pole, Middle & Superior Frontal Gyrus, Paracingulate Gyrus (L)	R/L	3.8	-8	42	50
3	1335	Frontal Pole	R/L	3.59	10	68	20
Expectancy Trend							
1	16947	Insula, Operculum, Inferior Frontal Gyrus, Precentral Gyrus, Intracalcarine Cortex, Lingual Gyrus, Occipital Pole, Putamen, Thalamus, Brain Stem	R/L	4.59	2	-92	-20
2	2712	Anterior Cingulate Gyrus, Supplementary Motor Cortex, Postcentral Gyrus (R), Precentral Gyrus (R), Superior Frontal Gyrus (R)	R/L	4.04	28	0	72
3	1386	Supramarginal Gyrus	L	4.34	-68	-30	30

# = the number of a cluster, ordered by size; k = the number of contiguous voxels in the cluster; Brain region = regions of local maxima included in the broader cluster. The region names are taken generally from the Harvard Oxford atlas in FSL; H = principal hemisphere of the cluster, right (R) or left (L); Z = maximum z-value from the cluster within the given brain region; MNI(X,Y,Z) = coordinates of the voxel with the maximum effect in the standardized space of the Montreal Neurological Institute (MNI), represented in units of millimeters (mm).

Table 3.2. CS-alone &gt; US+US and CS+US&gt; CS-alone BOLD clusters

#	k	Brain Region	H	Z	MNI		
					x	y	z
<b>Single CS+US &gt; Single CS Alone</b>							
1	48314	Amygdala, Middle & Superior Frontal Gyrus, Frontal Pole, Posterior Insula, Operculum, Intracalcarine Cortex, Lingual Gyrus, Posterior Cingulate Gyrus, Paracingulate Gyrus, Cuneal Cortex, Hippocampus, Inferior & Superior Lateral Occipital Cortex, Occipital Pole, Angular Gyrus, Superior & Middle Temporal Gyrus, Precentral Gyrus, Postcentral Gyrus, Putamen, Thalamus, Brain Stem	R/L	4.4	10	62	20
<b>Double CS+US &gt; Double CS Alone</b>							
1	1437	Inferior & Middle Temporal Gyrus, Inferior & Superior Lateral Occipital Cortex	R	3.57	70	-56	-6
<b>Triple CS+US &gt; Triple CS Alone</b>							
1	1410	Frontal Pole, Superior frontal Gyrus, Middle Frontal Gyrus (R), Paracingulate Gyrus (L)	R/L	3.51	-16	58	26
<b>Single CS Alone &gt; Single CS+US</b>							
n.s.							
<b>Double CS Alone &gt; Double CS+US</b>							
1	5047	Intracalcarine Cortex, Lingual Gyrus, Occipital Pole, Thalamus, Brain Stem	R/L	4.01	2	-90	-18
<b>Triple CS Alone &gt; Triple CS+US</b>							
1	15846	Anterior Insula, Operculum, Inferior Frontal Gyrus, Precentral Gyrus, Intracalcarine Cortex, Lingual Gyrus, Occipital Fusiform Gyrus, Hippocampus (L), Posterior Cingulate Cortex, Putamen, Thalamus, Brain Stem	R/L	4.28	-58	10	8
2	2372	Superior Frontal Gyrus, Superior Parietal Cortex, Precentral Gyrus, Postcentral Gyrus, Posterior Cingulate Gyrus	R	3.79	18	-8	82
3	1551	Operculum, Postcentral Gyrus, Anterior & Posterior Supramarginal Gyrus	L	4.22	-66	-30	30
4	1178	Anterior Cingulate Gyrus, Paracingulate Gyrus, Precentral Gyrus (R)	R/L	3.77	6	6	46

# = the number of a cluster, ordered by size; k = the number of contiguous voxels in the cluster; Brain region = regions of local maxima included in the broader cluster. The region names are taken generally from the Harvard Oxford atlas in FSL; H = principal hemisphere of the cluster, right (R) or left (L); Z = maximum z-value from the cluster within the given brain region; MNI(X,Y,Z) = coordinates of the voxel with the maximum effect in the standardized space of the Montreal Neurological Institute (MNI), represented in units of millimeters (mm).

