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Mental Imagery in Fear Extinction: A Multi-Component Examination Based on Behavioral, Physiological, and Neurological Measures

Xinrui Jiang

MENTAL IMAGERY IN FEAR EXTINCTION: A MULTI-COMPONENT EXAMINATION BASED ON BEHAVIORAL, PHYSIOLOGICAL, AND NEUROLOGICAL MEASURES.

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by
Xinrui Jiang
M.A., Louisiana State University, 2017
B.S., Colorado State University, 2014
B.S., East China Normal University, 2014
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Abstract

Imagery has long been utilized in clinical treatments of affective symptoms with the assumption that mental imagery can stand in for its perceptual counterpart and exert regulatory effects over emotional responses. While this assumption has its ground in theoretical framework of mental imagery supported by evidence of neurological overlaps between imagery and perception, and clinical applications of imagery interventions were found to be successful, very little has been done through means of experimental examinations.

This investigation began with a differential fear conditioning study (study 1) to simulate and assess imagery extinction. Results provided support for the efficacy of imagery exposure in that no spontaneous recovery was observed upon re-exposure based on skin conductance response/SCR. Study 2 sought to replicate the findings of study 1 with the adjustments of conditioning parameters to strengthen the conditioning effect, and the addition of neuroimaging data collection. Successful replication was achieved.

Efforts of engaging a range of measurement types were explicitly made in consideration of the multi-component view emotion. An area for future research in to include simultaneous behavioral indices of fear. To pave the ground, a third study (study 3) was conducted to inspect such possibility through a basic visual attention task. It was found that this specific task was sensitive to differential conditioning and did not lead to interference with conditioning as measured by self-reported fear and SCR supporting its use in similar conditioning designs.

Keywords: differential fear conditioning, extinction, mental imagery, SCR, self-reported fear, fMRI, anterior insular, dorsal anterior cingulate

Chapter 1. Introduction

1.1. Affective Mental Imagery and Its Theories

If you are like me, who is terrified of public speaking, then you might have received the recommendation, perhaps several times, to take on as many opportunities as you can to put yourself in front of a crowd and practice boldness. This could be difficult for some to manage, however, in that these opportunities can be hard to find and perhaps more importantly, the fear that comes with forcing oneself to take on this challenge may deter one from trying altogether. Indeed, in vivo exposure treatments' dropout rates are not low (Gould, Buckminster, Pollack, Otto, & Yap, 1997; Gould, Ott, & Pollack, 1995). Taking a step back, the next best option is perhaps imagining oneself being under a group's scrutiny to provide a more readily available and less intimidating opportunity to teach yourself the art of public speaking. Indeed, for tens of thousands years, humans have long attempted manipulations of emotions via means of mental imagery such as the ancient practice of shamanism (Achterberg, 2002) and the more modern imagery-based techniques of cognitive behavioral therapy such as imaginal exposure which involves repeated exposures to imagined feared stimuli/scenarios (Bryant, Moulds, Guthrie, Dang, & Nixon, 2003; Kandris & Moulds, 2008), and imagery rescripting through which imagined changes are made to aversive experiences (Holmes, Arntz, & Smucker, 2007). These imagery-based interventions are widely adopted with the assumption that mental imagery can substitute for the actual stimuli in affective processes to induce and regulate fear responses.

In the discussion of mental imagery, two major factions of theorists have held extensive and heated debates over what mental imagery is. One party regards imagery as a propositional construct while the other argues that imagery is pictorial in nature. An example from the first group and one of the earliest imagery theories is Lang's bio-information theory (Lang, 1979).

According to Lang's descriptions, emotional imagery is a propositional network consisting of information about the label of imagined stimulus (e.g., a snake), stimulus related semantics (e.g., snakes are dangerous), modality specific perceptual responses (e.g., seeing a snake), and motor programs for efferent output (e.g., heart racing). It was through the activation of this propositional network during imagery that modifications were made to emotional responses to the actual stimuli (Lang, 1977, 1979). Divergent from this propositional construction of mental imagery is the pictorial/depictive theory of mental imagery, which conceptualizes mental imagery as a quasi-pictorial image formed in the "visual buffer" based on information about the imagined object or scene stored in long-term memory (Kosslyn, 1981). According to this second school of imagery theories, mental imagery behaves like weaker versions of perceptual representations and thus can "stand in" for corresponding external stimuli in affective processes (Pearson, Naselaris, Holmes, & Kosslyn, 2015). This debate over whether mental imagery is propositional or depictive has been thoroughly discussed elsewhere (Kosslyn, Thompson, & Ganis, 2006; Pylyshyn, 2003) and will not be considered here. Regardless which side one is on, researchers agree that mental imagery has the capacity to elicit emotional responses similar to its perceptual counterparts.

In a review by Holmes and Mathews (2010), the authors proposed three pathways through which mental imagery can exert influences on emotional responses. The first pathway is through mental imagery's direct contacts with emotional systems in the brain. This is consistent with Lang's bio-informational theory (Lang, 1977, 1979) in that mental imagery is hypothesized to have the capacity to directly act upon cognitive processes and brain regions involved in emotion perception and regulation. The second pathway is built upon its affinity to perception supported by the overlap in neurological activations between imagery and perception (Kreiman,

Koch, & Fried, 2000; Phan, Wager, Taylor, & Liberzon, 2002; A. Schaefer et al., 2003). Based on this conceptualization, mental imagery behaves similarly to perception and thus elicits similar neural activities as external emotion eliciting stimuli. The third pathway was made possible by imagery's potential capacity to interact with past emotional memories and reactivate related affective states. This connection/overlap between imagery and autobiographical memory is supported by neuroimaging evidence that imagining the future and remembering the past may share a common brain system (Schacter, Addis, & Buckner, 2007). Holmes and Mathews (2010) proposed that as imagery generation draws upon autobiographical memory, if the accessed memory contains affect-related information, the constructed imagery could share the same emotion. It is worth noting that these three proposed pathways of emotion regulation through imagery are not mutually exclusive and they may all be constituting parts of the complete operations of affective mental imagery.

1.2. Clinical Implications of Affective Mental Imagery

Consistent with the theorizing of imagery's capacity to possess emotional characteristics, great emphasis has been made over the role of imagery in both symptom presentations and clinical treatments of various affective conditions. Evidence has shown that mental images often evoke stronger emotional consequences compared to verbal presentations (Holmes & Mathews, 2005; Holmes, Mathews, Mackintosh, & Dalgleish, 2008), especially in those with affective conditions such as anxiety and depression (Morina, Deeprose, Pusowski, Schmid, & Holmes, 2011). Frequent and intrusive imagery is also prominent in various emotional disturbances, such excessive negative images of oneself in social situations in social phobia (Hackmann, Clark, & McManus, 2000), unintentional re-experiencing of traumatic events in post-traumatic stress disorder (PTSD; Ehlers, Hackmann, & Michael, 2004), intrusive imagery of both the past and the

future in bipolar disorder (Gregory, Brewin, Mansell, & Donaldson, 2010), and intrusive prospective imagery in anxiety and major depressive disorder (MDD; Morina et al., 2011). In a review by Brewin et al. (2010), prevalence of recurrent negative intrusive images in different psychological disorders was found to be as high as 100% in certain patient populations. While healthy controls also reported occasional intrusive imagery, they are less distressing compared to patient groups (Brewin et al., 2010). More relevant to the current investigation, however, is that the great majority of the studies reviewed described these intrusive imageries as vivid and accompanied by intense physical and emotional reactions.

Abnormalities in imagery functioning has also been proposed to be an important component of the underlying causes of the affective complaints experienced by those with the above psychological disturbances. Some of these discussions were structured around the third pathway of connections between imagery and emotion proposed by Mathews (2010), specifically on the simulation of dreaded future outcomes/prospective imagery drawn from autobiographical memories of the past. Morina et al. (2011) compared patients with anxiety, MDD, and healthy controls, and found that the patient groups in contrast to the control group, experienced impoverished positive prospective imagery, and that the anxiety group in particular reported greater ability to generate vivid negative prospective imagery. Taken together, this deficiency of positive imagery and exaggerated negative imagery of the future, accompanied by a heightened emotional reactivity towards imagery (Morina et al., 2011), further aided by the amplifying effects of imagery on emotional responses (Holmes & Mathews, 2005; Holmes et al., 2008) is likely to play an important part in the manifestation and maintenance of affective symptoms in clinical populations.

While this proposed course of imagery dysfunctions to the etiology of affective conditions is only at the hypothesizing stage, and there lacks an integrative account of imagery's role in the maintenance of the above affective conditions, imagery has been readily involved in various clinical treatments and its efficacy is not without verifications. Two of the most popular strategies, as mentioned previously, are imaginal exposure (Bryant et al., 2003; Kandris & Moulds, 2008) and imagery rescripting (Holmes et al., 2007). Ample evidence has been found in support of the effectiveness of imaginal exposure in treatments of PTSD (for review see Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010) and other anxiety disorders such as phobias (Hecker, 1990; Turner, Beidel, & Jacob, 1994) and obsessive compulsive disorder (OCD; Abramowitz, 1996). Similarly, imaginal rescripting was assessed for and received confirmations on its effectiveness in treatments of phobias, depression, PTSD, and OCD, etc. (for review see Arntz, 2012). In imagery exposure and imagery rescripting, affective imagery was utilized as tools to activate feared object or situation and evoke changes in their corresponding emotional responses. In some other perhaps less frequently examined cases, imagery itself becomes the target of treatments. Examples include disrupting the reconsolidation of negative imagery (Holmes, James, Coode-Bate, & Deeprose, 2009; James et al., 2015) and promoting positive imagery (T. J. Lang, Blackwell, Harmer, Davison, & Holmes, 2012). Again, evidence gathered from these examinations provided support for the effectiveness of imagery-based interventions.

1.3. Neural Overlaps Between Imagery and Perception

In addition to theoretical foundations and successful clinical applications, evidence has also been gathered through neuroimaging research which provided support of the capacity of mental imagery to serve as a substitute for perceptual stimuli in emotional processing.

1.3.1. Higher Order Systems

Research has found that mental imagery shares neural overlaps with perceptual stimuli on both emotional and unemotional stimuli. Meta-analytic reviews reported multiple brain regions to be associated with the emotional processing of perceptual stimuli, such as medial prefrontal cortex (mPFC), anterior cingulate cortex (ACC), insula (INS), and amygdala (Kober et al., 2008; Murphy, Nimmo-Smith, & Lawrence, 2003; Phan et al., 2002). And activations of the same regions have been reported during affective mental imagery, including ventromedial prefrontal cortext (vmPFC; A. Schaefer et al., 2003), ACC, INS (Phan et al., 2002), and amygdala (Kreiman et al., 2000). Consistent with the idea of overlaps/parallels between mental imagery and perception, neural imaging research has also found evidence of similar content-directed selectiveness towards imagine and viewed objects. Such as the study by O'Craven and Kanwisher (2000) which reported selective activations in fusiform face area, a brain region sensitive to visually presented faces, when imagining faces but not places, and activations of parahippocampal place area, an area sensitive to viewing images of places, when imagining places but not faces.

1.3.2. Early Visual Areas

In addition to these frontal and temporal regions, activations of regions within the occipital cortex such as early visual areas were also commonly shared by imagery and perception, though with a smaller degree of overlaps in comparison to the other higher order regions with perception leading a stronger drive for activations (Ganis, Thompson, & Kosslyn, 2004). What is perhaps more interesting is the finding that mental imagery produced retinotopic maps with similar organizations to the corresponding perception maps both found in early visual areas (Slotnick, Thompson, & Kosslyn, 2005). These findings are of great significance because

they offer arguments for that mental imagery is at least in part depictive. “In part” because these activations within early visual areas have not been consistently reported across studies. Importantly, however, these variances were not random and can be accounted for by methodological differences (Kosslyn & Thompson, 2003).

1.3.3. Brain Lesion Evidence

Another area of supporting evidence comes from brain damage research in that there seem to be parallels between the imagery and perception disruptions experienced by patients. For example, a patient with left occipital damage experienced difficulties naming both imagined and visually presented colors (De Vreese, 1991). Another patient with a severe closed head injury exhibited impaired abilities to both generate and recognize images of faces (Young, Humphreys, Riddoch, Hellawell, & de Haans, 1994). These findings of functional and structural overlaps between mental imagery and perception during processing of both emotional and unemotional materials, compared to clinical evidence by itself, provide a more concrete ground for the intuition that imagery behaves similarly to perception and can act as its substitute.

Considering the private nature of mental imagery, these advances and discoveries in neuroimaging research provides a unique window to probe into the mechanisms of mental imagery in relation to perception. It is important to note, however, that while the abundance of evidence listed above confirms the close affinity between imagery and perception, it is not to say that the two processes are the same. In fact, many researchers have illustrated that these neural overlaps/parallels are restricted to a subset of brain regions (Ishai, Ungerleider, & Haxby, 2000; Kosslyn, Thompson, & Alpert, 1997), and the presence and absence of their activations are affected by methodological variances (Kosslyn & Thompson, 2003). In addition, in a review by Bartolomeo (2002), the author listed numerous cases where patients display symptoms of

dissociations between imagery and perception, specifically, some were found to experience disrupted imagery with intact perception and others exhibited normal imagery functioning while failing at perception tasks. In summary, neurological evidence provides support for overlaps and similarities between mental imagery and perception, though these two actions likely still have their respective specialized mechanisms.

1.4. Mental Imagery in Fear Conditioning and Extinction

Compared to the above theoretical discussions, assessments of clinical treatments, and neurological examinations, experimental research of emotional imagery has received little attention despite being the most direct way to investigate the assumed relationship between mental imagery and emotion regulation. Among the limited experimental literature, many opted to use associative learning paradigms such as differential fear conditioning to study emotion (Agren, Björkstrand, & Fredrikson, 2017; Greening et al., 2021; Grégoire & Greening, 2019; Koizumi et al., 2016; Reddan, Wager, & Schiller, 2018). In a typical differential fear conditioning paradigm, two initially neutral conditioned stimuli (CSs) are involved. While one of the CSs (CS+) is repeatedly paired with an aversive or threatening unconditioned stimulus (US; e.g., a loud noise or mild electric shock), the other CS (CS-) is never accompanied by the US (R. M. Carter, Hofstotter, Tsuchiya, & Koch, 2003). Following repeated pairing, the CS+ but not the CS- would exhibit a conditioned responses (CR) that is originally associated with the US (e.g., elevations in self-reported fear; greater skin conductance response, SCR; or engagement of escape behaviors; Carter et al., 2003; Critchley, Mathias, & Dolan, 2002). The degree of differential fear is quantified as the difference between the CS+ versus the CS- in their elicited CRs. Upon successful acquisition of differential fear, extinction procedures can be carried out to inhibit the learned CS-US association (Milad & Quirk, 2012), which involves the removal of US

from the presentations of the CS+ leading to a reduction or suppression of the acquired differential CR. It is this precise theorizing of extinction that the foundations of many imagery-based clinical interventions such as imaginal exposure are based on (Abramowitz, 1996; Hecker, 1990; Powers et al., 2010; Turner et al., 1994).

In a systematic review, Mertens, Krypotos, and Engelhard (2020) screened 1148 publications and were left with only 20 that met the criteria of including both mental imagery manipulation and fear conditioning. The authors concluded that the existing literature only offers "tentative confirmatory evidence" to the relationship between mental imagery and fear regulation due to the lack of research and the high degree of methodological heterogeneity. We found two studies that specifically evaluated the efficacy of imagery exposure in fear extinction (e.g., Agren et al., 2017; Reddan et al., 2018) and both reported supporting evidence. Specifically, Agren et al. (2017) found that imaginal exposure led to comparable reductions of fear as measured by SCR to perceptual extinction. Reddan et al. (2018) reported such reductions following imagined extinction in both neural activations and SCR upon re-exposure. In addition to the limitation of small volume, the existing literature of imagery extinction also suffers from an over-reliance on physiological measures. Based on the multi-system conceptualization of emotion (LeDoux & Pine, 2016), fear is expressed through ways including the conscious feeling of fear, its behavioral manifestations, in addition to the physiological expressions such as the ones used by Agren et al. (2017) and Reddan et al. (2018). To better answer the research question of whether imagery can stand in for perception in emotion regulation, specifically, if conditioned fear to a visual stimulus can undergo extinction via exposure through its mental imagery, further examination with a more diverse selection of outcome measures is needed.

1.5. Measures of Fear

In the present conception of emotion, fear is a multi-component construct that involves subjective feelings and thoughts, physiological activations, and behavioral responses (Cacioppo, Berntson, & Klein, 1992; Gross, 1998; P. J. Lang, 1993). Consistently, outcome measures of fear responses can also be grouped into these three categories. In this section, I will provide examples from each category and discuss their advantages and limitations briefly.

1.5.1. Subjective Measures

Subjective measures can assess both cognitive (e.g., US expectancy, CS-US contingency ratings; Hofmann, 2008) and affective (e.g., self-reported ratings of fear; Grégoire & Greening, 2019) aspects of fear responses. US expectancy and CS-US contingency ratings are ways to measure contingency awareness, which refers to one's explicit knowledge of the CS-US relationship (Weidemann, Satkunarajah, & Lovibond, 2016). It can be collected continuously/online (i.e., during CS presentations; R. M. K. Carter, O'Doherty, Seymour, Koch, & Dolan, 2006), intermittently (i.e., between trials/blocks; Dibbets, Lemmens, & Voncken, 2018), or retrospectively (i.e., after experimentation; Bechara et al., 1995). The same is true for affective evaluations. Self-reports of arousal, valence, or fear/anxiety can also be acquired online (Rossiter & Thornton, 2004), intermittently (Grégoire & Greening, 2019), or retrospectively (H. S. Schaefer, Larson, Davidson, & Coan, 2014). The decision on when to insert these behavioral read-outs, however, can be a difficult one. Online or intermittent reporting of US expectancy or CS-US contingency may draw attention to the contingency relationship itself resulting in contingency awareness, and as a result exerts unwanted influences over fear learning (Critchley et al., 2002; Tabbert, Stark, Kirsch, & Vaitl, 2006). On the other hand, data collected retrospectively may lead to serious underestimations of the actual fear responses during

conditioning (Lovibond & Shanks, 2002). To date, no agreed-upon guidelines have been established on rating procedures. The current project took the middle route and placed questionnaires about fear ratings and CS-US contingency at the conclusions of each experimental phase (i.e., at the end of acquisition and extinction).

1.5.2. Physiological Measures

Compared to subjective measures, psychophysiological indices have the advantages of not being susceptible to self-report biases and allowing connections with animal research (Lonsdorf et al., 2017). SCR and fear-potentiated startle (FPS) responses are the two most popular choices of physiological human fear response measures (Lonsdorf et al., 2017). Other commonly used measures include heart rate (e.g., Mueller et al., 2019; Neumann & Waters, 2006), pupillary response (e.g., Greenberg, Carlson, Cha, Hajcak, & Mujica-Parodi, 2013; Korn, Staib, Tzovara, Castegnetti, & Bach, 2017), and respiration rate (e.g., Demaree et al., 2006; Notarius & Levenson, 1979). Despite the aforementioned advantages, psychophysiological measures are not free from limitations. For example, SCR can be affected by various internal variables (e.g., age, gender), external factors (e.g., temperature and humidity), and medication (Boucsein et al., 2012). In addition, a small percentage of the general population do not produce measurable SCR thus limiting its application. In the case of FPS, problems arise due to startle probes. While startle probes are required to measure FPS responses, recent studies have found that the addition of startle probes may interfere with fear learning (de Haan et al., 2018; Sjouwerman, Niehaus, Kuhn, & Lonsdorf, 2016). In all three studies in this investigation, continuous recordings of SCR were collected and anconsidering the availability of previous literature using the same measure and general guidelines for data collection and analysis (e.g., Boucsein et al., 2012).

1.5.3. Behavioral Measures

Compared to subjective reports and psychophysiological activations, the third category of behavioral responses has not been frequently employed in human fear conditioning research. In Mertens' review (Mertens et al., 2020), only one out of the 20 selected publications included a behavioral measure (i.e., avoidance response; Krypotos, Mertens, Leer, & Engelhard, 2019). Lonsdorf et al. (2017) postulated that this is due ethical and methodological considerations in human research, that human fear conditioning paradigms are rarely intense enough to elicit a clear behavioral response. In comparison, animal research relies heavily on behavioral measures including freezing (e.g., Quirk, Russo, Barron, & Lebron, 2000) and approach/avoidance (e.g., Leiner & Fendt, 2011) considering subjective/verbal reports are not applicable in animal models. As a result, this lack of behavioral descriptions restricts human and animal research translations to only discussions based on physiological (e.g., Leiner & Fendt, 2011; McEchron, Tseng, & Disterhoft, 2000) and neurological (for a review, see Delgado, Olsson, & Phelps, 2006) responses. Among those who incorporated behavioral measures in human fear conditioning research, many selected reaction time (RT) and it was shown to be a sensitive measure of human fear conditioning (Lewis, O'Reilly, Khuu, & Pearson, 2013; Meulders, Vansteenwegen, & Vlaeyen, 2011; Öhman, Flykt, & Esteves, 2001; Silvers et al., 2016). Others forms of behavioral measures less frequently used in human conditioning research include facial expressions (Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005) and avoidance behavior (Grillon, Baas, Cornwell, & Johnson, 2006), etc.

1.5.4. Neurological Representations

In addition to subjective, physiological, and behavioral measures, another important way of measuring fear is through neuroimaging tools. Previous functional magnetic resonance

imaging (fMRI) studies have reported various brain regions to be associated with fear conditioning and/or extinction, including the amygdala, anterior insula (AIC), dorsal anterior cingulate cortex (dACC), hippocampus, precuneus, ventral medial prefrontal cortex (vmPFC), and other medial prefrontal regions, etc. (M. M. R. Delgado, Nearing, LeDoux, & Phelps, 2008; LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998; Lissek et al., 2014; Milad et al., 2007; Phelps, Delgado, Nearing, & Ledoux, 2004). In two recent meta-analyses, Fullana and colleagues examined the neurological signatures of fear conditioning (Fullana et al., 2016) and fear extinction (Fullana et al., 2018). Unlike many previous independent studies on fear conditioning, the meta-analysis (Fullana et al., 2016) did not find robust involvement of the amygdala, instead, the authors found consistent reporting of activations of AIC and dACC, and deactivations of vmPFC and posterior cingulate cortex in reviewed studies. In the fear extinction meta-analysis (Fullana et al., 2018), the authors again reported no significant amygdala involvement with similar brain activation patterns to fear conditioning with involvement of AIC and dACC but not vmPFC regions. Based on existing discoveries on the neural overlap between mental imagery and perception, it is hypothesized that imagery extinction would engage similar brain regions as perceptual extinction, perhaps more consistently in AIC and dACC.

1.6. The Need and Challenges of Employing Multiple Measures

Among the studies reviewed by Mertens et al. (2020), a wide range of measures were recorded and analyzed, such as self-report of affective judgements (Grégoire & Greening, 2019), US expectancy (Dibbets et al., 2018), SCR (Agren, Björkstrand, & Fredrikson, 2017), heart rate (Mueller et al., 2019), FPS responses (Mueller et al., 2019), and fMRI activations (Reddan et al., 2018). Comparisons between studies using different measures can only be made if these indices can be treated interchangeably. However, most theories and studies all assumed concordance

among the subjective, physiological, and behavioral response systems as they are regarded as the expressions of a specific emotion (Hollenstein & Lanteigne, 2014), that is, that these measures are unified expressions of the same emotion construct notwithstanding evidence suggesting that different measures are sensitive to different aspects of an emotional state and lack a strong connection (Mauss & Robinson, 2009).

In the case of fear, concordance means that one would exhibit a set of synchronized responses including self-reported distress, elevated SCR amplitude, and hastened RT. Just like the hypothesized regulatory effect of mental imagery on emotion, this concordance assumption has not been evaluated by many. When it is put under scrutiny, however, concordance has received inconsistent support. While some reported substantial concordance between these categories (e.g., there were high levels of concordance between subjective and physiological measures, Friedman, Stephens, & Thayer, 2014; and between subjective and behavioral measures, Rosenberg & Ekman, 1994), others made the opposite conclusion of moderate to low degrees of concordance (e.g., physiological measures only moderately correlated with subjective feelings and behavior; Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005). Employment of multiple measures and the assessment of concordance between measures are needed to inform better interpretations of results.

Challenges can emerge, however, when collections of multiple measures are carried out simultaneously. One form of challenge has to do with experimental designs. Hollenstein and Lanteigne (2014) reviewed and proposed three probable sources for the inconsistency in concordance research, one of them being methodological variances. To enable a better examination of concordance, a few considerations must be taken into account when designing a study, with one being that the target emotion needs to be accurately and adequately evoked

(Hollenstein & Lanteigne, 2014; Mauss et al., 2005) to allow the examination of concordance. Differential fear conditioning paradigm can serve as a candidate as it provides a more stringent test of fear conditioning compared to classical conditioning (Lockhart & Grings, 1963; Miskovic & Keil, 2012). A second area of concern was regarding the selection of between-subject designs by many studies while the concordance assumption refers to within-individual associations (Hollenstein & Lanteigne, 2014; Mauss & Robinson, 2009). Thus, an ideal experimental design should carry out concordance assessment within individuals. Third, is the reliance on paired associations between pairs of measures selected from either across or within categories of subjective, physiological, and behavioral measures (Mauss et al., 2005). Such designs failed to capture the essence of the concordance assumption which addresses a process that has at least three components (i.e., subjective, physiological, and behavioral; Hollenstein & Lanteigne, 2014). A more appropriate design would include one outcome measure from each of the three categories (i.e., self-report as the subjective measure, SCR as the psychophysiological measure, and RT as the behavioral measure) and apply multivariate analyses.

Another area of consideration is the potential interferences between measures. One potential example of such interference is the effect of online or intermittent reporting of US expectancy or CS-US contingency. When such measures results in changes in contingency awareness, fear learning as measured by other read-outs would be affected (Critchley et al., 2002; Tabbert et al., 2006). Another example is the influence of startle probes when measuring FPS responses. Two recent publications reported changes in fear learning as measured by SCR, fear ratings (Sjouwerman et al., 2016) and pupil dilation (de Haan et al., 2018) that were the results of the use of startle probes. In summary, faced with the multitude of options, caution is needed when selecting outcome measures. Considerations of the characteristics of different

measures should be taken into account. Additional evaluations are needed when one opts to use more than one index, as some combinations may lead to interferences between measures.

1.7. Overall Goal and Central Hypothesis

The overall goal of my dissertation is to answer the question of whether conditioned fear to a visual stimulus can go through extinction via imagery exposure. The rationale for this hypothesis is two-fold supported by the discussions described above. First is the powerful impact of imagery on emotion supported by clinical, psychophysiological, and neurological evidence (Holmes & Mathews, 2010). Second is the similarities and overlaps between emotional imagery and perception in their neurological representations (Kober et al., 2008; Kreiman et al., 2000; Murphy et al., 2003; Phan et al., 2002; A. Schaefer et al., 2003; Slotnick et al., 2005). Evaluations were first made with self-reported fear and SCR, followed by the addition of brain activations. An additional investigation was carried out to assess whether RT would be suitable in the same fear learning and extinction paradigm.

1.7.1. STUDY 1: Psychophysiological Evidence for Fear Extinction Learning via Mental Imagery

Experimental literature on imagery extinction is lacking and relied on physiological measures of fear without considerations of subjective feelings. To determine whether extinction of fear responses towards a perceptual stimulus through imaginal exposure to its imagery, we conducted fear conditioning following by imagery exposure. CRs were measured and assessed in terms of both subjective (i.e., self-reported fear) and physiological (i.e., SCR) responses. We hypothesized that consistent with the limited literature, imaginal exposure could lead to reductions or eliminations of conditioned fear similar to viewed extinction.

1.7.2. STUDY 2: Psychophysiological and Neurological Evidence for Fear Extinction Learning via Mental Imagery

In an effort to replicate our findings from self-reported fear and SCR evidence in study 1, similar conditioning and extinction procedures were carried out with the addition of fMRI data collection. Based on existing literature on the neurological overlap and parallels between imagery and perception, we hypothesized that there would be measurable effects of conditioning and extinction in brain regions that were consistently involved in fear conditioning and extinction, i.e., dACC and AIC. Considering the inconsistencies between measures in study 1, it is predicted that conditioned fear responses as measured by self-reported fear, SCR, and brain activations would all or in part undergo extinction after repeated imagined exposure.

1.7.3. STUDY 3: Complete the Triangulation: Quantifying Differential Fear Conditioning With a Noninterfering and Sensitive Behavioral Measure Along With Self-Report and Physiological Measures

In contrast with animal research, examination of human fear conditioning has put little emphasis on behavioral descriptions. One major area for concerns is the potential interference that can be brought by behavioral probes during the process of concurrent behavioral tasks. To assess whether the chosen behavioral task could offer a sensitive and non-interfering measure of differential fear conditioning, we compared degrees of conditioning as measured by self-reported fear and SCR between two groups of participants with one containing behavioral probes and the other without. Based on previous RT-based human conditioning research, we hypothesized that the behavioral probe task adopted here would be able to detect differential fear conditioning. And considering its low task demand, it is expected that it will not cause interference with conditioning as measured by the other two indices (i.e., self-reported fear and SCR).

Chapter 2. Psychophysiological Evidence for Fear Extinction Learning via Mental Imagery

2.1. Introduction

From as early as the practices of shamanism 20,000 some years ago (Achterberg, 2002) to today's imagery-based cognitive behavioral therapy techniques (Holmes, Arntz, & Smucker, 2007), mental imagery has been harnessed for its efficacy as a cognitive process that affects emotion perception and regulation. It is commonly referred to as a perceptual-like experience in the absence of external sensory input (Kosslyn, Thompson, & Ganis, 2006), and is recognized as an important component of various fear-related affective conditions in terms of both their symptom presentations (e.g., intrusive images in depression, flashbacks in post-traumatic stress disorder or PTSD; Matthews, Collins, Thakkar, & Park, 2014; Weßlau & Steil, 2014), and clinical treatments (e.g., imaginal exposure, Abramowitz, 1996; Hecker, 1990; Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010; Turner, Beidel, & Jacob, 1994; imagery rescripting, Arntz, 2012). The primary account for the imagery's impact in these examples is that it can substitute for the actual stimuli in affective processes to regulate fear responses. Yet, little experimental research has been done to support this explanation.

While some have suggested that informational processing attributed to mental imagery is purely propositional, an abundance of behavioral and brain imaging research suggests that mental imagery is at least partially depictive or pictorial (Kosslyn, 1981, 2005; Kosslyn, Ganis, & Thompson, 2001). According depictive theory, mental imagery generates a neural representation that functions like a weaker version of perception and is associated with the subjective experience of, for example, "seeing with the mind's eye" (Kosslyn et al., 2001). Thus, imagery of an object can "stand in" for the corresponding external stimulus in various cognitive processes including associative learning and other affective processes (Lewis, O'Reilly, Khuu, &

Pearson, 2013; Pearson & Kosslyn, 2015; Pearson, Naselaris, Holmes, & Kosslyn, 2015). On the other hand, the bio-informational theory which is directly concerned with the relationship between imagery and emotion noted that mental imagery contains not only the perceptual information of the imagined stimulus but also its conceptual information stored as propositions such as "relationships, descriptions, interpretations, labels, and tags" (Lang, 1977, 1979). The bio-informational theory posits that it is through the activation of this propositional network during imagery that emotional modifications occur (Lang, 1977, 1979). Regardless of the precise nature of mental imagery, it is acknowledged by both theoretical perspectives that mental imagery has the capacity to elicit emotional characteristics similar to its perceptual counterparts. In addition to successful clinical applications and theoretical foundations, neuroimaging research has also provided evidence that mental imagery contributes to the elicitation or modification of emotional reactivity. For example, meta-analytic reviews of the brain regions associated with the emotional processing of perceptual stimuli report activations in regions such as medial prefrontal cortex (mPFC), anterior cingulate cortex (ACC), insula (INS), and amygdala (Kober et al., 2008; Murphy, Nimmo-Smith, & Lawrence, 2003; Phan, Wager, Taylor, & Liberzon, 2002). Importantly, activations of the same regions have been reported during elicitation of emotions via mental imagery, including mPFC (Schaefer et al., 2003), ACC, INS (Phan et al., 2002), and amygdala (Kreiman, Koch, & Fried, 2000). Taken together, the existing research appears to support the intuition that mental imagery of an emotional stimulus can substitute for its external presentation. However, experimental research regarding the relationship between visual mental imagery and emotion is lacking despite being a direct way to investigate the assumed relationship between mental imagery and emotion/fear regulation.

Among the few existing studies that investigated the connection between mental imagery and emotion, many based their task paradigms on differential fear conditioning (Agren, Björkstrand, & Fredrikson, 2017; Greening et al., 2021; Grégoire & Greening, 2019; Koizumi et al., 2016; Reddan, Wager, & Schiller, 2018). Such paradigm typically involves one initially neutral conditioned stimulus (CS+) which is repeatedly paired with an aversive or threatening unconditioned stimulus (US; e.g., a loud noise or mild electric shock), and a second CS (CS-) which is never accompanied by the US (Carter, Hofstotter, Tsuchiya, & Koch, 2003). Upon such pairing, the CS+ but not the CS- exhibits a conditioned responses (CR) that is similar to the type of response elicited by US (e.g., increased self-reported fear; increased skin conductance response, SCR; increased heart rate; or, escape behavior; Carter et al., 2003; Critchley, Mathias, & Dolan, 2002). The acquisition of differential fear conditioning is quantified as the difference in the CR between the CS+ versus the CS-. Greening et al. (2021) observed recently that visual imagery of conditioned stimuli elicited a significant differential fear conditioned response as measured by self-reported fear, SCR, and activation of the right INS. Following the acquisition of differential fear, fear extinction learning is commonly used for inhibiting the fear conditioning association (Milad & Quirk, 2012). It involves repeated presentations of the CS+ in the absence of the US such that a novel safety associated memory is formed, which leads to a reduction or suppression of the differential CR. Many imagery-based clinical interventions such as imaginal exposure (Abramowitz, 1996; Hecker, 1990; Powers et al., 2010; Turner et al., 1994) are premised on such extinction theorizing.

Though limited in number, existing research has provided supporting evidence for the efficacy of imagery exposure in the down-regulation of differential fear conditioning via fear extinction (e.g., Agren et al., 2017; Reddan et al., 2018). Agren et al. (2017) found that exposure

to either an imagined or perceptual CS+ during extinction led to comparable degrees of reduction in SCR. Reddan et al. (2018) reported reductions in both threat-relevant neural predictive pattern expression and SCR upon re-exposure to conditioned auditory CS+ following imagined extinction during which participants were asked to play the conditioned CS+ tones in their head. Koizumi et al. (2016) also managed to reduce conditioned fear responses as measured by SCR and neural activations using counter conditioning by pairing implicit imagery of the CS+ with monetary reward using neurofeedback. Notably, the above cited studies all relied on physiological indices of differential conditioning without assessments of the subjective experiences of fear. This stands in contrast to the multi-system conceptualization of emotion that emotion is expressed through both the conscious feeling of fear and also the corresponding behavioral and physiological expressions (LeDoux & Pine, 2016), and that over-reliance on any single response system will be limiting to our understanding of the emotion being studied (Frijda, 1986; Gross, 2013; Jiang, Burleigh, & Greening, 2021; Lang, 1993; Larsen & Prizmic-Larsen, 2006; LeDoux & Pine, 2016).

The current study aimed to evaluate whether visual mental imagery could produce fear extinction following the acquisition of differential fear conditioning to visual objects, in terms of both self-reported fear and SCR. To do so, we used a within-subject design in which two CS+s and one CS- underwent acquisition of differential conditioning (Acquisition), followed by in vivo, perceptual extinction of one of the CS+s (CS+V) and imagery extinction of the other (CS+I) during Extinction Phase 1. Both of the CS+s were then viewed again in Extinction Phase 2. Considering the ample evidence supporting the effectiveness of imagery-based clinical interventions on the reduction of negative affect (Heyes, Lau, & Holmes, 2013; Holmes & Mathews, 2010; Weßlau & Steil, 2014) and the above research findings on imagery in fear

down-regulation (Agren et al., 2017; Koizumi et al., 2016; Reddan et al., 2018), our overall prediction was that conditioned fear responses (as measured by both self-report and SCR) to perceived visual stimuli would reduce after repeated imaginary exposure to the same stimuli without the accompany of US. The accuracy of this overall prediction was evaluated on the basis of two specific experimental predictions. First, we hypothesized that imagining the CS+I during Extinction Phase 1 would elicit a significant CR compared to the CS-, as the fear association would generalize from viewing the CS+I during Acquisition to imagining the CS+I during Extinction Phase 1 (Greening et al., 2021). Second, if fear extinction learning via imagery exposure generalized back to viewing the CS+I, then we would observe no significant differential conditioning during Extinction Phase 2 between CS+I versus CS-. Conversely, if imagery exposure did not produce extinction to the visual CS+I, we would predict a spontaneous recovery of differential CR in Extinction Phase 2 as reflected in a significant difference between the CS+I and CS-.

2.2. Method

2.2.1. Participants

A total of 61 Louisiana State University students taking undergraduate-level psychology courses were recruited and completed this study. Five participants were removed from the final analyses due to excessive noise in SCR throughout or a lack of SCR response to the US, i.e., the shock, leaving a final sample of 56 individuals (32 females, mean age of 19.28, *SD* = 1.18; demographic information is missing from 3 participants). This study was approved by the Institutional Review Board of the Louisiana State University. Written informed consent was given to each participant prior to the start of experiment sessions. All participants were reimbursed by way of research credits.

2.2.2. Stimuli

All stimuli were created and presented in MATLAB R2018a with the Psychophysics Toolbox extensions (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997). Three capital letters were selected as the CSs: letters “J” and “H” were paired with the US functioning as two distinct CS+s and letter “F” was used as the CS- and it was never paired with the US. All stimuli were presented at the center of the screen in 4-by-5 grids drawn on a grey background (figure 2.1 A). A single mild electric shock of 5-ms durations as the US was delivered to the distal phalanx of each participant’s ring finger and pinky on his/her non-dominant hand through attached electrodes using the Biopac MP-150 system and AcqKnowledge software (for 5 participants, the shock electrodes were placed on their index and middle fingers). Whenever the US was delivered it co-terminated with the CS+. The intensity of the US was customized to each participant such that it was rated as “uncomfortable but not painful.” Shock intensity was checked and adjusted after the first half of Acquisition for each participant to avoid desensitization or sensitization to the US.

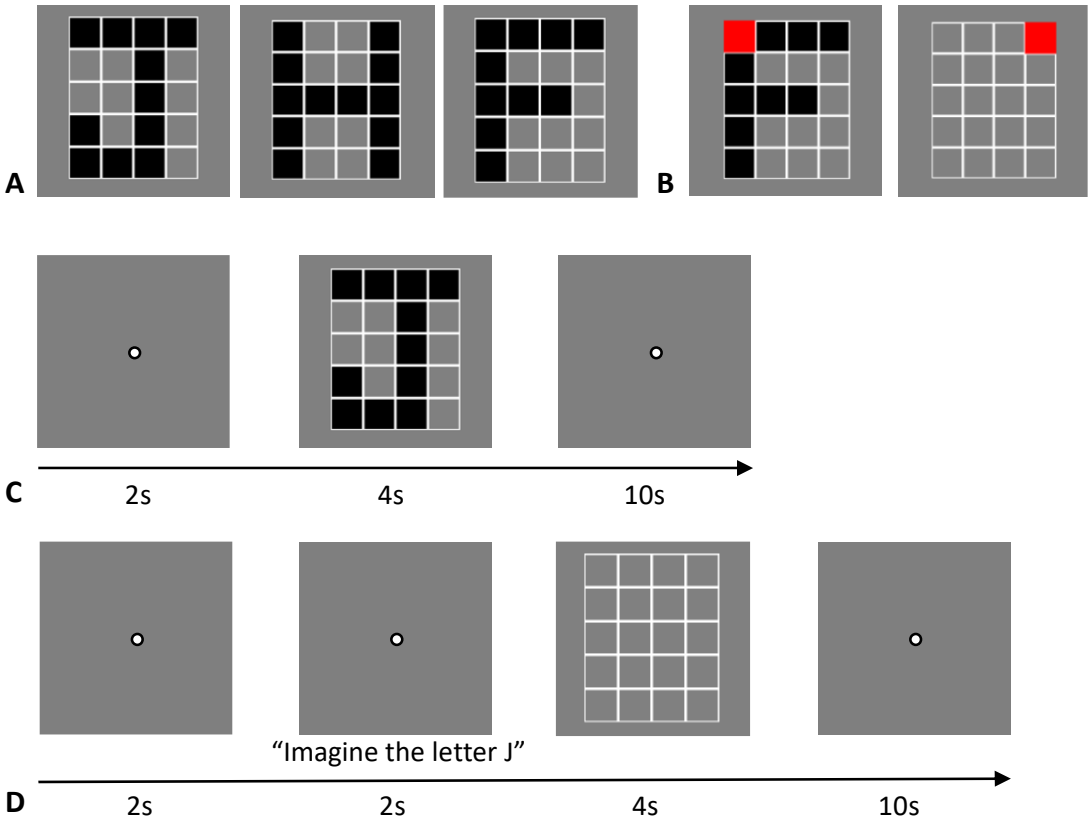

Figure 2.1. Letter stimuli (A), probe (B), and trial designs for view (C) and imagine (D) trials.