## DISCUSSION

This study tested the prediction that there are dissociable brain networks reflecting the associative strength model and the expectancy model of Pavlovian fear conditioning, consistent with two-systems theories of threat and fear reactivity. We observed that trial-by-trial self-reported expectancy trended negatively with repeated CS+US pairings consistent with the expectancy model prediction. Neurologically, we observed a significant linear effect in the right amygdala and lateral occipital cortex as the number of sequential CS+US trials increased consistent with the associative strength model, and a significant linear increase in aIn and dACC activity as the number of sequential CS-alone trials increased consistent with the expectancy model. More broadly, we found two dissociable networks, one related to the associative strength model and the other to the expectancy model. Our findings are consistent with a two-systems model of fear processing, though regions implicated in each of the systems differ somewhat from those proposed by LeDoux and Pine (2016).

Self-reported expectancy ratings in this study were consistent with the expectancy model. We observed a significant linear effect such that participants' expectation of receiving shock increased with the number of sequential CS-alone trials and decreased with the number of sequential CS+US trials. This is consistent with previous research using similar paradigms (Moratti and Keil, 2009; Perruchet, 1985), as well as the gambler's fallacy (Burns and Corpus, 2004). Our findings were distinct from several studies using the Perruchet paradigm (Perruchet, 2015) which have reported that CRs parallel associative strength when measuring somatic (Weidemann, Broderick, Lovibond, & Mitchell, 2012) and autonomic (Perruchet et al., 2016) CRs, as well as in cued reaction time tasks (Perruchet, Cleeremans, & Destrebecqz, 2006).

The linear fMRI contrast revealed several regions significantly associated with the associative strength model. First, the whole-brain analysis revealed elevated activity in the right lateral occipital cortex and bilateral superior and middle frontal gyri. Involvement of the lateral occipital cortex is consistent with face stimuli activating the right occipital face area (Grill-Spector, Kourtzi, & Kanwisher, 2001), as well as evidence that sensory cortices associated with the CS increase in activity following associative learning (Greening et al., 2016; Miskovic & Keil, 2012; Moratti & Keil, 2009; Weinberger, 2004). While activity in the middle and superior frontal gyrus was not predicted, the bilateral activity observed in these regions extends posteriorly into the premotor cortex and frontal eye fields (Kastner et al., 2007). These regions are consistent with previous behavioral research in humans demonstrating that reaction times and eyeblinks mirror the associative strength model (Perruchet 2015), as well as research with non-human primates demonstrating that reward-related associative learning affects activity in dorsal fronto-parietal areas associated with eye movements (Schultz & Dickinson, 2000). Our small volume analysis of the amygdala also revealed a significant linear relationship consistent with the associative strength model. This is in keeping with research suggesting that the amygdala adapts on a trial-by-trial basis to the strength of the association between the CS and US (Belova et al., 2008; Li et al., 2011). The separate contrast of the single sequences only (CS+US > CS-alone) demonstrated that the bilateral amygdala was robustly active following the first CS+US pairing (Figure 3.5). Together, the results of the present study are consistent with the amygdala's role in the rapid detection of fear-relevant stimuli, the prioritization of attention, and the priming of defensive behaviors (Holland & Gallagher, 1999; LeDoux & Pine, 2016; Roesch, Calu, Esber, & Schoenbaum, 2010).

Regarding the early visual cortex, we observed medial visual regions associated with expectancy. This is distinct from Moratti and Keil (2009) in which visual cortex activity appeared to reflect the associative strength theory. Two potential factors may have contributed to this difference. First, the properties of the stimulus chosen as the CS may have influenced where the impact of associative strength occurred. Moratti and Keil (2009) used a basic visual grating (i.e., a 45-degree contrast grating) as their CS. This low-level stimulus-type is primarily processed in the primary visual cortex, which has been shown to respond to a low-level visual stimulus undergoing fear conditioning (McTeague, Gruss, & Keil, 2015; Padmala & Pessoa, 2008). Conversely, we used a human face image. Faces are preferentially processed in a more holistic manner later in the ventral visual stream, primarily in the right lateral occipital cortex and right fusiform cortex (Grill-Spector et al., 2001). Consistent with this, in the present study we observed that the right lateral occipital cortex responded according to the associative strength theory, increasing in activity as the number of sequential CS+US trials increased. Secondly, our stimulus is distinct from Moratti and Keil (2009) in terms of biological relevance to fear or threat (i.e., fear-relevant stimuli). Fear-relevant stimuli such as faces (or snakes and spiders) have been found to fear condition more readily and extinguish more slowly compared either fear-irrelevant stimuli such as flowers, mushrooms, or artifactual images (Atlas & Phelps, 2018; Mineka & Öhman, 2002). However, findings regarding the relationship between fear-relevant stimuli and rates of conditioning and extinction are mixed (Åhs et al., 2018).