2.2.3. Procedures

Each participant first completed two training runs (12 trials/run) in which participants both viewed (figure 2.1. C) or were instructed to imagine (figure 2.1. D) the selected three letters. During each trial a probe appears, which was a single square in the grid would be filled-in in red (figure 2.1. B) and participants were instructed identify via button press whether the probe was on the letter viewed/imagined or off the letter. This probe task was added to the training phrase to initially facilitate participants' attention to the task and ensure the instructions were understood regarding imagery. No shock was involved during this training phase of the experiment, which allows the trials in this phase to as habituation trials for the CSs. However, no probes were present during the remaining phases of the experiment out of a concern that they could interfere with the differential conditioning (Carter et al., 2003).

During fear conditioning/Acquisition (12 trials/run x 4 runs), all trials were view trials (i.e., there was no mental imagery). The two CS+ letters were paired with shock on 50% of trials and the CS- was never paired with shock. The order of stimuli presentation was pseudorandomized in a way that the first and last trials were always CS- and that the second and thirst trials were always the two CS+ stimuli with shock. The second CS+ with shock trials were always in the second half of the run. In addition, no more than two consecutive trials were the same. Upon completion of Acquisition, participants proceeded into the Extinction Phase 1 (12 trials/run x 2 runs) in which shock was removed from CS+ presentations. One CS+ continued to be viewed (CS+V) and the other was imagined (CS+I) for the entire phase. The assignment of which CS+ letter (i.e., letters "J" and "H") was the CS+V versus the CS+I was counterbalanced across participants. The CS- (i.e., letter "F") was always viewed during Extinction Phase 1. The last phase of the experiment was Extinction Phase 2 (12 trials/run x 2 runs), in which all stimuli were viewed without the presence of electric shocks. The order of stimulus presentation for both Extinction Phase 1 and Extinction Phase 2 was pseudorandomized with no more than two of the same CS trials in a row. Details of the trial schedule for each phase is listed in table 2.1.

Table 2.1. Trial schedule for each phase of the study.

	Training/Habituation	Acquisition	Extinction Phase 1
CS+I with US		8 view trials	
CS+V with US		8 view trials	
CS+I without US	4 view, 4 imagine trials	8 view trials	8 imagine trials
CS+V without US	4 view, 4 imagine trials	8 view trials	8 view trials
CS-	4 view, 4 imagine trials	16 view trials (8 excluded in analyses)	8 view trials

2.2.4. Self-Report Measures

After Acquisition, Extinction Phase 1 and 2, participants were asked to complete a series of self-report questionnaires on their level of fear towards receiving a shock, and on their perceived likelihood of being shocked for each CS. They were instructed to report how much they feared receiving a shock using a 7-point Likert scale (between 1 = "Not at All" and 7 = "Very Much So"). A 10-point Likert scale (between 0% and 100% with intervals of 10%) was provided for reporting estimations of shock likelihood.

2.2.5. Skin Conductance Response

During each trial, participants' SCRs were collected and sampled at 2000 Hz. SCR analysis was carried out in MATLAB R2018a (Version 9.4). A first-order Butterworth bandpass filter was applied during preprocessing with cut-off frequencies of .01 and 5 Hz (Bach, Flandin, Friston, & Dolan, 2010). The time series were then down-sampled to 100 Hz. Based on previous

research (Grégoire & Greening, 2019; Schiller, Kanen, LeDoux, Monfils, & Phelps, 2013; Vervliet, Vansteenwegen, Baeyens, Hermans, & Eelen, 2005) SCRs to the CSs were calculated by subtracting baseline (1 second before stimulus onset) from peak amplitude (during 1-3.995 seconds after stimulus onset). Peaks were zeroed if their distance from the baseline was smaller than .02 μS. The difference scores were then square root transformed. Consistent with previous research (Grégoire & Greening, 2019), we only included unreinforced CS+ trials (i.e., trials without US) in subsequent analyses. Lastly, the first and last trials of the Acquisition run were always CS- trials, which were excluded from the analyses to avoid the potential confounding orienting effect of the first trials, and to ensured that there was an equal number of CS+ and CS- trials included in the analyses (Grégoire & Greening, 2019; Lonsdorf et al., 2017).

2.2.6. Data Analysis

Based on recommendations by Lonsdorf et al. (2017), in order to maintain the most generalizable sample possible we only excluded participants from the analysis who displayed no clear SCR response to the US or whose overall SCR data was of poor quality even after filtering and down-sampling. No outlier removal was undertaken. Mean values of square-rooted SCR were calculated for each CS types (i.e., CS+I, CS+V, and CS−) separated into Acquisition, early Extinction Phase 1 (first half of trials), late Extinction Phase 1 (second half of trials), early Extinction Phase 2 (first half of trials), and late Extinction Phase 2 (late half of trials). Self-reported fear and shock estimations were collected at the end of each study phase and thus were not broken down into early and late responses for each of the three CSs. Repeated measures analyses of variance (ANOVAs) were conducted with Greenhouse–Geisser correction for non-sphericity when needed. Post hoc paired t-tests without corrections were conducted when

significant interactions or main effects were found (Saville, 1990). Specific analyses are described in the results section.

2.3. Results

2.3.1. Acquisition

SCR: Acquisition was analyzed using a repeated-measures ANOVA with CS type (i.e., CS+I, CS+V, and CS-) as the within-subject factor on mean SCR during Acquisition (figure 2.2.). There was a main effect of CS type, $F(2, 110) = 3.80$, $p = .025$, $\eta^2 = .06$. Post hoc t-tests revealed that while there was a significant difference between the CS+I ($M = .23$, $SD = .21$) and the CS- ($M = .17$, $SD = .14$), $t(55) = 2.59$, $p = .012$, $d = .35$; the CS+V ($M = .20$, $SD = .19$) did not differ from CS- ($M = .17$, $SD = .14$), $t(55) = 1.40$, $p = .167$. Moreover, the two CS+s (i.e., CS+I and CS+V) did not differ from each other, $t(55) = 1.46$, $p = .151$. Together, based on the mean SCR, CS+I but not CS+V acquired differential fear at the group-level. Thus, we did not include the CS+V in the subsequent analyses in the extinction phases with respect to the SCR data.

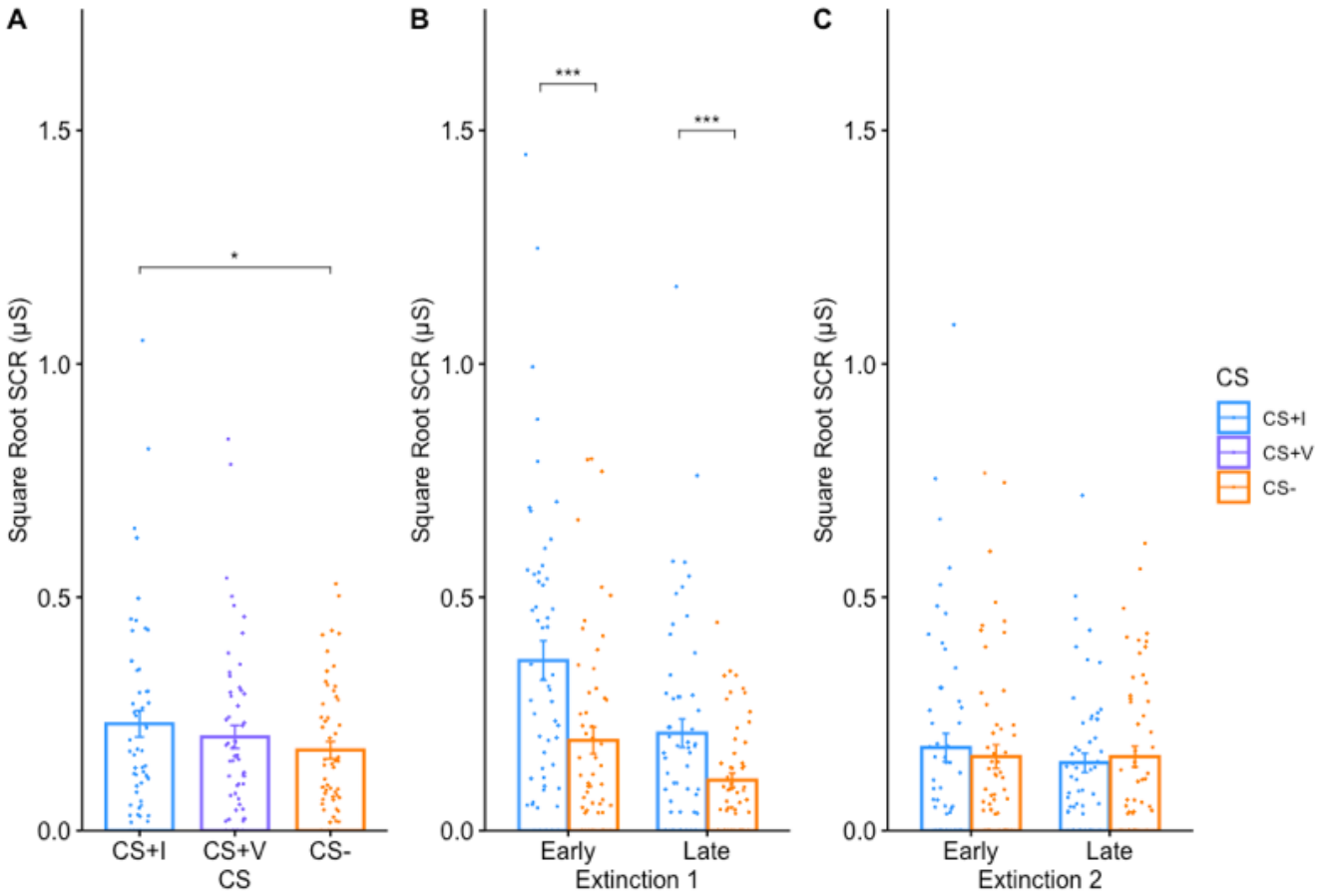

Figure 2.2. Mean square-rooted SCR for each CS type during Acquisition (A), and early and late Extinction Phase 1 (B) and Extinction Phase 2 (C). Due to insignificant difference between CS+V and CS- during Acquisition, CS+V was not included in Extinction Phase 1 and Extinction Phase 2. Error bars show ± 1 standard error. Each dot represents one subject.
* p < .05. ** p < .01. *** p < .001. **** p < .0001.

Self-Report: The same repeated ANOVA was applied to self-reported fear (figure 2.3. A) and shock estimations (figure 2.3. B). In contrast to SCR, these two self-report measures revealed differential conditioning of both CS+I and CS+V. Specifically, for self-reported fear there was a main effects of CS-type, $F(1.38, 76) = 32.59$, $p < .0001$, $\eta^2 = .37$. Post hoc t-tests indicated that participants reported higher fear ratings for both CS+I ($M = 4.20$, $SD = 1.63$) and CS+V ($M = 4.23$, $SD = 1.67$) compared to the CS- ($M = 2.14$, $SD = 1.43$), with respective statistics of $t(55) = 6.61$, $p < .0001$, $d = .88$, and $t(55) = 7.13$, $p < .0001$, $d = .95$. The two CS+s did not differ, $t(55) = -.12$, $p = .901$. As for shock estimation, a main effect of CS type was also

found, $F(1.71, 94.22) = 59.95$, $p < .0001$, $\eta^2 = .52$. Post hoc t-tests showed that participants reported higher likelihood of shock for both CS+I ($M = 49.82$, $SD = 17.11$) and CS+V ($M = 49.64$, $SD = 18.39$) compared to the CS- ($M = 17.86$, $SD = 20.95$): CS+I vs CS-, $t(55) = 8.45$, $p < .0001$, $d = 1.13$; CS+V vs CS-, $t(55) = 8.07$, $p < .0001$, $d = 1.08$). The two CD+s, again, did not differ, $t(55) = .06$, $p = .951$.

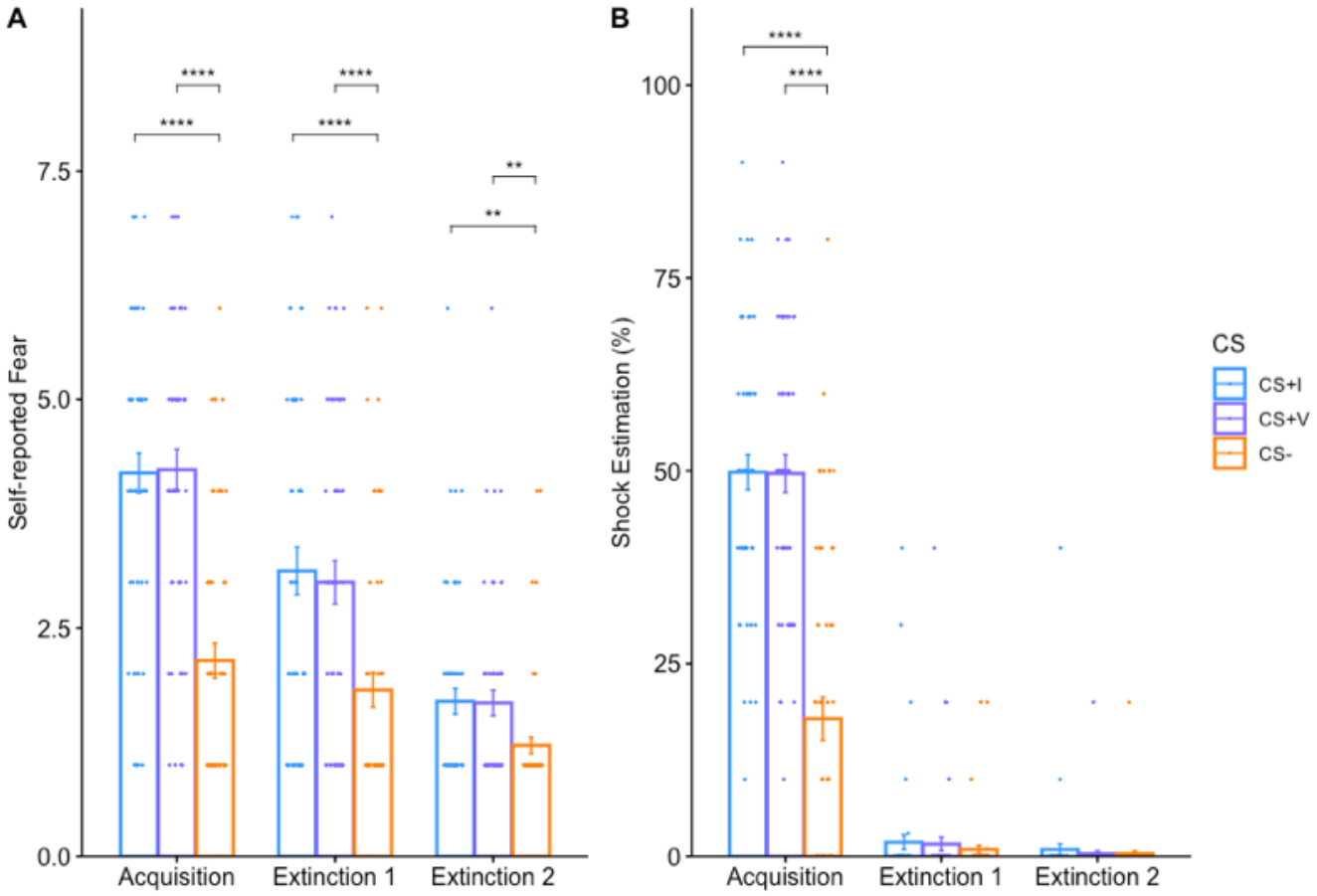

Figure 2.3. Mean self-reported fear ratings (A) and shock estimations (B) for each CS type. Error bars show ± 1 standard error. Each dot represents one subject.
* p < .05. ** p < .01. *** p < .001. **** p < .0001.

2.3.2. Extinction Phase 1: Differential Fear Generalization to CS+ Imagery

SCR: During Extinction Phase 1, participants imagined the CS+I and continued to view the CS-, and the US was never delivered. A 2x2 ANOVA with CS-type (i.e., CS+I, CS-) and timing (i.e., early trials, late trials) as the within subject factors were conducted on SCR data

during Extinction Phase 1 (figure 2.2. B). This analysis revealed significant main effects for both CS type, $F(1, 55) = 21.12$, $p < .0001$, $\eta_p^2 = .28$, and timing $F(1, 55) = 41.45$, $p < .0001$, $\eta_p^2 = .43$. There was no CS type x timing interaction, $F(1, 55) = 2.91$, $p = .094$. Post hoc t-tests indicated that CS+I was significantly different from CS- during both early (CS+I: $M = .38$, $SD = .32$; CS-: $M = .19$, $SD = .20$), $t(55) = 4.03$, $p < .001$, $d = .54$; and late (CS+I: $M = .22$, $SD = .24$; CS-: $M = .11$, $SD = .12$), $t(55) = 3.55$, $p < .001$, $d = .47$ trials of Extinction Phase 1. Both CS+I and CS- had greater SCR during early compared to their respective late trials of Extinction Phase 1 (CS+I: $t(55) = 5.53$, $p < .0001$, $d = .74$; CS-: $t(55) = 3.10$, $p = .003$, $d = .41$). As noted previously, CS+V was not included in SCR analyses for Extinction Phase 1 and 2. However, a graph containing all three CSs separated into early and late Extinction Phase 1 and 2 is provided in supplementary figure 2.S1 in Appendix A.1.

Self-Report: Results of a one-way repeated measures ANOVA with CS-type (i.e., CS+I, CS+V, and CS-) as the within-subject factor on self-reported fear (figure 2.3. A) also supported generalization of fear to imagery with a main effect of CS-type, $F(1.75, 96.49) = 15.88$, $p < .0001$, $\eta_p^2 = .22$. Based on post hoc t-tests, CS+I ($M = 3.28$, $SD = 1.96$) and CS+V ($M = 3.16$, $SD = 1.77$) were both rated significantly higher than CS- ($M = 1.92$, $SD = 1.45$), with $t(55) = 4.36$, $p < .0001$, $d = .58$, and $t(55) = 5.10$, $p < .0001$, $d = .68$, respectively. The two CS+s did not differ from each other, $t(55) = .55$, $p = .588$. These elevations of both physical and subjective fear responses during Extinction Phase 1 were apparent despite participants' accurate knowledge of shock estimations (figure 2.3. B). The same one-way repeated measures ANOVA applied to shock estimations indicated that all CS's (i.e., CS+I, CS+V, and CS-) were reported to be paired with shock close to 0% of the time during Extinction Phase 1 (CS+I: $M = 1.84$, $SD = 7.16$;

CS+V: M = 1.61, SD = 6.54; CS-: M = .91, SD = 3.94) with no effect of CS type, F(1.47, 81.02) = 1.15, p = .308.

2.3.3. Extinction Phase 2: Imagery Exposure Led to Differential Fear Extinction Learning

SCR: During Extinction Phase 2, participants now viewed both the CS+I and the CS-, and as with Extinction Phase 1 the US was never delivered. We predicted that if mental imagery of CS+I was effective then we would observe no main effect of CS type. As predicted, a 2x2 ANOVA with CS-type (i.e., CS+I, CS-) and timing (i.e., early and late extinction) as the within subject factors (figure 2.2. C) resulted in no interaction (F(1, 55) = .52, p = .476) nor main effects (CS type: F(1, 55) = .02, p = .882; timing: F(1, 55) = .49, p = .485).

Self-Report: Regarding self-reported fear, a one-way repeated measures ANOVA with CS-type (i.e., CS+I, CS+V, and CS-) as the within-subject factor (figure 2.3. A) revealed a main effect of CS type, F(1.75, 96.24) = 14.25, p < .0001, η_p^2 = .21. Importantly, a post hoc t-test revealed no significant difference in self-reported fear for the CS+I (M = 1.70, SD = 1.06) versus CS+V (M = 1.68, SD = 1.05), t(55) = .10, p = .924. Additional post hoc t-tests revealed higher fear ratings for both CS+I and CS+V than the CS- (M = 1.21, SD = .68), with t(55) = 2.89, p = .006, d = .39, and t(55) = 3.00, p = .004, d = .40, respectively. Although this result may appear to suggest that self-reported fear was not extinguished, in the following section we carried out an additional analysis across the 3 main experimental phases to demonstrate that the magnitude of self-reported differential fear was reduced via both visual and imagery extinction. Regarding self-reported shock estimation, accurate estimations were reported (figure 2.3. B) with respect to Extinction Phase 2 with close to 0% estimations for CS+I (M = .89, SD = 5.49), CS+V (M = .38, SD = 2.67), and CS- (M = .36, SD = 2.67) with no main effect of CS type, F(1, 55) = 1.83, p = .182.

2.3.4. Self-Reported Fear Across Acquisition, Extinction Phase 1 and Extinction Phase 2

In order to evaluate the magnitude of differential fear conditioning as measured by self-report across the three main experimental phases we conducted a 3x2 ANOVA on the difference scores of self-reported fear with study phase (i.e., Acquisition, Extinction Phase 1, Extinction Phase 2) and CS contrast (i.e., CS+I minus CS-, CS+V minus CS-) as the within-subject factors. This revealed only a main effect of study phase, $F(1.71, 94.27) = 17.84$, $p < .0001$, $\eta_p^2 = .24$. Notably, there was neither a main effect of CS contrast, $F(1, 55) = .13$, $p = 721$, nor interaction, $F(1.45, 79.87) = .23$, $p = .724$. As there was no main effect of CS contrast and no interaction, the contrast scores were averaged together (i.e., producing one aggregate measure of the CS+ vs CS- difference) and compared between study phases. Post-hoc t-tests revealed significant reductions from Acquisition ($M = 2.07$, $SD = 2.48$) to Extinction Phase 1 ($M = 1.24$, $SD = 1.81$), $t(55) = 2.83$, $p = .007$, $d = .38$; and from Extinction Phase 1 to Extinction Phase 2 ($M = .47$, $SD = .77$), $t(55) = 3.73$, $p = .000$, $d = .50$. These results suggest that the magnitude of differential fear conditioning (CS+ minus CS-) as measured with self-reported fear significantly decreased throughout extinction (i.e., Extinction Phase 1 and 2). Moreover, the reduction in differential self-reported fear was the similar regardless of whether or not imagery was employed during Extinction Phase 1.

2.4. Discussion

Mental imagery has long played an important part in our understanding and treatments of various affective conditions. The assumption is that imagery performs like its perceptual counterpart and can exert regulatory effects on emotion in its place. While efforts have been made in the theorizing and assessment of imagery-based emotion regulatory strategies, experimental examination is lacking. The current investigation sought to determine if visual

mental imagery could contribute to fear extinction as measured by both physiology (i.e., SCR) and self-reported fear, as this has not been done in the current literature (Agren et al., 2017; Reddan et al., 2018). First, we found that conditioned fear acquired by visual stimuli generalized to visual imagery as indicated by elevated SCR and self-reported fear. Second, following repeated visual imagery of the CS+I, there was no significant differential SCR upon re-exposure to the CS+I compared to the CS-. In addition, based on self-reported fear, imagery-based and perceptual extinction led to similar degrees of reductions in the differential conditioned fear response, consistent with the SCR-based findings of Agren et al. (2017).

As the main research question of the current investigation is whether imagery exposure to the CS+ leads to fear extinction initially acquired to a perceptual (i.e., visual) CS+, our observation of significantly greater SCR for CS+I versus the CS- during acquisition allows us to make valid inferences regarding mental imagery's impact on extinction despite the lack of clear differential conditioning between the CS+V and the CS-. Our first observation supporting the impact of mental imagery on extinction comes from the observation of the generalization of conditioned fear from perception to imagery during Extinction Phase 1 in terms of both SCR and self-reported fear. An alternative possibility is that the elevation of SCR when imagining the CS+I could be the result of the act of imagery, which may require more effort than simply viewing in the case of CS-. The initial purpose of including the CS+V during Extinction Phase 1 was to help evaluate this possibility. On the other hand, previous research on the generalization of differential fear conditioning from visual to imagined objects did not observe evidence of an elevated SCR response to mental imagery compared to viewing, though they did observe a significant SCR difference between the CS+ versus the CS- (Greening et al., 2021). Another study by Agren et al. (2017) reported that while the conditioned response measured by SCR

difference between CS+ and CS- was initially larger in the imaginal extinction group, the imagery and in vivo/perceptual extinction groups were comparable by late extinction. Based on these findings, it is unlikely that the SCR difference can be completely accounted for by the difference between viewing versus visual imagery per se, rather than being an expression of the generalized conditioned fear response.

The second piece of evidence supporting the use of mental imagery for fear extinction learning comes from Extinction Phase 2. Specifically, even during the early trials (i.e., the first four trials per condition) the CS+I no longer exhibited a greater SCR compared to the CS-. Had imagery fear extinction not affected the fear conditioned association between the perceptual in vivo CS+I and the CS- one would have predicted a spontaneous recovery of differential conditioning upon re-exposure to the in vivo CS+I during Extinction Phase 2 (Huff, Hernandez, Blanding, & LaBar, 2009), which was not observed. Unlike SCR, differential fear measured as self-reported fear did persist to some degree throughout extinction. However, this differential was significantly reduced from Acquisition to Extinction Phase 1 and from Extinction Phase 1 to Extinction Phase 2 irrespective of the type of CS+ (i.e., for both CS+I – CS- and CS+V – CS-). This is in line with previous research on self-reported fear (Lau et al., 2008; Shechner et al., 2015), and may reflect that individuals maintain stable declarative knowledge regarding the difference between the CS+s and CS- even after extinction.

Unexpectedly, only one of the two CS+'s (i.e., CS+I) was found to exhibit threat related differential physiological reactivity (i.e., greater SCR for CS+I vs. CS-) following the acquisition phase in the current study. Considering that the selections of CS+I and CS+V were counterbalanced across participants, this could not be attributed to differences between the letter stimuli of "J" and "H". One possibility is that the nature of the stimuli and the use of two CS+s

in a within-subject designed made the stimulus discriminability for the purposes of differential conditioning difficult. Additionally, compared to evolutionarily fear-relevant objects (e.g., images of snakes, human faces), stimuli lacking in evolutionary fear-relevance, such as the letter stimuli used in the current study, undergo fear conditioning less readily (Öhman & Mineka, 2001). Future research could consider using more fear-relevant objects (e.g., snakes or spiders), or a between-group design to avoid require two CS+s (e.g., Agren et al., 2017; Reddan et al., 2018). The inconsistency observed in the current study could also be a manifestation of the noise and measurement error in SCR.

Altogether, the present results from both SCR and self-reported fear suggest that repeated exposure to the mental image of an in vivo CS+ can facilitate extinction learning. Both the complementary findings and inferential similarities revealed between the subjective and physiological measures also demonstrates the importance of collecting multiple outcome measures based on a multi-component view of emotion (Frijda, 1986; Gross, 2013; Lang, 1993; Larsen & Prizmic-Larsen, 2006; LeDoux & Pine, 2016). While further investigations are needed to confirm and evaluate the underlying cognitive mechanisms of emotion regulation by affective mental imagery, the current study along with the limited experimental literature (Agren et al., 2017; Reddan et al., 2018) provide preliminary support for the clinical application of extinction-based imagery treatments in fear-related affective conditions.

Chapter 3. Psychophysiological and Neurological Evidence for Fear Extinction Learning via Mental Imagery

3.1. Introduction

Mental imagery is the perceptual-like experience of previously perceived stimuli without sensory input from external stimuli (Lewis et al., 2013). It has been frequently mentioned in the literature of affective psychopathology, including anxiety, depression, bipolar, and post-traumatic stress disorder (PTSD). It is recognized as an important component of both symptom presentations of these conditions (e.g., intrusive images in depression, flashbacks in PTSD; Matthews, Collins, Thakkar, & Park, 2014; Weßlau & Steil, 2014), and their clinical treatments, mainly cognitive behavioral therapy (CBT) techniques (e.g., imaginal exposure therapy, image-based cognitive modification; Heyes, Lau, & Holmes, 2013; Holmes & Mathews, 2010; Weßlau & Steil, 2014). The widely used but surprising not adequately supported assumption here is the link between mental imagery and emotion, more specifically, that mental imagery can elicit strong emotional responses and that the latter can in turn be modified through the former.

Among the few existing studies that investigated this connection between mental imagery and emotion, many selected task paradigms are based on associative learning (Agren et al., 2017, 2012; Grégoire & Greening, 2019; Lewis et al., 2013; Reddan et al., 2018). Briefly, associative learning involves the acquisition of the association between an initially neutral stimulus or the conditioned stimulus (CS), and a meaningful stimulus or the unconditioned stimulus (US; Carter, Hofstotter, Tsuchiya, & Koch, 2003). One form of associative learning that is particularly popular is fear conditioning, in which a CS is repeatedly paired with an aversive or threatening US (e.g., a loud noise or mild electric shock). Upon such pairing, the CS subsequently elicits fear responses (e.g., increased heart rate, escape behavior) that were previously associated with the US (R. M. Carter et al., 2003; Critchley et al., 2002). The learned fear responses can then be

attenuated or eliminated with repeated exposures to the CS without the accompanying US pairing (Agren et al., 2017).

Previous functional magnetic resonance imaging (fMRI) studies have reported various brain regions to be associated with fear conditioning and/or extinction, including amygdala, anterior insula cortex (AIC), anterior cingulate cortex (dACC), hippocampus, precuneus, ventral medial prefrontal cortex (vmPFC), and other medial prefrontal regions, etc. (M. M. R. Delgado et al., 2008; LaBar et al., 1998; Lissek et al., 2014; Milad et al., 2007; Phelps et al., 2004). However, not all of these regions were reported in these studies. This inconsistency in research findings is mirrored by methodological heterogeneities among existing research. In two recent meta-analyses, Fullana and colleagues examined the neurological signatures of fear conditioning (Fullana et al., 2016) and fear extinction (Fullana et al., 2018). Unlike many previous independent studies on fear conditioning, the meta-analysis (Fullana et al., 2016) did not find robust involvement of the amygdala, instead, the authors found consistent reporting of activations of AIC and dACC, and deactivations of vmPFC and posterior cingulate cortex in reviewed studies. In the fear extinction meta-analysis (Fullana et al., 2018), the authors again reported no significant amygdala involvement with similar brain activation patterns to fear conditioning with involvement of AIC and dACC but not vmPFC regions.

The current study aims to determine whether fear conditioned association can undergo the process of extinction via mental imagery, and whether such imagery-driven extinction recruits distinct brain regions from experiential extinction learning circuitry (i.e., AIC and dACC). Considering the ample evidence supporting the effectiveness of imagery-based clinical interventions on the reduction of negative affect (Heyes, Lau, & Holmes, 2013; Holmes & Mathews, 2010; Weßlau & Steil, 2014), we hypothesized that fear responses (as measured by

both self-report, skin conductance response [SCR], and brain activations) to visual stimuli would reduce after repeated imaginary exposure to the same stimuli without the accompany of US.

3.2. Method

3.2.1. Participants

Twenty-eight undergraduate students (2 males, mean age of 20.00, *SD* = 2.40) completed this study as part of a larger two-day study. The data presented here was from Day 2 of the study. Day 1 data was described previous publication (Jiang, Burleigh, & Greening, 2021). Seven participants were removed from SCR analyses (2 due to missing data files, 5 due to excessive noise in SCR). Analyses on all the other measures (i.e., self-reported fear, shock estimation, and fMRI) were based on the complete sample. This study was approved by the Institutional Review Board of the Louisiana State University and written informed consent was acquired from all participants prior to the beginning the experiment.

3.2.2. Materials

A set of three letters (i.e., "J," "H," and "F," see figure 3.1. A) were used as the CSs. The US were 100-ms mild electric stimulations which were delivered to the distal phalanx of each participant's ring finger and pinky on his/her non-dominant hand through attached electrodes. The mild electric stimulation used was customized to each participant and a shock level was selected when it was reported to be "uncomfortable but not painful" and was administered through the STMISOC and STM100C modules of BIOPAC Systems.

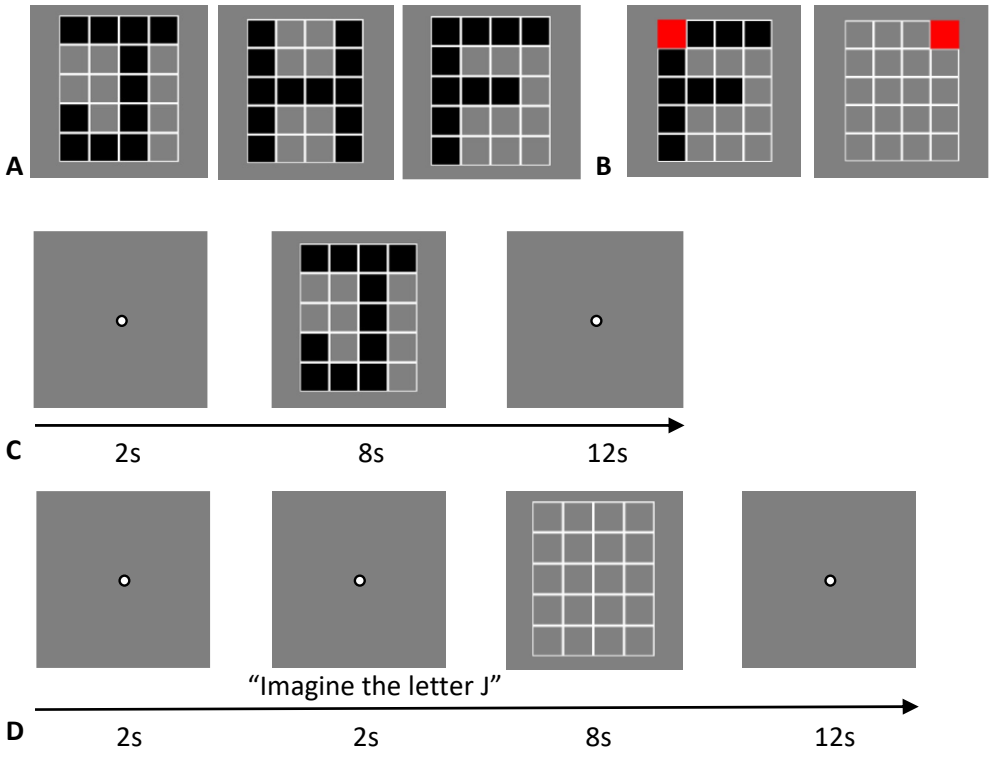

Figure 3.1. Study materials (A), probe task (B), and examples of view (C) and imagine (D) trials.

3.2.3. Procedure

The experimental paradigm and study protocol are illustrated in figure 3.2. and table 3.1. The current study was composed of two habituations, one acquisition, and two extinctions in order. In habituations, participants were instructed to view and imagine the CSs, i.e., "J," "H," and "F". After completion of the first habituation (habituation 1), which occurred outside the scanner, participants proceeded with the remaining procedures in the scanner starting with the second habituation (habituation 2). In acquisition, visual images of the CSs were presented to the participants. The CS+s (i.e., "J" and "H") were paired with the US 50% of the time while the CS- (i.e., "F") was never paired with the US. Following acquisition, all participants continued to the first extinction (extinction 1) in which they were instructed to image one of the CS+s (i.e., CS+IV; "J" or "H," counterbalanced across participants) and the CS-. In the second extinction

(extinction 2) all CSs were visually presented again. Stimuli presentation scheduling details see figure 3.2.

A separate functional localizer task was added to the end of the study. Twenty fear and 20 neutral images were selected from the International Affective Picture System (P. J. Lang, Bradley, & Cuthbert, 2008) and the Nencki Affective Picture System (Marchewka, Żurawski, Jednoróg, & Grabowska, 2014). All images were transformed into black and white and their low level visual properties (i.e., luminance and contrast) were controlled using the SHINE Matlab toolbox (Willenbockel et al., 2010). The images were visually presented to each participant using a block design (see figure 3.2. D for scheduling details). The presentation was randomized both in terms of the block order and images within each block. Each block was presented for 10 s (2.5 s for each image) with intervals of 10 s between blocks.

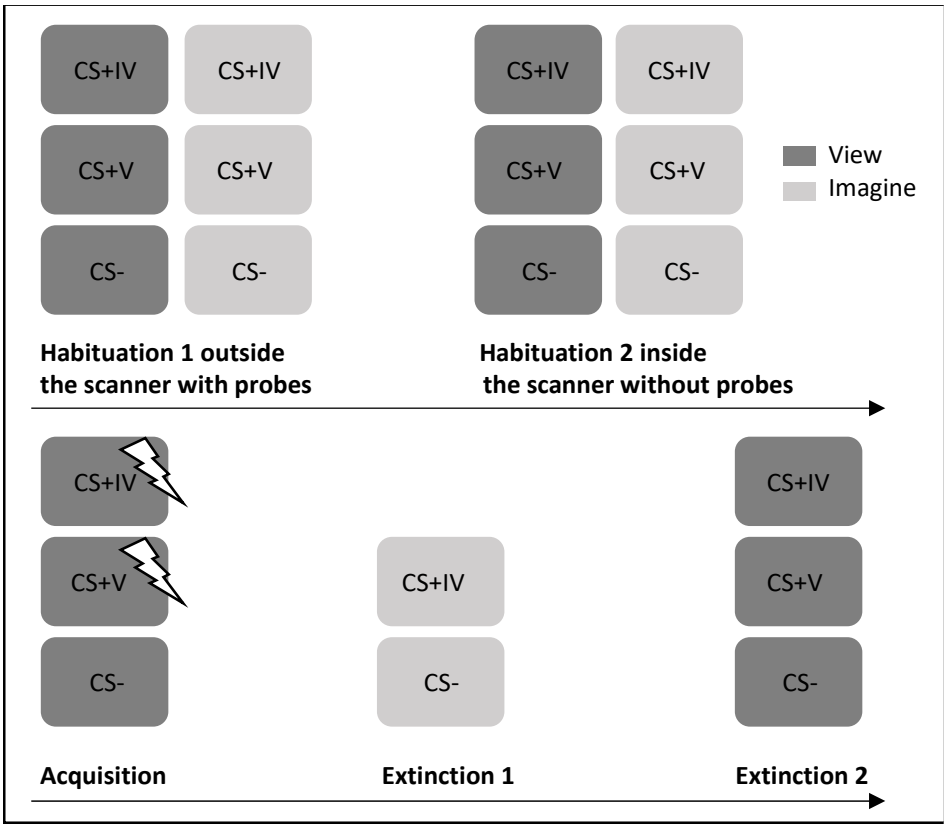

Figure 3.2. Study procedure including habituation/practice 1 and 2 during which participants viewed and imagined all three CSs (i.e., CS+IV, CS+V, CS-); acquisition where participants viewed all three CSs and the CS+s were paired with shock 50% of the time; extinction 1, where participants imagined CS+IV and CS-; and extinction 2, where participants viewed all CSs again.

Table 3.1. Trial compositions for the study.

Fear Learning	Functional Localizer
Habituation 1 and 2 2 view and 2 imagine CS+IV 2 view and 2 imagine CS+V 2 view and 2 imagine CS- x 2 runs	5 Fear blocks 5 Neutral blocks (4 difference images in each block)
Acquisition 2 view CS+IV and 2 view CS+IV/US 2 view CS+V and 2 view CS+V/US 4 view CS- x 4 runs	
Extinction 1 6 imagine CS+IV 6 imagine CS- x 2 runs	
Extinction 2 4 view CS+IV 4 view CS+V 4 view CS- x 2 runs	

3.2.4. Probe

Probes were added to habituation 1 as a way of making sure that participants are picturing the letters correctly and also as a measure of how well they are able to imagine the letters. A single square in the grid filled in in red appearing at a location randomly selected from a set of positions on the 4 x 5 grid was used as the probe (see figure 3.1. B). The participants were instructed to respond quickly as possible by either pressing 1 if he/she thought the probe was on the letter presented/imagined or 2 if the probe was deemed to be off the letter. A response window of 2s was applied. Within each run, the probe had a 50% chance to be on the target letter. Probes were added to each trial at either 4, 5, or 6 s after stimulus onset. This

randomization of probe timing should reduce or eliminate expectancy so that participants' reaction time to probes were more representative of their scanning and mental formation of images of letter stimuli.

3.2.5. Subjective Ratings

Participants were surveyed on their fear of shock and the estimated percentage of shock paired with each CS after acquisition, extinction 1 and 2. Participants reported their fear of each CS on a 7-point Likert scale (between 1 = "Not At All" and 7 = "Very Much So"). A 10-point Likert scale (between 0% and 100% with intervals of 10%) was used as estimations of shock contingency of each CS. Participants also provided self-reported evaluations of their vividness of the mental images on a 7-point scale ranging (from 1 = "Non-Existent" to 7 = "Very Strong") and their effort when forming mental images on a 7-point scale ranging (from 1 = "Not At All" to 7 = "Very Hard"). Participants were followed up after functional localizer task on their fear levels of each image presented. A 5-point Likert scale was used here (from 1 = "Not At All" to 5 = "Very Much So").