We observed a wide network of regions displaying a linear relationship consistent with the expectancy model. Most notably, activity in the bilateral aIn and bilateral dACC, as well as aspects of the dorsomedial prefrontal cortex (dmPFC), trended positively with expectancy. Both regions have been observed in studies of instructed fear conditioning in which the CS+ is never

physical paired with the US (Mechias et al., 2010), suggesting that both regions contribute to the conscious expectation of an aversive US. However, Mechias et al. (2010) and a more recent meta-analysis (M. A. Fullana et al., 2016; Miquel A. Fullana et al., 2018) of fear conditioning have observed aIn and dACC involvement in differential fear conditioning. Most studies included in these meta-analyses used partial reinforcement schedules in which the potential contributions of expectancy versus associative strength are not isolated from one another. Nevertheless, partial reinforcement schedules generally elevate uncertainty regarding when the US will occur, which has been associated with aIn and dACC/dmPFC activity (Morris, Gell, & van Reekum, 2019). Similarly, anxious anticipation of potential threat in fear conditioning is also associated with increased activity in the aIn and dACC/dmPFC (Harrison et al., 2015). Another potential explanation is that this network reflects interoceptive awareness of one's fear state as a component of subjective appraisal (Critchley, Wiens, Rotshtein, Öhman, & Dolan, 2004). Consistent with the role of aIn in interception, we observed significant activity in aspects of the brainstem and diencephalon potentially associated with autonomic arousal. Additionally, brain lesion research involving fear conditioning has found that the aIn and dACC/dmPFC are not required for the acquisition of fear conditioning, though they are necessary for the expression (Shi & Davis, 1999) or conscious modulation of fear (Kroes et al., 2019). More generally, aIn lesions have been associated with alexithymia in humans, a condition in which one has difficulty subjectively experiencing emotional state (Hogeveen, Bird, Chau, Krueger, & Grafman, 2016). Together, our results and the previous findings are consistent with aIn and dACC participation in a network involved in conscious appraisal of threat.

Rather than supporting either associative strength or expectancy models, our results are most consistent with two-systems models of fear such as that proposed by LeDoux and Pine



(2016). LeDoux and Pine differentiate changes induced by associative learning from those related to the conscious state of fear and anxiety. This two-system view poses that both systems can be active simultaneously but targeted separately for analysis or intervention. The associative strength network we identified is conceptually similar to the proposed “defensive responding” circuit, while our expectancy network can be considered a component of “feeling states” relevant to fear. Although distinct, it remains unlikely that these networks operate in isolation. The anterior insula’s involvement in associative learning under uncertainty noted by Morriss et al. (2019) was accompanied by elevated activity in the amygdala. Moreover, research in the emotion regulation literature has found evidence that the insula can exert a down-regulatory influence on the amygdala (Nicholson et al., 2017). Together, these studies indicate the possibility of integration between the amygdala and insula during appraisal.

Cumulatively, the results from this study support the presence of two dissociable networks reflecting the associative strength between a CS and a US versus the expectancy of receiving a US given the presence of a CS. This begins to reconcile some of the competing findings in the literature, though it also points to the need for future research to better understand the contributions of associative strength versus expectancy in behavioral, physiological, and subjective aspects of fear. For example, future research could evaluate whether the presence of a safe conditioned stimulus (i.e., CS-) and use of differential conditioning affects associative strength, as single cue conditioning may be more automatically acquired (Carter, Hofstotter, Tsuchiya, & Koch, 2003). Moreover, future research is required to determine under which conditions the networks identified in this study compete or cooperate, as it not possible to determine with the current paradigm. While self-report findings in the present study reflected the expectancy theory, future research could benefit from the inclusion of behavioral or peripheral

physiological measures, which should reflect the associative strength model (Perruchet et al., 2006, 2016).