3.2.6. Physiological Responses Recording

Electrodermal activity was recorded with the Biopac MP-150 system and AcqKnowledge software (BIOPAC systems, Goleta, CA, USA) and was sampled at 2000 Hz.

Analyses were carried out in MATLAB R2018a (Version 9.4) on SCR signals. A first-order Butterworth bandpass filter was applied with cut-off frequencies of .01 and 5 Hz (Bach, Flandin, Friston, & Dolan, 2010). Time series were then down-sampled to 100 Hz. SCRs to the CSs were calculated by subtracting baseline (1 second before stimulus onset) from the peak amplitude (during 1-7.9 s after stimulus onset; Grégoire & Greening, 2019; Leys, Ley, Klein, Bernard, & Licata, 2013; Milad et al., 2007; D. Schiller, Kanen, LeDoux, Monfils, & Phelps, 2013; Daniela

Schiller et al., 2010; Vervliet, Vansteenwegen, Baeyens, Hermans, & Eelen, 2005). Peaks were removed if their distance from the baseline was smaller than .02 µS or if it appeared outside of the 1-7.9 s timeframe. The difference scores were then square root transformed. Shock trials were excluded as these SCRs may be more reflective of the unconditioned responses to the US instead of the conditioned ones to the CS (Greening, Lee, & Mather, 2016), though these US trials were included as nuisance regressors in first level fMRI analyses. The first and last trial of each acquisition run was a CS- trial which was also excluded from the analyses, though they were again included in fMRI analyses as nuisance regressors. This was done to avoid the potential confounding orienting effect of the first trials (Grégoire & Greening, 2019; Lonsdorf et al., 2017) and to ensure that each condition had an equal number of trials in the primary analyses.

3.2.7. MRI Data Collection and Analysis

MRI Acquisition: Participants were scanned during day two procedures from the beginning of habituation 2 to the end of functional localizer. Imaging data was collected on a GE MR750w 3.0T system with a 32-channel MR Instruments head coil at Pennington Biomedical Research Center, Baton Rouge, Louisiana. T1-weighted structural images were acquired using a three-dimensional fast spoiled gradient-echo (FSPGR) sequence (TR = 8.7 ms, TE = 3.8 ms, flip angle = 8°, 256 × 256 matrix, phase encoding direction anterior to posterior, FOV = 25.6 cm). One hundred eighty sagittal slices covering the entire brain were acquired in sequential order producing a voxel resolution of 1mm isotropic. T2*-weighted functional scans were acquired using gradient-echo echo-planar imaging (EPI; TR = 2000 ms, TE = 25 ms, flip angle = 90°, 64 x 64 matrix, phase encoding direction anterior to posterior, FOV = 22.4 cm). Thirty-six axial slices covering the whole brain were acquired with a voxel resolution of 3.5 mm isotropic with no gap. Slices were acquired in interleaved ascending order. Each functional scan began with

three dummy volumes to account for equilibrium effects, and these dummy volumes were discarded from the analyses during preprocessing. The number of volumes varied for each portion of the experiment. Specifically, each habituation run had 130 volumes, each acquisition run had 124 volumes, each extinction 1 run had 136 volumes, each extinction 2 run had 124 volumes, and the functional localizer run had 108 volumes.

fMRI Preprocessing and Whole-Brain Univariate Analyses: fMRI data was analyzed using FEAT (FMRI Expert Analysis Tool) Version 6.0, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Registration to participant structural and standard space images was carried out using FLIRT (Jenkinson, Bannister, Brady, & Smith, 2002; Jenkinson & Smith, 2001). Pre-statistics processing applied include: motion correction using MCFLIRT (Jenkinson et al., 2002); slice-timing correction using Fourier-space time-series phase-shifting; non-brain removal using BET (Smith, 2002); spatial smoothing using a Gaussian kernel of FWHM 7mm; grand-mean intensity normalization by a single multiplicative factor; and highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma=50.0s). The time-series modeling was carried out using FILM with local autocorrelation correction (M. W. Woolrich, Ripley, Brady, & Smith, 2001).

At the single-subject level each run was modelled separately. A double-gamma hemodynamic response function convolution was used on each of the conditions of interest/explanatory variables (i.e., CS+IV, CS+V, CS-, CS+IV/US, CS+V/US, and first and last CS- trials in acquisition) inputted in Custom (3 column format) basic shape. Temporal derivatives of each condition of interest were added. Several nuisance regressors were added, including six original motion parameters, extended motion parameters, and framewise displacement (FD) = 0.9 mm motion censoring (Siegel et al., 2014) using the fsl_motion_outliers

function. A second-level analysis was performed to average over contrast estimates from the first level analysis for each experimental phase (e.g., acquisition) for each participant. As noted previously US (i.e., CS+IV/US, CS+V/US) trials and the first and last CS- trials in acquisition were not used in higher-level analyses. These analyses were carried out using a fixed effects model in FLAME (FMRIB's Local Analysis of Mixed Effects), with the random effects variance forced to zero (Beckmann, Jenkinson, & Smith, 2003; M. Woolrich, 2008; M. W. Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004). Group-level analyses were carried out using FLAME (FMRIB's Local Analysis of Mixed Effects) stage 1 (Beckmann, Jenkinson, & Smith, 2003; M. Woolrich, 2008; M. W. Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004). The resulting z (Gaussianised T/F) statistic images were thresholded using clusters determined by z > 2.3 and a cluster significance threshold of $p = 0.05$ (Worsley, 2001).

3.3. Results

3.3.1. Acquisition

Subjective and Physiological Data: Acquisition was examined using repeated-measures analyses of variance (ANOVAs) with CS type (i.e., CS+IV, CS+V, and CS-) as the within-subject factor on self-reported fear, mean SCR, and shock estimation separately (figure 3.3. B). Greenhouse–Geisser correction for non-sphericity was applied when needed. Significant findings were followed by post hoc paired *t*-tests without corrections (Saville, 1990). These three ANOVAs returned consistent results with significant main effects of CS type on self-reported fear ($F(1.64, 44.26) = 70.16$, $p < .001$, $\eta_p^2 = .72$), SCR ($F(1.53, 30.69) = 5.85$, $p = .012$, $\eta_p^2 = .23$), and shock estimations ($F(2, 54) = 77.58$, $p < .001$, $\eta_p^2 = .74$). Post-hoc *t*-tests revealed differential conditioning for both of the two CS+s (i.e., CS+IV and CS+V) on all three measures. Specifically, participants had greater self-reported fear for CS+IV ($M = 5.11$, $SD = 1.26$; $t(27) =$

9.04, $p < .0001$) and CS+V($M = 5.11$, $SD = 1.37$; $t(27) = 9.46$, $p < .0001$) than the CS- ($M = 1.96$, $SD = 1.57$). They also had larger SCR for CS+IV ($M = .20$, $SD = .21$; $t(20) = 2.55$, $p = .02$) and CS+V($M = .20$, $SD = .19$; $t(20) = 2.72$, $p = .01$) compared to the CS- ($M = .10$, $SD = .11$). Higher likelihood of shock was reported for CS+IV ($M = 59.29$, $SD = 16.31$; $t(27) = 9.22$, $p < .0001$) and CS+V ($M = 58.57$, $SD = 14.07$; $t(27) = 10.88$, $p < .0001$) than the CS- ($M = 9.64$, $SD = 19.53$). The two CS+s did not differ on any of these measures (self-reported fear: $t(27) = .00$, $p = 1.00$; SCR: $t(20) = .00$, $p = 1.00$; shock estimation: $t(27) = .20$, $p = .85$).

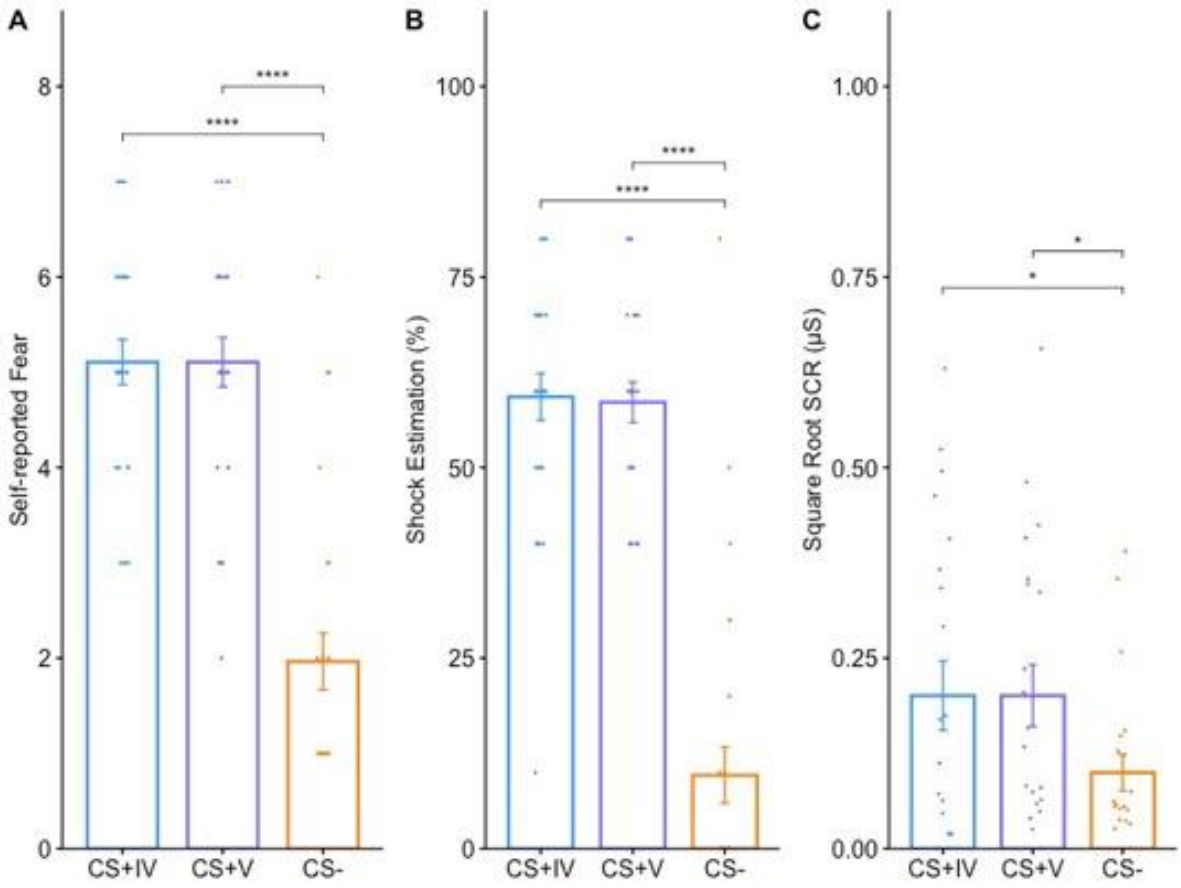

Figure 3.3. Self-reported fear (A), shock estimation (B), and mean SCR (C) during acquisition. Error bars show ± 1 standard error. Each dot represents one subject.
* $p < .05$. ** $p < .01$. *** $p < .001$. **** $p < .0001$.

Univariate Whole Brain Data: A network of regions associated with differential fear conditioning (Fullana et al., 2016) were found to exhibit significant functional activation during

acquisition. Specifically, significantly greater signals were found in parts of bilateral AIC and bilateral dACC when viewing both CS+s compared to the CS- (figure 3.4.).

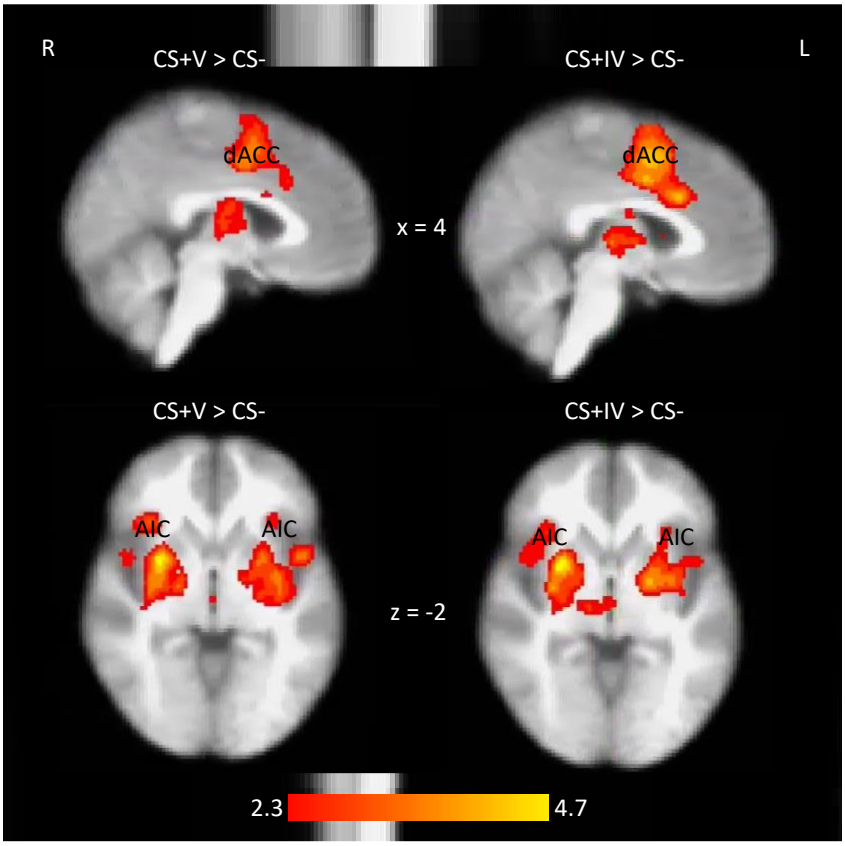

Figure 3.4. Univariate whole brain analysis results during acquisition comparing CS+V and CS- (left) and CS+IV and CS- (right).

Univariate Region-Of-Interest (ROI) Analysis: Based on univariate whole brain results, ROI masks were created in left AIC (L-AIC), right AIC (R-AIC), and bilateral dACC using meta-analysis results by Fullana et al. (2016). These ROI masks were then applied to univariate whole brain data during acquisition. The same ANOVAs from subjective and physiological data analyses were conducted on mean brain activations during acquisition within each ROI (figure 3.5.). Significant main effects of CS type were found in all three ROIs, including L-AIC ($F(1.55, 41.85) = 3.55$, $p = .048$, $\eta_p^2 = .12$), R-AIC ($F(1.56, 42.20) = 9.33$, $p = .001$, $\eta_p^2 = .26$), and bilateral dACC ($F(2, 54) = 13.55$, $p < .001$, $\eta_p^2 = .33$). Post-hoc *t*-tests provided support for both

CS+s in R-AIC and bilateral dACC, and only for CS+V in L-AIC. Specifically, in R-AIC, CS+IV (M = 2.82, SD = 1.27; $t(27) = 3.70$, $p < .001$) and CS+V (M = 2.58, SD = 1.33; $t(27) = 2.89$, $p = .008$) both had greater activations than the CS- (M = 1.52, SD = 1.65). No difference was found between the two CS+s ($t(27) = 1.06$, $p = .30$). The same pattern was found in dACC (CS+IV: M = 2.50, SD = 1.74; CS+V: M = 2.54, SD = 1.72; CS-: M = .88, SD = 1.66; CS+IV vs CS-: $t(27) = 4.33$, $p < .001$; CS+V vs CS-: $t(27) = 4.01$, $p < .001$; CS+IV vs CS+V: $t(27) = -.13$, $p = .90$). In L-AIC, however, differential fear was only evident for CS+V (M = 1.88, SD = 1.48; $t(27) = 2.20$, $p = .04$) when compared with CS- (M = 1.07, SD = 1.62). CS+IV (M = 1.77, SD = 1.76) did not differ from CS- ($t(27) = 1.87$, $p = .07$) or CS+V ($t(27) = -.50$, $p = .63$).

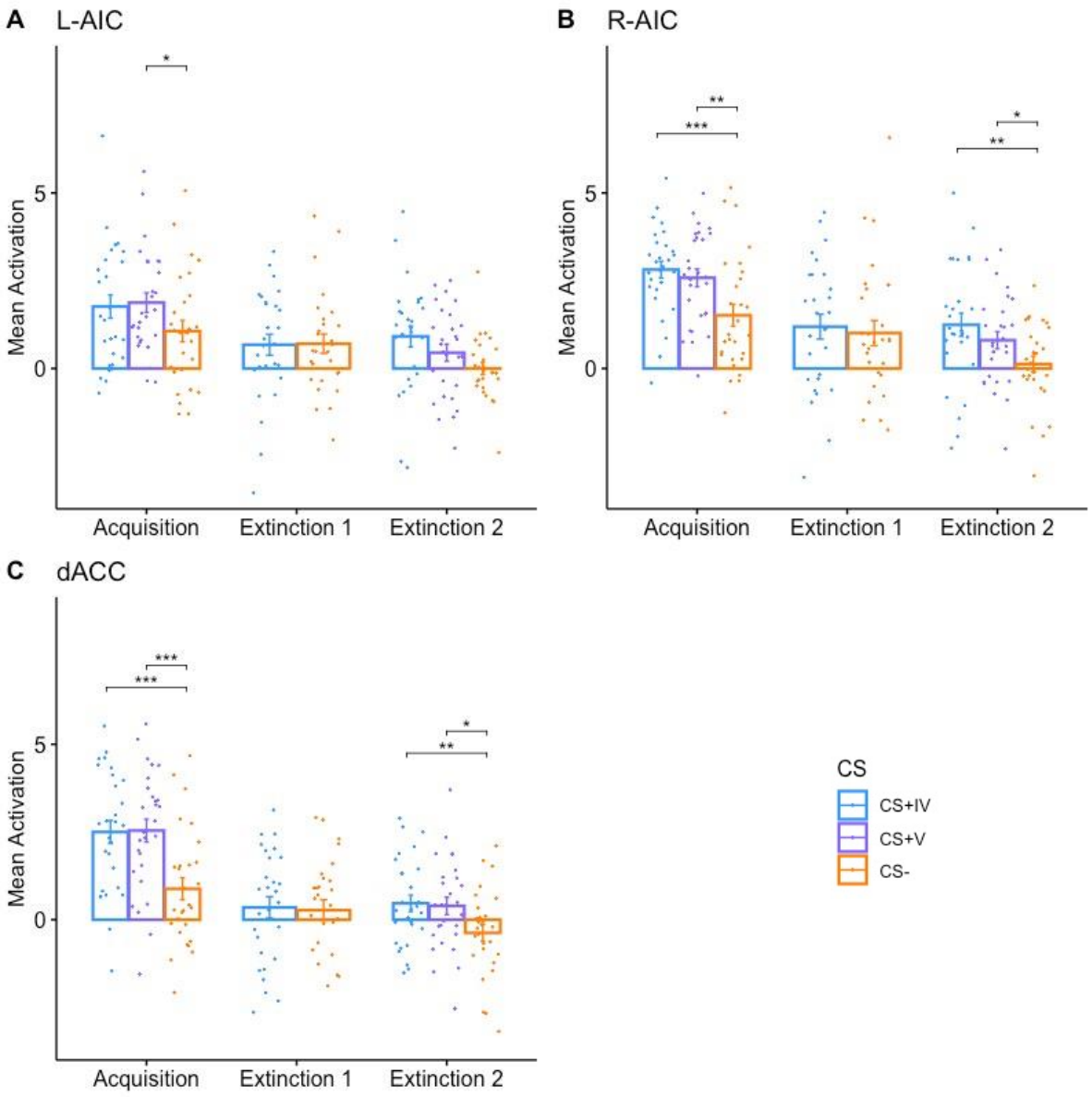

Figure 3.5. Results of ROI analyses of mean brain activations during each study phase in ROIs L-AIC (A), R-AIC (B), and bilateral dACC (C). Error bars show ± 1 standard error. Each dot represents one subject.
* $p < .05$. ** $p < .01$. *** $p < .001$. **** $p < .0001$.