## SUMMARY AND CONCLUSIONS

The primary objective of this investigation was to assess the effectiveness of mental imagery in regulating differentially conditioned fear. We hypothesized that using mental imagery to distract oneself from the conditioned stimulus would downregulate fear response. Results from Study 1 demonstrated that mental imagery functioned as an effective target for distraction, with similar effectiveness to an object-based distracter in terms of self-reported fear. These findings were further supported by study 2, in which both self-report and BOLD activity in the anterior insula were reduced while attending to either the mental imagery-based distracter or the object-based distracter, again with comparable effectiveness. Our results were consistent with the biased-competition model's prediction that top-down attentional control can modulate representation of a fearful stimulus in the brain.

Study 2 also examined the neural correlates of mental imagery-based distraction, identifying modulation in the anterior insula related to the downregulation of conditioned fear. This is consistent with previous research demonstrating involvement of the aIn in emotional appraisal and subjective fear (Buhle et al., 2014; Delgado et al., 2008; Fullana et al., 2016). However, this investigation did not identify amygdala modulation by distraction in Study 2, despite showing elevated amygdala activity in response to the CS+. This is again consistent with prior studies noting a lack of amygdala response in some forms of emotion regulation (Fullana et al., 2016), despite the amygdala's common inclusion in fear networks. This examination of the roles played by the aIn and amygdala in subjective and associative fear was continued in Study 3, in which both the aIn and amygdala were identified as components in dissociable networks relating to expectation and associative strength respectively.

Additionally, self-reported difficulty results from Study 1 and Study 2 revealed that mental-imagery was significantly more difficult than the object-based distraction. Study 2 examined this contrast in the brain and identified regions of the prefrontal cortex in which activity was elevated during the mental imagery task. This supported the implication from Study 1 that distraction via mental imagery requires greater cognitive resources than object-based distraction. Greater engagement of cognitive processing does not contradict the assumption of biased-competition for visual processing, but may raise questions regarding how mental imagery interacts with other cognitive elements in emotion regulation paradigms.

### **REGULATION OF CONDITIONED FEAR**

Our findings confirmed that differential fear conditioning can be regulated via attentional effects, however, there were notable differences between the regions of interest described in the literature and those identified by our results. Namely, response in the amygdala was considerably less robust than predicted. The absence of significant amygdala modulation in Study 2 and presence of significant, but less robust modulation of the amygdala than predicted in Study 3 suggests that both object-based and mental imagery-based distraction may have a weaker influence on differentially conditioned amygdala reactivity than reactivity to inherently fearful stimuli. Additionally, the aIn downregulation identified in Study 2, paired with the robust aIn involvement in the expectancy trend in Study 3, suggests that the effects of differential conditioning in the aIn are more strongly modulated by distraction than in the amygdala. These findings allow us to infer that associative fear response, while induced by fear conditioning, was only weakly regulated by mental imagery-based and object-based distraction. Subjective fear appraisal, however, reacted strongly to both distraction paradigms. That these two components of

fear processing were dissociable in Study 3 supports the theory that the two can be affected to different degrees.

While the amygdala was identified as part of the associative strength network, amygdala activity was most strongly elevated following initial shock trials in a sequence and did not greatly increase for following sequential trials. This suggests that while associative strength increases with sequential shock pairings, the strongest influence is induced by the first shock trial following an absence of shock. The aIn, in contrast, demonstrated a robust positive trend following subsequent no-shock trials in a sequence. To further explore these trends, we propose expanding the current paradigm of Study 3 to include longer sequences of shock and no-shock trials. This would help clarify whether the described trends continue linearly or exhibit non-linear effects in longer sequences. In the case of the associative strength results, diminishing returns seem likely with subsequent shock pairings. Study 3 again reinforced that associative fear and subjective expectancy, while related, can be influenced separately.

A regulatory disconnect between affective strength and subjective appraisal may also help explain the SCR findings from Studies 1 and 2. While self-report identified a clear regulatory effect on subjective fear, SCR consistently lacked this robust downregulation. Elevated SCR in the presence of the CS+ face confirmed the establishment of differential fear conditioning, but neither the external nor the internal regulation significantly reduced SCR. This suggests that our distraction paradigm did not regulate autonomic response despite apparent regulation of subjective fear. Disassociating these components is not a typical goal in fear regulation research. However, this is consistent with recent research on the specific regulation of differentially conditioned fear (Wiemer et al., 2021). The distinct expectancy and associative strength networks identified in Study 3 support the assertion that subjective and associative fear

are dissociable. Comparing these results to literature using affective images suggests that differentially conditioned fear responds differently to regulation by distraction than inherently fearful images. Further research will be necessary to compare fear elicitors under this regulation paradigm.

## **CONCLUSIONS**

While our primary hypothesis that mental imagery could effectively regulate fear response was supported, differentiating the effectiveness of mental imagery-based distraction from object-based distraction was not possible using self-reported fear, SCR, or BOLD intensity. However, the considerably higher difficulty of mental imagery-based distraction revealed by self-reported difficulty and BOLD measures in the prefrontal cortex makes it necessary to qualifying this effectiveness. Both techniques resulted in comparable downregulation of subjective fear, but the greater difficulty required by the internal task suggests that, given equal effort, mental imagery-based distraction may be less effective than object-based distraction. In our paradigm, sufficient cognitive resources were available to perform either task. Were these tasks to be performed in tandem with a task that requires considerable cognitive effort, it is possible that the internal task would underperform due to this occupation of necessary resources.

Emotion regulation research notes that some regulation tactics perform better in high or low affective intensities, rather than being equally effective across stimuli. In particular, reappraisal-based regulation is less effective under high intensity negative stimuli, while distraction is more effective at high intensity. Notably, the prefrontal activity in the mental imagery-based distraction task identified in Study 2 is similar to that found in fMRI studies of reappraisal (Buhle et al., 2014; Ochsner, Silvers, & Buhle, 2012), particularly the involvement of

the dlPFC and mPFC. If the difference in effectiveness between reappraisal and general distraction is due to higher cognitive demand, then this difference should apply to between mental imagery-based and object-based distraction as well. To address this possibility, future paradigms could consider comparing high and low intensity stimuli using differential fear conditioning. Including a low and a high intensity shock stimulus, paired to separate conditioned stimuli, could be explored to produce stimuli with higher and lower fear response respectively. Replicating the paradigms used in Study 1 and 2 using multiple fear stimulus intensities could reveal whether object-based and mental imagery-based distraction regulate their effects with different degrees of success.

In both distraction and other regulation tactics, elements of mental imagery may be contributing more significantly to task efficacy than previously predicted. As noted, the dlPFC regions revealed in the internal task by Study 2 and mPFC activity identified by both Study 2 and Study 3 have similarities to prefrontal regions identified in reappraisal literature (Buhle et al., 2014; Ochsner et al., 2012). Reappraisal is assumed to downregulate fear via different mechanisms than distraction (i.e. by changing meaning while maintaining attention, rather than redirecting attention). However, many reappraisal paradigms include components of mental imagery. Consequently, reappraisal techniques may themselves rely on mental imagery components to a greater degree than assumed. Examining both this relationship and differences in mental imagery effectiveness by condition will help determine which tactics are more effective in a given situation. Understanding effectiveness by situation is necessary for targeting regulation in therapy and clinical settings, as well as for day-to-day management of emotion.

To our knowledge, this investigation is the first direct demonstration of mental imagery as an attentional target for regulating differentially conditioned fear. Prior research has shown the

effectiveness of visual distraction in regulating inherently fearful stimuli (Kanske et al., 2011; McRae et al., 2010; Scheibe et al., 2015; Strauss et al., 2016), and many cognitive emotion regulation tasks include mental imagery components. However, this investigation appears to be the first to explicitly target mental imagery and conditioned fear response. Additionally, the distraction regulation applied in Study 1 and Study 2 uses a novel visual distraction design targeting object-based and mental imagery-based distraction separately, unlike many existing paradigms that mix elements of visual and mental distraction (Kanske et al., 2011; McRae et al., 2012). Finally, while the paradigm used in Study 3 was created by Perruchet et al. (2016), this investigation was the first to examine the neural correlates resulting from this design. Cumulatively, these results introduce several novel contributions to the field. Our findings should encourage existing studies to consider how mental imagery plays a part in their existing paradigms, and how evidence of dissociable subjective and associative components of fear can influence future designs.



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## **VITA**

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