3.3.2. Extinction 1

Subjective and Physiological Data: Mean SCR were separated into early (first half of trials) and late (second half of trials) extinction 1 responses. A 2x2 repeated measures ANOVA

with CS type (i.e., CS+IV and CS-) and time (i.e., early and late) as the within-subject factors revealed significant main effects of both CS type ($F(1, 20) = 7.58$, $p = .01$, $\eta_p^2 = .27$) and time ($F(1, 20) = 4.68$, $p = .04$, $\eta_p^2 = .19$), with no interaction ($F(1, 20) = 0.71$, $p = .410$). Paired *t*-tests were then carried out on mean SCR across early and late extinction 1 in addition to self-reported fear and shock estimation during extinction 1 to contrast CS+IV and CS- (figure 3.6.). Results based on self-reported fear and SCR supported a generalization of differential fear from viewing to imagining CS+IV. Specifically, CS+IV had greater self-reported fear ($M = 3.18$, $SD = 2.02$; $t(27) = 2.78$, $p = .01$) and SCR ($M = .17$, $SD = .11$; $t(20) = 2.75$, $p = .01$) than the CS- (self-reported fear: $M = 2.00$, $SD = 1.83$; SCR: $M = .13$, $SD = .10$) when imagined during extinction 1. These elevations of subjective and physical fear responses were apparent despite participants' accurate knowledge of shock estimations during extinction 1. Close to 0% of shock likelihoods were reported for both CS+IV ($M = 2.75$, $SD = 7.55$) and CS- ($M = 5.00$, $SD = 14.78$), and a paired *t*-test revealed no significant difference $t(27) = -1.06$, $p = .30$. Paired *t*-test contrasting early and late mean SCR responses across CS type indicated that participants had larger SCR during early extinction 1 ($M = .17$, $SD = .12$) compared to late extinction 1 ($M = .14$, $SD = .10$), $t(20) = 2.16$, $p = .04$.

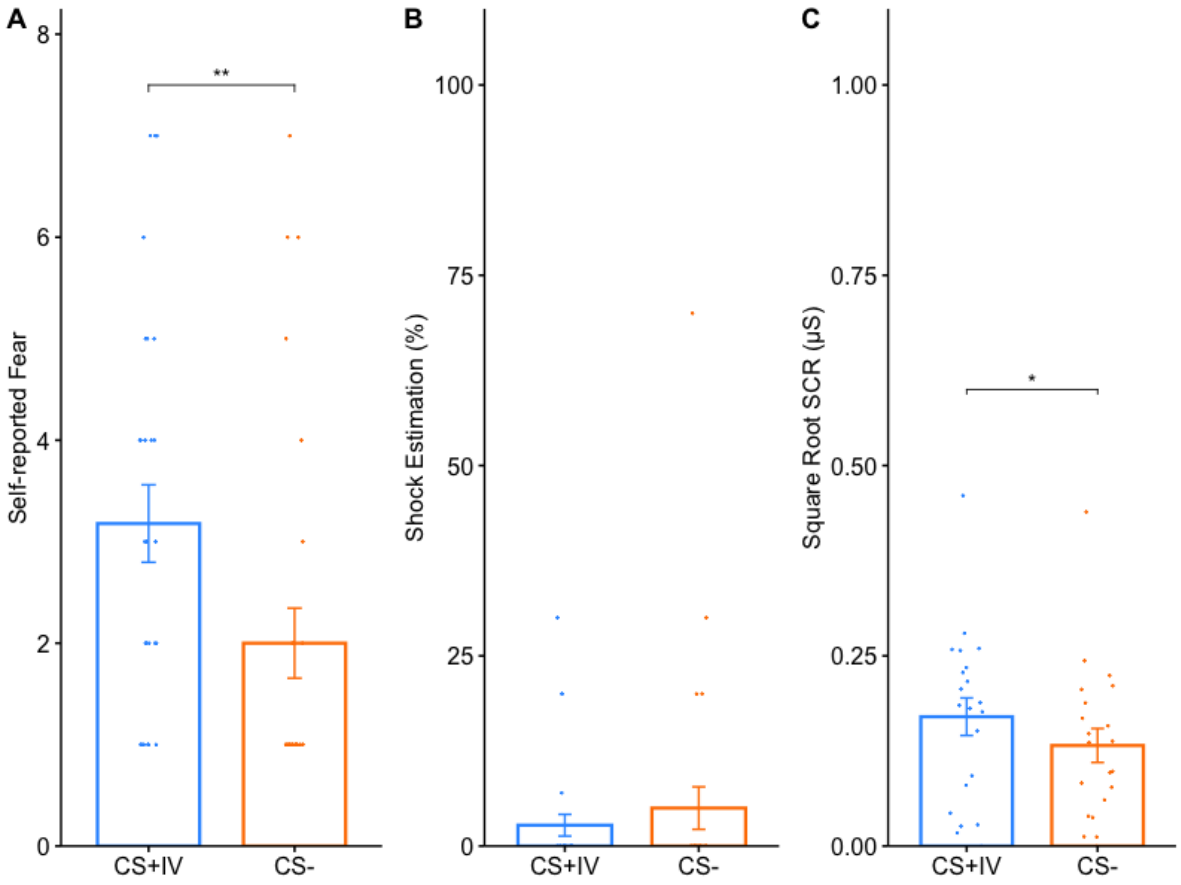

Figure 3.6. Self-reported fear (A), shock estimation (B), and mean SCR (C) during extinction 1. Error bars show ± 1 standard error. Each dot represents one subject.
* $p < .05$. ** $p < .01$. *** $p < .001$. **** $p < .0001$.

Univariate Whole Brain Data: Univariate whole brain analysis contrasting imagining CS+IV and CS- during extinction 1 yielded no significant findings.

Univariate ROI Analysis: As L-AIC ROI did not possess evidence of differential fear for both CS+s during acquisition, it was not included in extinction analyses. Paired *t*-tests were conducted on mean activations during extinction 1 within ROIs R-AIC and bilateral dACC comparing imagining CS+IV and CS- (figure 3.5.). No significant results were found in either of the two selected ROIs. In R-AIC, CS+IV ($M = 1.19$, $SD = 1.87$) showed no elevation compared to CS- ($M = 1.01$, $SD = 1.89$), $t(27) = .42$, $p = .68$. The same was found in dACC, where CS+IV

(*M* = .35, *SD* = 1.60) and CS- (*M* = .27, *SD* = 1.56) had similar levels of activations, *t*(27) = .19, *p* = .85.

3.3.3. Extinction 2

Subjective and Physiological Data: Mean SCR were again separated into early (first half of trials) and late (second half of trials) extinction 2 responses. A 3x2 repeated measures ANOVA with CS type (i.e., CS+IV, CS+V, and CS-) and time (i.e., early and late) as the within-subject factors reported significant main effects of CS type ($F(2, 40) = 3.58$, $p = .04$, $\eta_p^2 = .15$) and time ($F(1, 20) = 8.52$, $p = .008$, $\eta_p^2 = .30$). No significant interaction was found ($F(2, 40) = 2.10$, $p = .14$). The same ANOVAs carried out on acquisition data were then repeated on extinction 2 data (figure 3.7.). While self-reported fear ($F(2, 54) = 6.49$, $p = .003$, $\eta_p^2 = .19$) and SCR ($F(2, 40) = 3.58$, $p = .037$, $\eta_p^2 = .15$) analyses both reported significant main effects of CS type, post-hoc analyses yielded somewhat different results. Based on self-reported fear data, differential fear was still apparent for both CS+s during extinction 2. Specifically, participants reported higher levels of fear for CS+IV (*M* = 2.54, *SD* = 1.69; *t*(27) = 2.70, *p* = .01) and CS+V (*M* = 2.57, *SD* = 1.62; *t*(27) = 3.42, *p* = .002) in contrast to the CS- (*M* = 1.64, *SD* = 1.10) with no difference between the two CS+s, *t*(27) = -.13, *p* = .90. Paired *t*-tests on mean SCR, however, provided evidence of differential fear only for the CS+V (*M* = .21, *SD* = .16; *t*(20) = 2.28, *p* = .03) and not for the CS+IV (*M* = .20, *SD* = .18; *t*(20) = 2.04, *p* = .06) in contrast with CS- (*M* = .14, *SD* = .11). Again, the two CS+s did not differ, *t*(20) = -.43, *p* = .67. Similar to extinction 1, averaged SCR across early and late extinction 2 was larger during the first half (*M* = .21, *SD* = .15) compared to the second half of trials (*M* = .16, *SD* = .13), *t*(20) = 2.92, *p* = .008.

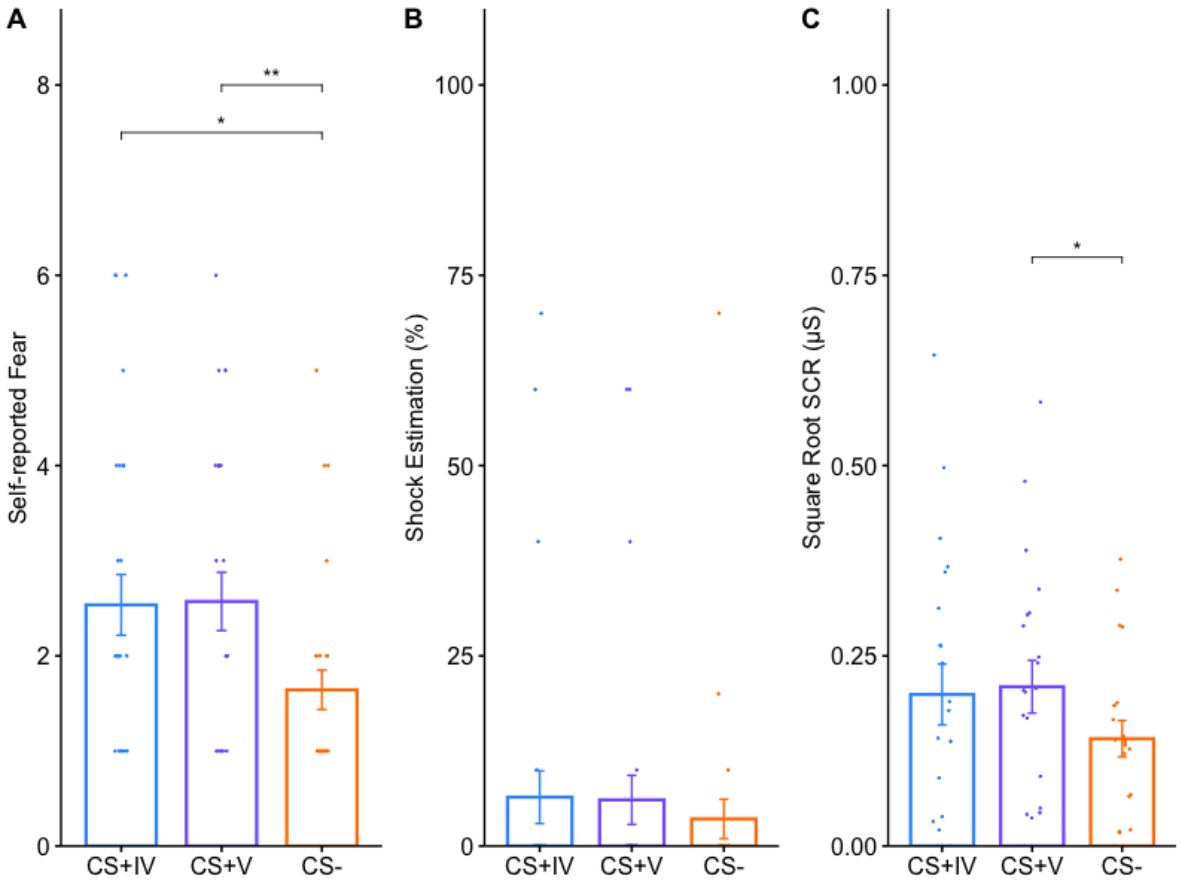

Figure 3.7. Self-reported fear (A), shock estimation (B), and mean SCR (C) during extinction 2. Error bars show ± 1 standard error. Each dot represents one subject.
* $p < .05$. ** $p < .01$. *** $p < .001$. **** $p < .0001$.

Univariate Whole Brain Data: Again, no significant findings were found by univariate whole brain analysis during extinction 2 in any contrast pairing of CS conditions.

Univariate ROI Analysis: The same ANOVAs applied to acquisition ROI analysis were repeated here in ROIs R-AIC and bilateral dACC (figure 3.5.). It was found that differential fear was still evident based on mean activations in both ROIs. Specifically, there were significant main effects of CS type in R-AIC ($\eta_p^2 = .12$) and bilateral dACC ($\eta_p^2 = .33$). Results of post-hoc *t*-tests revealed that in R-AIC, CS+IV ($M = 1.24$, $SD = 1.75$; $t(27) = 3.46$, $p = .002$) and CS+V ($M = .81$, $SD = 1.29$; $t(27) = 2.26$, $p = .03$) both had greater activations than the CS- ($M = .13$, $SD = 1.19$). No difference was found between the two CS+s ($t(27) = 1.36$, $p = .19$). The same was

true in dACC, where CS+IV (M = .47, SD = 1.25; $t(27) = 2.93$, p = .007) and CS+V (M = .39, SD = 1.31; $t(27) = 2.65$, p = .01) had significant elevations compared to the CS- (M = -.37, SD = 1.25). Again, no difference was found between the two CS+s ($t(27) = .27$, p = .79).

3.4. Discussion

The current study sought to assess the assumption that mental imagery has the capacity to regulate emotions similar to perceptual counterpart and its underlying psychophysiological and neurological mechanisms. We found that both CS+ (i.e., CS+IV and CS+V) acquired differential fear supported by elevations in self-reported fear and SCR. After applying ROI masks to fMRI data, we observed evidence of differential fear in R-AIC and bilateral dACC consistent with findings by Fullana el al. (2016) confirming the relevance of AIC and dACC in fear learning. This conditioned fear then generalized to mental imagery captured by greater self-reported fear coupled with SCR in CS+IV in comparison to CS- during imagery in extinction 1. However, no such difference was found in ROIs (i.e., R-AIC and bilateral dACC). Considering that generalized fear was evident in the other two measures (i.e., self-reported fear and SCR), this lack of discrimination in the selected ROIs may indicate that affective perception and imagery may involve different brain regions. Upon re-exposure to viewing CSs in extinction 2, results from analyses of physiological responses (i.e., SCR) indicated that only CS+V but not CS+IV still exhibited differential fear. This suggested that after repeated mental imagery exposure, conditioned fear was no longer apparent (in the case of CS+IV). Importantly, the CS that did not went through imagery exposure (i.e., CS+V) still evidenced differential fear indicative of a spontaneous recovery of differential conditioning (Huff, Hernandez, Blanding, & LaBar, 2009). This contrast between CS+IV and CS+V confirmed that fear extinction took place via imagery exposure.

The above descriptions of SCR results in extinction 2 provided confirmatory answers to the main research question, however, self-reported fear and ROI analyses provided results. Specifically, participants reported higher fear ratings for both CS+s (i.e., CS+IV and CS+V) than the CS-; and in both ROIs (i.e., R-AIC and bilateral dACC), the two CS+s (i.e., CS+IV, CS+V) similarly had greater activations in contrast to the CS-. This persistence of elevated self-reported fear is consistent with previous findings (Lau et al., 2008; Shechner et al., 2015), and may be indicative of stable declarative knowledge of CS-US pairing even after extinction. Subsequently, this declarative knowledge may have driven the significant differential activations in AIC and dACC (Tabbert et al., 2011). Future research may further explore this inconsistency between SCR measures with self-reported fear and brain activations by introducing manipulations of contingency awareness.

Taken together, findings of this investigation provided support for the assumption that repeated exposure to the mental imagery of an CS+ can result in extinction of conditioned fear consistent with the limited existing experimental literature (Agren et al., 2017; Reddan et al., 2018). While findings were mostly consistent across different fear indices (i.e., self-reported fear, SCR, and brain activations), differences emerged during extinction 2, emphasizing the importance of recruiting multiple sources of measurement in emotion research (Frijda, 1986; Gross, 2013; P. J. Lang, 1993; Larsen & Prizmic-Larsen, 2006; LeDoux & Pine, 2016). The current study also confirmed that brain regions including AIC and dACC are involved in differential fear learning (Fullana et al., 2016). However, unlike Greening et al. (2021), we did not observe activations of the insular in response to visual imagery of conditioned stimuli. This is perhaps the result of methodological differences. Specifically, while here the CS+ was imagined after completion of perceptual conditioning, in Greening et al. (2021), the CS+ was imagined

during conditioning. Further research is needed to assess brain regions involved in affective imagery in fear conditioning.

Chapter 4. Complete the Triangulation: Quantifying Differential Fear Conditioning with a Noninterfering and Sensitive Behavioral Measure Along with Self-report and Physiological Measures

4.1. Introduction

Emotions, such as fear, are multi-component construct that involve subjective feelings and thoughts, physiological activation, and behavioral responses (Frijda, 1986; Gross, 2013; Lang, 1993; Larsen & Prizmic-Larsen, 2006). Since the Little Albert study (Watson & Rayner, 1920), Pavlovian fear conditioning has been one of the most popular experimental paradigms in fear research. Fear conditioning has unique translational values as the mechanisms and outcomes of fear conditioning can be studied across a range of animal models in addition to both typical and clinical human populations (Hofmann, 2008; Marks & Tobeña, 1990). One type of popular fear conditioning paradigm is differential fear conditioning, which involves two conditioned stimuli (CS). While one (CS+) is paired with an unconditioned stimulus (US) such as a mild shock such that subsequent presentations of the CS+ without the US produce a conditioned response (CR), the other CS (CS-) is never paired with the US and thus does not acquire the CR. The differences between CR to the CS+ versus the CS- are taken as indices of fear and serve as the measurements of conditioning.

More recently, discussions around the issue of reproducibility and replicability in fear conditioning research have arisen (Lonsdorf et al., 2017). One subject of particular interest is the selection of outcome measures for the quantification of the CR. Some of the most common dependent variables in human fear conditioning literature include self-report (e.g., ratings of fear to the CS or expectancy of US), and physiological measures (e.g., skin conductance responses/SCRs, fear-potentiated startle responses/FPS, heart rate; Lonsdorf et al., 2017) during CS presentations. In contrast, while research has demonstrated that following acquisition, fear

conditioned stimuli can affect subsequent behavioral measures in tasks such as affective priming (e.g., Hermans, Vansteenwegen, Crombez, Baeyens, & Eelen, 2002) and dot-probe (e.g., Haddad, Lissek, Pine, & Lau, 2011), very few studies with human participants included behavioral measures, such as reaction time (RT), during the acquisition phase of fear conditioning. One cited concern is that the addition of concurrent behavioral probes may affect the acquisition of fear conditioning itself, or interfere with the other dependent measures (Lipp, 2007). To the authors' knowledge, this specific concern has not been addressed in previous human conditioning studies that included a concurrent behavioral assay (e.g., visual response probes) involving RT measures (Critchley, Mathias, & Dolan, 2002; Gottfried & Dolan, 2004; Hermans et al., 2005; Koster, Crombez, van Damme, Verschuere, & de Houwer, 2005; Morris & Dolan, 2004; Romaniuk et al., 2010).

On the one hand, if fear conditioning can be acquired automatically then there is no concern that concurrent behavioral probes will interfere with acquisition of differential conditioning. For example, some studies reported that unconscious fear conditioning can be observed under certain conditions, such as during delay conditioning but not trace conditioning (Knight, Nguyen, & Bandettini, 2006), when differential conditioning is measured using FPS assays such as the eye-blink startle reflex in humans instead of the SCR (Sevenster, Beckers, & Kindt, 2014) and when the CSs are fear-relevant instead of fear-irrelevant (Esteves, Parra, Dimberg, & Öhman, 1994). However, a systematic review by Mertens and Engelhard (2020) concluded that there is no evidence of specific conditions under which differential fear conditioning occurs in a strictly automatic fashion.

Considering the multi-component view that emotion cannot be captured by any measure alone (Lang, 1968; Mauss & Robinson, 2009; Rachman, 1978), it is necessary to find ways to

incorporate behavioral descriptions in emotion research. Moreover, if fear conditioning is not strictly an automatic process, research is needed to evaluate whether a certain behavioral probe interferes with other outcome measures of differential conditioning (e.g., the SCR, or self-reported fear). Additionally, research is needed to evaluate whether a certain behavioral probe produces a behavioral index that is sensitive to conditioning (e.g., differential RT to the CS+ versus the CS-). Thus, an optimal concurrent behavioral measure of differential fear conditioning would not disrupt other measures of conditioning, and would be sensitive to differences in the CS+ versus the CS-. One recent example is eye gaze pattern (Xia, Melinscak, & Bach, 2020), though its utilization requires eye-tracking equipment and is limited to visually presented CSs. Another option are traditional response-based assays of behavior such as RT as mentioned previously (Critchley et al., 2002; Gottfried & Dolan, 2004; Hermans et al., 2005; Koster et al., 2005; Morris & Dolan, 2004; Romaniuk et al., 2010).

Two noteworthy studies have found that a concurrent behavioral task interacts with fear conditioning, and that the magnitude of interference increases with task demands (Carrillo, Gabrieli, & Disterhoft, 2000; Carter, Hofstotter, Tsuchiya, & Koch, 2003). Carrilo et al. (2000) combined secondary tasks (i.e., watching silent movie, verbal shadowing) with both single-cue and differential conditioning. Analyses of conditioned eye-blink startle indicated that while single-cue conditioning was not affected by the distraction tasks, the degree of difference in differential conditioning was significantly reduced in the presence of distractions. Based on SCR analyses, Carter et al. (2003) found that both differential delay and trace conditioning are affected by a concurrent working-memory task, though delay conditioning still occurred when the working memory load was low (i.e., a 1-back task). While these two studies provide some support that low-demand behavioral tasks may be carried out concurrently while conserving a

degree of differential conditioning as measured by eye-blink startle response and SCR separately, neither examined whether the behavioral measures (i.e., RT or accuracy) themselves were sensitive measures of differential fear conditioning. Moreover, neither study evaluated subjective fear response, leaving the triangulation of fear incomplete with only physiological but not subjective or behavioral descriptions.

The scarcity of behavioral assays in human fear conditioning research stands in strong contrast to animal models, which rely greatly on behavioral measures such as freezing (e.g., Quirk, Russo, Barron, & Lebron, 2000) and approach/avoidance (e.g., Leiner & Fendt, 2011) behaviors. Considering that subjective/verbal reports do not apply to animal research, the lack of behavioral descriptions restricts translations between human and animal research to physiological (e.g., Leiner & Fendt, 2011; McEchron, Tseng, & Disterhoft, 2000) and neurological (for a review, see Delgado, Olsson, & Phelps, 2006) responses. With the support of non-interfering behavioral probes and sensitive behavioral measures, researchers can bridge this gap in translational studies. Further, this would allow simultaneous employment of behavioral in addition to verbal and psychophysiological measures echoing the multi-component view that emotion cannot be captured by any measure alone (Lang, 1968; Mauss & Robinson, 2009; Rachman, 1978). Indeed, evidence suggests that although subjective, behavioral, and physiological measures are meant to quantify the same construct of emotion, they do not necessarily converge (Hollenstein & Crowell, 2014; Mauss & Robinson, 2009). One explanation for this is that the various measures reflect independent sources of information which combine in specific patterns to reflect a given emotion (Bulteel et al., 2014; Kragel & LaBar, 2013). Thus, a diverse pool of outcome measures is required for a comprehensive quantification of fear. An

ideal design would include indices from all of the above three categories (i.e., subjective, behavioral, and physiological) constituting a complete triangulation of fear.

The primary purpose of the current study was twofold. First, the present study sought to assess whether a basic visual attention task influenced differential visual fear conditioning as measured by subjective (i.e., self-reported fear, shock estimation) and physiological (i.e., SCR) measures. Second, the study aimed to determine if the corresponding behavioral measure associated with the attention task (i.e., RT) was sensitive to differential conditioning as indicated by a significant difference between the CS+ and the CS-. The study also considered an exploratory investigation of the relationship between the different measures, including self-reported fear, shock estimation, SCR, and RT.

4.2. Method

4.2.1. Participants

One hundred and sixty-nine undergraduate students completed this study as day 1 of a two-day study. This study was conducted in a 30-minute session, which precluded the collection of individual differences measures, including demographic information. Regarding the full sample (N = 169), data from 7 participants were excluded (2 due to excessive noise, 2 due to lack of SCR response to any presentation of the US via visual inspection, 2 due to incomplete missing data, 1 due to invalid self-report data, i.e., scoring outside of provided range) leaving a total sample of 162 individuals recruited from the undergraduate research pool at Louisiana State University. The participants were further randomly assigned to one of two groups: the probe group (n = 86) or the no-probe group (n = 76). Probes were added in habituation/training for both groups, and during acquisition for the probe group only. Our chosen sample size was selected based on existing literature of similar studies. An examination of differential fear conditioning

studies that included either SCR or RT measures returned a wide range of numbers with the lowest found of 6 subjects per group with a total of 36 participants (Carter et al., 2003)to the highest found of a within-subject design with 66 subjects (Koster et al., 2005). We aimed to collected 70-80 participants per group. The data presented in this manuscript were from a study completed during Day 1 of a two-day protocol in which a sub-sample of the participants completed an independent study on their second visit (the Day 2 data will be described in a future publication). This study was approved by the Institutional Review Board of the Louisiana State University and written informed consent was acquired from all participants prior to the beginning the experiment.

4.2.2. Materials

Two letters (i.e., "L" and "O") drawn on 4 by 5 grids were selected as the CSs (see figure 4.1. A). These two letters were selected to minimize overlap between the two CSs on the grid. While they differ in terms of number of composing pixels, the selection of which letter was CS+ and which was CS- was counterbalanced across participants. The USs were 100-ms mild electric stimulations which were delivered to the distal phalanx of each participant's ring and pinky finger on their non-dominant hand through attached electrodes. The mild electric stimulation was customized to each participant such that the intensity of the shock was set to a level that was "uncomfortable but not painful" and was administered through the STMISOC and STM100C modules of BIOPAC Systems (mean intensity = 1.61 mA, *SD*= 1.16).

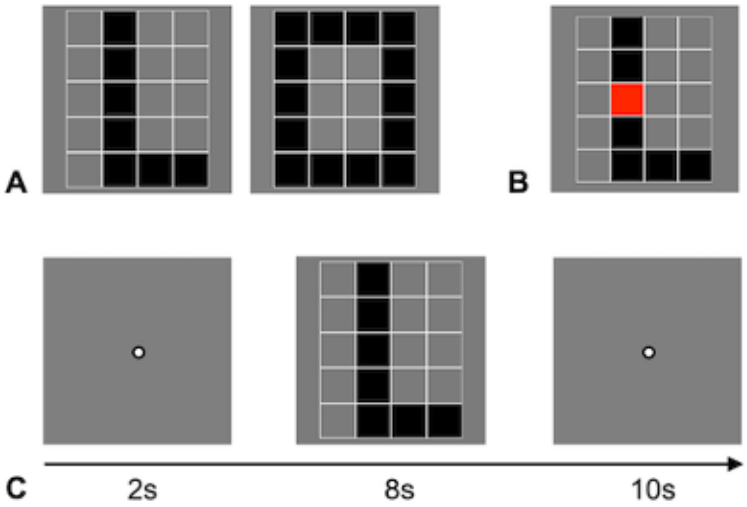

Figure 4.1. Letter stimuli (A), probe (B), and trial design (C).

4.2.3. Procedure

The study was composed of one habituation run and one acquisition run. In habituation, participants were instructed to view and imagine both CSs (i.e., "L" and "O"). The habituation run consisted of 6 trials of each of the four CS identity and modality combinations (i.e., view CS+, imagine CS+, view CS-, imagine CS-) leading to a total of 24 trials. In acquisition, the visual images of CSs were presented to the participants with the instruction to observe the stimuli. The CS+ was always paired the US (i.e., 100% reinforcement rate) while the CS- was never paired with the US (i.e., 0%). The acquisition run contained 8 view CS+ trials and 8 view CS- trials. Each trial began with a fixation point at the center of the screen for 2 s. Next, one of the two CSs was presented for 8 s ending with another fixation of 10 s (figure 4.1. C). Mild electrical stimulation was delivered on every CS+, 7.9 s after CS+ onset and co-terminated with the stimulus.

4.2.4. Probe

The habituation phase was used as practice for the behavioral probe task. Probes were added to each trial at either 4, 5, or 6 s after stimulus onset. On a given trial a probe was

randomly placed in a single square in the 4 x 5 grid (see figure 4.1. B). Within each run, the probe had a 50% chance of being on the target letter. Participants were instructed to indicate if the probe was on or off the letter by responding as quickly and accurately as possible via button press with their dominant hand. The probe timing was randomized to reduce or eliminate expectancy. All participants went through the same habituation procedure. For those in the probe group, probes were also presented during acquisition. Specifically, probes were added to each trial at either 4.5, 5, 5.5, or 6 s after stimulus onset. Any response that took place longer than 2 s after probe onset was not recorded.

4.2.5. Subjective Ratings

At the end of the experimental task, participants were surveyed on their self-reported fear of receiving a shock and their shock estimation after acquisition (i.e., their estimate of the percentage trials that were paired with shock) for each CS. Participants reported their fear of each CS on a 7-point Likert scale (between 1 = "Not at All" and 7 = "Very Much So"). A 10-point Likert scale (between 0% and 100% with intervals of 10%) was provided for participants' estimations of shock for each CS.

4.2.6. Physiological Responses Recording

Electrodermal activity was recorded with the Biopac MP-150 system and AcqKnowledge software (BIOPAC systems, Goleta, CA, USA) and was sampled at 2000 Hz. SCR analysis was carried out in Matlab R2018a (Version 9.4). During preprocessing, a first-order Butterworth bandpass filter was applied with cut-off frequencies of .01 and 5 Hz (Bach, Flandin, Friston, & Dolan, 2010). Time series were then down-sampled to 100 Hz. Based on previous research (e.g., Grégoire & Greening, 2019; Leys, Ley, Klein, Bernard, & Licata, 2013; Milad et al., 2007; D. Schiller, Kanen, LeDoux, Monfils, & Phelps, 2013; Daniela Schiller et al., 2010; Vervliet,

Vansteenwegen, Baeyens, Hermans, & Eelen, 2005), SCRs to the CSs were calculated by subtracting baseline (1 second before stimulus onset) from the peak amplitude (during 1-7.9 seconds after stimulus onset). Peaks were removed if their distance from the baseline was smaller than .02 μS or if it did not appear in the 1 to 7.9 s timeframe. The difference scores were then square root transformed. The first two trials of the acquisition run were always a CS- trial then a CS+ trial, respectively, which were excluded from the analyses to avoid the potential confounding orienting effect of the first trials, and to avoid including data from a CS+ trial prior to the association with the US actually occurring (Grégoire & Greening, 2019; Lonsdorf et al., 2017). This also ensured that there was an equal number of CS+ and CS- trials included in the analysis.

4.2.7. Probe Task Behavioral Responses

RT and accuracy during the probe task (probe group only) were collected and analyzed. The first two trials were removed, consistent with SCR data analysis. The RT of each participant was averaged across trials for each stimulus type (i.e., CS+ and CS-), and only correct trials were included (i.e., pressing 1 when the probe was on the letter, or pressing 2 when the probe was off the letter). Accuracy was averaged across all trials including both probe on the letter and probe off the letter trials.

4.2.8. Data Analysis

Based on recommendations by Lonsdorf et al. (2017), the following analyses were conducted on the complete sample (n = 162; probe group, n = 86; no probe group, n = 76) without outlier removals. The primary research question is whether the addition of the visual attention task described above (i.e., probe task) would affect differential fear conditioning. The secondary question of the study asked whether the visual attention task was a sensitive

behavioral fear conditioning measure. To answer these two questions, separate mixed model ANOVAs were conducted on self-reported fear, shock likelihood estimations, and SCR, with CS type (i.e., CS+, CS-) as the within subject factor and probe task assignment (i.e., probe group, no probe group) as the grouping factor.

In a previous study examining the effect of inserting an additional outcome measure in fear acquisition, Sjouwerman et al. (2016) demonstrated that the inclusion of startle probes delayed the acquisition of differential fear responses in terms of SCR and fear ratings. Moreover, task uncertainty, such as the temporal uncertainty with respect to probe onset during trials in the present study, can increase vigilance thereby potentially affecting the acquisition rate of differential conditioning (Morriss, Gell, & van Reekum, 2019). To assess whether behavioral probes in the current study affected the rate of acquisition, a 2x2 ANOVA with timing (i.e., early, late) as the within subjects factor and probe group assignmeny (i.e., probe group, no probe group) was conducted on differential SCR data (i.e., CS+ - CS-). As stated earlier, the first two trials (one CS- and one CS+) were excluded in SCR analyses. Thus, the SCR responding here is separated into eary and late conditioning by averaging between trials 2-4 and 6-8 respetively. Self-reported fear is only collected after completion of conditioning and thus is not analyzed here.

Considering that SCR is sensitive to error detection (Hajcak, McDonald, & Simons, 2003), a follow-up paired t-test was carried out contrasting SCR during correct and incorrect trials using data from the probe group. After observing larger differential SCR on error trials, we sought to determine if either higher arousal/SCR prior to probe onset increased the number of errors or if it was error detection that led to an increased SCR after probe onset. Thus, SCR was divided into early/before probe (i.e., 1-4.5 s after stimulus onset) and late/after probe (i.e., 4.5-

7.9 s after stimulus onset) components, followed by a 2x2 ANOVA with timing (i.e., before probe, after probe) and key press accuracy (i.e., correct, incorrect) as the within subject factor. The study also undertook exploratory individual differences analyses aimed to investigate the degree of response synchronization and response patterning observed between the different measures of fear conditioning. Response synchronization refers to the degree of similarity between measures, which we operationalized as correlations between each pair of the selected measurements. Considering the potential influence of contingency awareness on differential conditioning (Critchley et al., 2002; Tabbert, Stark, Kirsch, & Vaitl, 2006; Weidemann, Satkunarajah, & Lovibond, 2016), our shock estimation measure was also included in the analyses. Correlation analyses were conducted on difference scores between CSs (i.e., CS+ - CS-) as indicators of differential fear conditioning discriminability. Response patterning, on the other hand, refers to the degree of unique patterning found between various dependent measures that combine to produce an emotional state. In other words, one would also expect that when it comes to predicting individual differences in self-reported fear, the other dependent measures should be unique explanatory variables (i.e., they should explain unique variance in self-reported fear). Separate multiple regression analyses were performed on the SCR, shock estimation (complete sample and probe group), and RT (probe group only) entered as predictors for predicting self-reported fear.

4.3. Results

4.3.1. The Influence of a Basic Visual Attention Task on Differential Conditioning

Evidence of successful fear conditioning was found in both the no-probe group and the probe group as indicated by higher ratings of fear and shock estimation, larger SCR components,

and faster probe task responses during CS+ compared to CS- presentations. Results from each of these measures are reported in the remainder of this section.

4.3.1.1. Self-Report Data

Self-reported fear data revealed a significant main effect of CS type, $F(1, 160) = 237.52$, $p < .001$, $\eta_p^2 = .60$. There was no main effect of probe task assignment $F(1, 160) = .36$, $p > .05$; nor an interaction between CS type and probe task, $F(1, 160) = 1.20$, $p > .05$. Follow-up paired t-tests (figure 4.2. A) confirmed the success of differential fear conditioning, with greater self-reported fear in CS+ than CS- in both probe and no probe groups. Specifically, participants in the probe group reported significantly higher levels of fear in CS+ ($M = 4.17$, $SD = 1.80$) than in CS- ($M = 1.71$, $SD = 1.30$) trials, $t(85) = 9.69$, $p < .0001$, $d = 1.04$. The same was true in the no probe group where CS+ fear ratings ($M = 4.46$, $SD = 1.60$) were higher than CS- fear ratings ($M = 1.62$, $SD = 1.23$), $t(75) = 12.55$, $p < .0001$, $d = 1.44$.

The same pattern was found in the shock estimation data. There was a significant main effect of CS type, $F(1, 160) = 395.04$, $p < .001$, $\eta_p^2 = .71$. No main effect of probe task assignment, $F(1, 160) = .06$, $p > .05$; nor interaction, $F(1, 160) = .97$, $p > .05$. Follow-up paired t-tests (figure 4.2. B) found significantly higher estimations of shock in CS+ than CS- in probe (CS+: $M = .83$, $SD = .26$; CS-: $M = .15$, $SD = .24$; $t(85) = 13.19$, $p < .0001$, $d = 1.42$) and no probe groups (CS+: $M = .86$, $SD = .22$; CS-: $M = .11$, $SD = .22$; $t(75) = 15.14$, $p < .0001$, $d = 1.74$).

4.3.1.2. SCR Data

SCR results were consistent with the self-report data. There was a significant main effect of CS type, $F(1, 160) = 89.59$, $p < .001$, $\eta_p^2 = .36$. Neither main effect of probe task assignment, $F(1, 160) = 3.52$, $p > .05$; nor the interaction, $F(1, 160) = 3.77$, $p > .05$ were significant.

According to the follow-up paired t-tests (figure 4.2. C), the probe group had significantly larger SCR on CS+ (M = .31, SD = .29) than CS- (M = .17, SD = .18) trials, $t(85) = 5.68$, $p < .0001$, d = .61. The same was observed in the no probe group, with SCR on CS+ trials (M = .41, SD = .31) significantly greater than on the CS- trials (M = .19, SD = .19), $t(75) = 7.55$, $p < .0001$, d = .87.

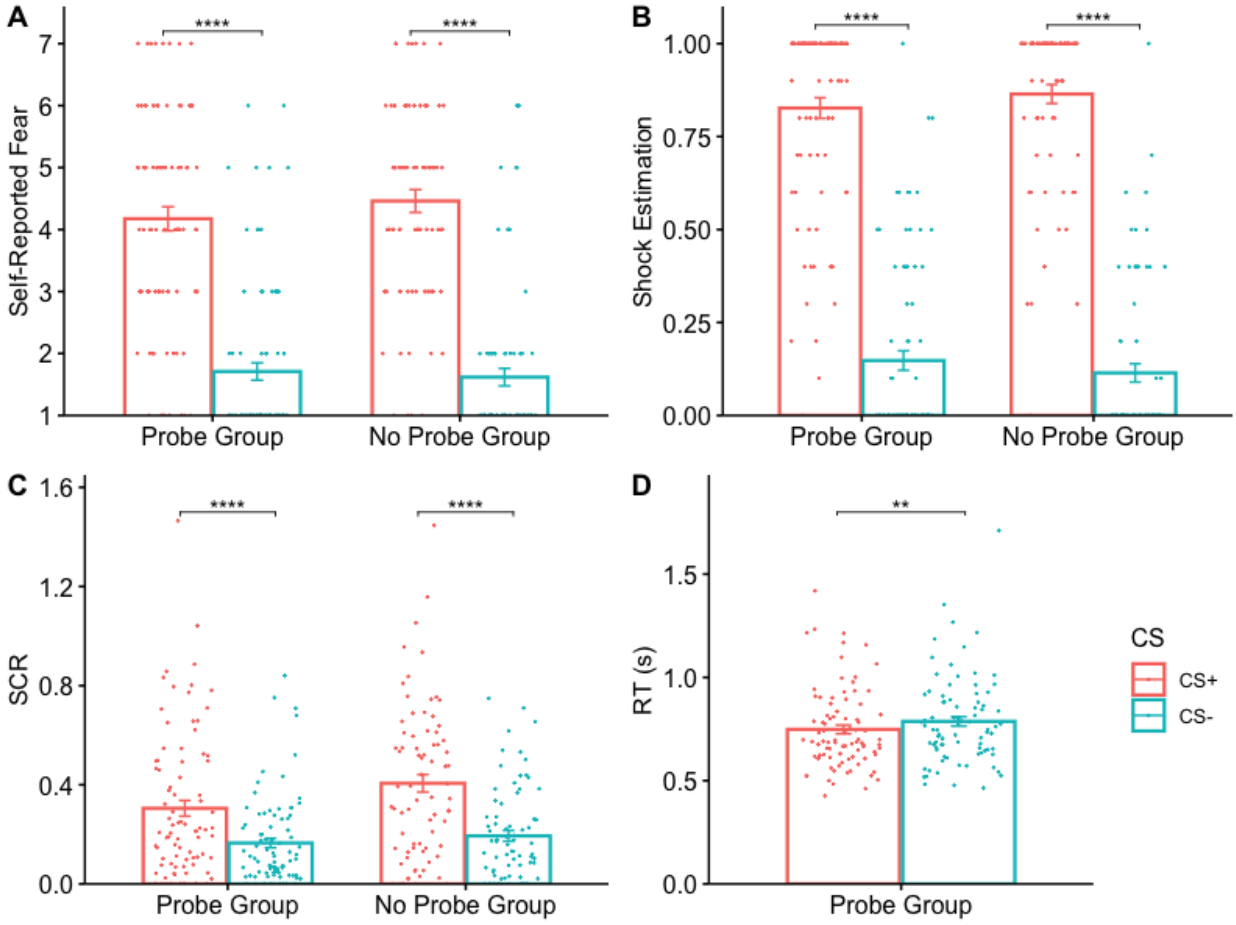

Figure 4.2. Effects of CS type (i.e., CS+, CS-) and probe task grouping (i.e., probe group, no probe group) on self-reported fear (A), shock estimations (B), and SCR (C). Comparison of RT between CS+ and CS- in the probe group (D). Error bars show ± 1 standard error. Each dot represents one subject.
* p < .05. ** p < .01. *** p < .001. **** p < .0001.

To evaluate whether the presence of probes affect the rate of acquisition we compared early and late differential conditioning (i.e., CS+ - CS-) across groups. Importantly, we observed neither a significant probe task by time interaction ($F(1, 160) = .00$, $p > .05$) nor a main effect of group ($F(1, 160) = 3.06$, $p > .05$). This indicated that the presences of the behavioral probes did

affect the magnitude of differential conditioning over time (early versus late acquisition). There was, however, a significant main effect of time, $F(1, 160) = 6.20$, $p < .05$, $\eta_p^2 = .04$, suggesting that SCR difference scores were higher during early acquisition ($M = .21$, $SD = .32$) than late acquisition ($M = .14$, $SD = .29$). See supplementary figure 4.S1 in Appendix A.2. for trial-by-trial data.

4.3.2. Influence of Differential Fear Conditioning on Behavior

As the probe group also provided behavioral data, we analyzed RT and accuracy for the probe group. A paired t-test revealed that participants were faster (i.e., lower RT) at responding to probes on CS+ trials ($M = .75$, $SD = .20$) compared with CS- trials ($M = .79$, $SD = .21$), $t(85) = -2.64$, $p < .01$, $d = -.29$ (figure 4.2. D). Another paired t-test revealed no significant difference in accuracy between CS+ ($M = .87$, $SD = .17$) and CS- ($M = .87$, $SD = .17$), $p > .05$.

While RT was averaged across only correct trials, SCR was derived from both correct and incorrect trials. To assess whether behavioral performance influenced SCR, a paired t-test was conducted comparing SCR on correct versus incorrect trials. It revealed that SCRs were smaller in correct trials ($M = .25$, $SD = .20$) than in incorrect trials ($M = .36$, $SD = .39$), $t(64) = -2.88$, $p < .01$, $d = -.37$. Two potential explanations could account for this difference: 1) higher arousal/SCR prior to the behavioral probe onset led to more mistakes; or 2) errors during the probe task caused elevations in SCR following probe onset. Out of the 85 participants in the probe group, 21 responded with 100% accuracy. Based on SCR data from the remaining 65 participants in the probe group, a 2x2 ANOVA revealed a significant interaction between timing (i.e., before probe, after probe) and key press accuracy (i.e., correct vs. incorrect), $F(1, 64) = 6.43$, $p < .05$, $\eta_p^2 = .09$. Follow-up t-tests revealed that SCR was larger on incorrect trials only after probe (correct trials: $M = .19$, $SD = .19$; incorrect trials: $M = .28$, $SD = .37$; $t(64) = -2.34$, $p < .05$, $d = -.22$), not before

probe (correct trials: M = .13, SD = .17; incorrect trials: M = .17, SD = .29; $t(64) = -1.05$, $p >$ .01; figure 4.3.). Together these findings are consistent with the explanation that errors cause a larger SCR and rule out the explanation that a larger SCR early-on to the CSs causes the errors.

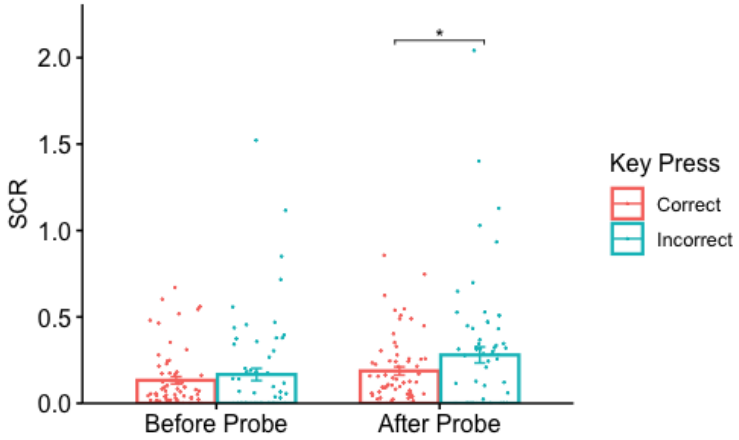

Figure 4.3. Effects of timing (i.e., before or after probe) and key press accuracy (i.e., correct, incorrect) on SCR. Error bars show ± 1 standard error. Each dot represents one subject.
* p < .05.

4.3.3. Correlations Between Measures

Based on data from the complete sample (figure 4.4. A), there were significant correlations between self-reported fear and SCR difference scores, $r(160) = .31$, $p < .001$; SCR and shock estimations, $r(160) = .28$, $p < .001$; and self-reported fear and shock estimations, $r(160) = .60$, $p < .001$. This remained true when evaluating the two groups separately. Specifically, in the no probe group (figure 4.4. B), there were significant correlations between self-reported fear and SCR difference scores, $r(74) = .34$, $p < .01$; SCR and shock estimations, $r(74) = .34$, $p < .01$; and self-reported fear and shock estimations, $r(74) = .53$, $p < .001$. In the probe group (figure 4.4. C), there were significant correlations between self-reported fear and SCR difference scores, $r(84) = .28$, $p < .01$; SCR and shock estimations, $r(84) = .21$, $p < .05$; and self-reported fear and shock estimations, $r(84) = .64$, $p < .001$. Examining the relationship between the RT and the other measures was only possible in the probe group. This revealed no

significant correlations between differential RT and differential self-reported fear ($r(84) = .14$, $p > .05$), SCR ($r(84) = -.14$, $p > .05$), or shock estimations ($r(84) = .02$, $p > .05$).

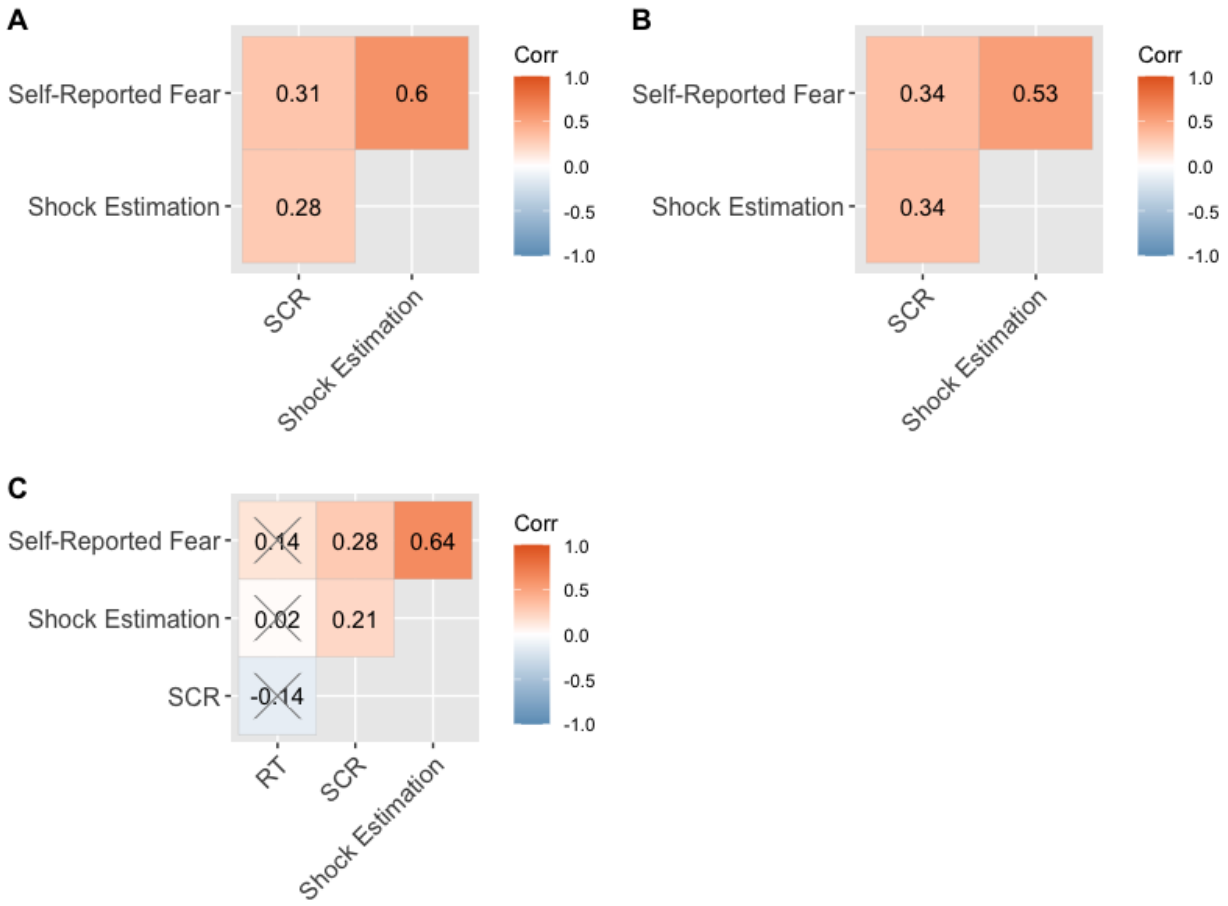

Figure 4.4. Correlations between pairs of outcome measure difference scores (CS+ - CS-) for all participants (A), no probe group only (B), and probe group only (C). Crossed out cells indicate insignificant correlations (p > .05).

4.3.4. Multiple Regression Predicting Self-Reported Fear

Three linear multiple regression models were carried out to test if self-reported fear can be predicted by the other outcome measures. Based on an analysis of the complete sample, shock estimation and SCR together explained 38.56% of the variance in self-reported fear ($F(2, 159) = 49.88$, $p < .001$), and both shock estimation ($\beta = 2.68$, $p < .001$) and SCR ($\beta = 1.42$, $p < .05$) were significant predictors. A second model included RT as a predictor using data from only the probe group. Results indicated that shock estimation, SCR, and RT explained 45.89% of the variance in

self-reported fear ($F(3, 82) = 23.18$, $p < .001$). Shock estimation ($\beta = 2.99$, $p < .001$) and SCR ($\beta = 1.76$, $p < .05$) were significant predictors, but not RT ($\beta = 2.64$, $p > .05$). To determine whether the addition of RT led to an improvement of the predictive model, another model without RT was assessed based on probe group data. In this model, shock estimation and SCR explained 43.61% of the variance in self-reported fear ($F(2, 83) = 32.09$, $p < .001$) with shock estimation being a significant predictor ($\beta = 3.03$, $p < .001$) but not SCR ($\beta = 1.52$, $p > .05$). Comparing to this model, an *F*-test revealed that the addition of RT in the second model did not have a significant improvement in model fit ($F(1, 83) = 3.46$, $p > .05$).

4.4. Discussion

Compared to verbal and physiological indices, behavioral measures are much less frequently used in human Pavlovian/classical conditioning studies. The lack of behavioral measures, such as RT, restricts translations between human and animal research. It also limits one's ability to fully evaluate fear (in the case of fear conditioning) as a multi-component construct (Lang, 1968; Mauss & Robinson, 2009; Rachman, 1978). One of the concerns regarding inserting concurrent behavioral tasks during the acquisition phase of differential fear conditioning is that a behavioral probes might interfere with acquisition due to processes such as distraction (Lipp, 2007). Consistent with this concern, some researchers have reported a reduction in fear conditioning in the company of demanding secondary tasks (Carrillo et al., 2000; Carter et al., 2003). In the present study, a simple visual attention task employing behavioral probes was evaluated as a concurrent behavioral measure that would not interfere with differential fear conditioning as measured by self-reported fear and SCR. Specifically, we compared differential fear conditioning alone (i.e., no probe group) to conditioning with a secondary visual attention task (i.e., probe group).

Results from the present study demonstrated that the addition of behavioral probes (i.e., visual attention task in the current study) did not interfere with fear conditioning as measured with SCR and self-reported fear collected immediately following the acquisition trials. Both probe and no probe groups exhibited successful fear conditioning as indicated by greater self-reported fear, larger shock estimations, and higher SCR for CS+ compared to CS-. Group assignment did not make a difference in fear conditioning based on any of these measures. These results are consistent with research findings that simple tasks with a low cognitive demand cause little or no interference on the acquisition of differential conditioning (Carrillo et al., 2000; Carter et al., 2003) as accuracy of the current probe task was relatively high for both CS+ and CS- with the same average of 87% accuracy. Further, unlike the findings on startle probes in Sjouwerman et al. (2016), the addition of behavioral probes in the current study did not delay or affect the magnitude of fear learning supported by the lack of a two-way interaction between probe group and acquisition time and a non-significant main effect of probe group on differential SCR (i.e., CS+ - CS-). The concurrent behavioral task in the present study was also a sensitive behavioral measure of fear conditioning. Specifically, RT was shorter during CS+ trials than CS- trials, consistent with previous human differential fear research findings (Critchley et al., 2002; Gottfried & Dolan, 2004; Hermans et al., 2005; Koster et al., 2005; Morris & Dolan, 2004; Romaniuk et al., 2010).

One consideration did, however, emerge regarding the behavioral task and its influence on the SCR. Specifically, it was found that incorrect trials were associated with a larger differential SCR than correct trials. A follow-up analysis found that while SCR did not differ between correct and incorrect trials before probes, there was a significant SCR increase during incorrect trials after probe presentations. One interpretation of this effect is that participants

detected their errors during the behavioral task which resulted in greater arousal, as indicated by elevated SCR (Hajcak et al., 2003). It should be noted that as accuracy was very high (86%) on the behavioral task there were relatively few error trials, with 21 participants making no errors at all. Thus, the impact of error trials when pooled with correct trials did not significantly influence the differential SCR magnitude as compared to the no probe group.

Taken together, results from the current study support the inclusion of the described visual attention task in differential fear conditioning research as a behavioral measure of conditioning that does not interfere with other measures of conditioning such as SCR or self-report measures. Considering the influence of incorrect responses/error detection on SCR, future research adopting a similar experimental design may need to account for this by either excluding incorrect trials or sampling SCR from before the onset of the behavioral probes. As it is a common practice when analyzing RTs to average across correct responses (e.g., Derryberry & Reed, 2002; Oliver & Page, 2003; Yates, Ashwin, & Fox, 2010), it would be consistent to use the same procedure when processing the SCR data. As for the second alternative of extracting SCR from a time window before probes, depending on the temporal design, such analysis may unintentionally cross over with the literature of first- and second-interval SCR in fear conditioning (Jentsch, Wolf, & Merz, 2020; Luck & Lipp, 2016). Additionally, while the current CS presentation time of 8 s allowed for parcellating the epoch in two sufficiently large windows of time, shorter presentation times might not support such a parcellation considering the latency of SCR (R. Sjouwerman & Lonsdorf, 2019). A third possibility is to ensure that accuracy on the behavioral task is sufficiently high such that error trials will have a negligible effect on the mean SCR, which also appears to have been the case in the present study.

Given the relatively large sample size and the inclusion of the behavioral measure, the current study was also able to examine the relationship between subjective, physiological, and behavioral measures. We observed that while there were significant correlations between subjective (i.e., self-reported fear, shock estimations) and physiological (i.e., SCR) measures consistent with Friedman et al. (2014), the behavioral measure (i.e., RT) did not correlate with the subjective nor physiological measures, which is inconsistent with Mauss et al. (2005) who reported concordance between subjective, behavioral, and physiological measures. Some methodological differences might explain the discrepant findings. First, the present study used RT, while Mauss et al. (2005) selected facial behavior (i.e., facial expression) as the behavioral measure. Second, the emotional responses in Mauss et al. (2005) were elicited by film-watching instead of differential fear conditioning. Third, while the present study collected the self-reported data immediately following the experimental manipulation, Mauss et al. (2005) collected their subjective measure concurrent with their task.

In addition to the correlation measures, we also observed that we could explain a significant portion of the variance in self-reported fear using the other measures including shock estimation and SCR. The addition of RT, however, did not lead to an improvement in model fit. Together, results from the current investigation suggest that while RT was a sensitive measure of differential fear conditioning, it did not converge with the other measures, including self-reported fear, shock estimations, and SCR. This is consistent with previous findings that emotion is multiply determined and cannot be accounted for by a single measure (Hollenstein & Crowell, 2014; Mauss & Robinson, 2009). The lack of correlation between RT and other measures needs some additional consideration. One potential factor is that the low task-demand produced a narrow range of between-subject variances, which is sub-optimal for individual differences

analyses (Hedge, Powell, & Sumner, 2018). While increasing the difficulty of the behavioral task may improve the between-subject variance, higher task demand may result in significant interference with differential conditioning itself (Carrillo et al., 2000; Carter et al., 2003). Further research is needed to establish whether or not between-subject variance could be increased without disrupted acquisition of differential conditioning and where the balance might lie, as well as to clarify the relationships across and within subjective, physiological, and behavioral descriptions of emotion.

A couple of limitations are worth noting and discussing. First, although we observed that the simple visual attention task described here did not affect differential conditioning as measured with SCR and self-reported fear, it is unclear how our task might affect other measures of differential conditioning. For example, future research should consider the impact of a simple visual attention task on the brain activity associated with differential conditioning. Second, we did not collect any individual personality characteristics data, such as state anxiety. Such measures should be incorporated into future research considering that previous literature (Lonsdorf et al., 2019) has found individual differences in state anxiety to be influential over differential fear learning.

In summary, the present investigation provides important new evidence that a simple behavioral task can be performed along with differential fear conditioning, such that it does not interfere with other measures (i.e., self-reported fear and SCR) of differential condition and is itself a sensitive measure of fear conditioning. In addition, the individual difference findings (i.e., correlations and multiple regression) emphasize the value of measuring the multi-components of emotion in the advancement of our basic understanding of emotions such as fear.

Chapter 5. General Discussion and Future Directions

The main goal of the current investigation is to experimentally evaluate the assumption that extinction of conditioned fear towards a perceptual stimulus can take place through imagined exposure to its imagery. We observed that conditioned fear responses underwent extinction during imagined exposure supported by the lack of spontaneous recovery upon re-exposure. In addition to providing supporting evidence for the central research hypothesis, the three studies discussed here also strengthened the importance of multi-component assessments when it comes to emotions such as fear. Specifically, that different forms of fear expressions were not always consistent. The following sections of the general discussion will summarize the three studies' findings, discuss their implications, and some limitations along with future directions.

5.1. Acquisition of Differential Fear

The requirement of successful conditioning must first be met before one can examine the extinction of the acquired fear responses. All three studies from this investigation shared a similar design of differential fear conditioning with the same material for CS (i.e., letters) and US (i.e., shock). Successful conditioning was achieved across all three studies, with the exception of one of the two CS+s in study 1 as measured by SCR. It is worth noting, however, that while this specific CS+ in study 1 failed to exhibit SCR evidence of discrimination between CS+ and CS-, self-reported fear and shock estimations were supportive of differential fear. Thus, the issue here may be partially a product of SCR noise and measurement error. When placed in the context of the whole inquiry with the remaining measurements in study 1 and the other two studies showing consistent and apparent CS+-CS- discrimination, one may speculate that this unexpected case of incomplete conditioning in study 1 was likely the result of methodological

variances, including number of CSs, CS presentation duration, CS-US contingency, and US duration. Explicitly, study 1 included two CS+s while study 3 only had one. Also, the CSs in study 1 were presented for 4 s which is half of the duration in study 3. In addition, study 1 had a lower CS-US contingency, i.e., the CS+s were paired with the US 50% of the time, while the CS+ in study 3 always co-terminated with the US. Further, the US in study 3 was set to extend a period of 100 ms, in contrast to a duration of 5 ms in study 1. While study 2 has the same number of CS+s and an identical CS-US contingency as study 1, study 2 had the benefits of longer periods of both CS (i.e., 8 s) and US (i.e., 100 ms) presentations. Future studies using a similar fear conditioning paradigm should choose experiment parameters similar to either study 2 or 3 to ensure robust SCR conditioning results.

With that being said, the unconditioned CS+ in study 1 (i.e., CS+V) was less relevant to the main research question. The CS+ that went through imaginal exposure (i.e., CS+I) in study 1 was found to have successfully acquired differential SCR fear responses in addition to self-reported fear, which permitted examination of extinction processes during imagination. Additionally, with the aforementioned adjustments in conditioning procedure, the CS+ in study 1 and the two CS+s in study 2 (i.e., the one that went through imaginal exposure/CS+IV and the one that did not/CS+V) both exhibited evidence of conditioning as measured by self-reported fear (studies 2 and 3), SCR (studies 2 and 3), and brain activations (study 3). Further support comes from the RT-based behavioral measurement in study 3 which evinced discrimination between CS+ and CS- despite the low task demand. Taken together, the current conditioning design was effective in eliciting differential fear as measured by the selected indices.

5.2. Generalization of Fear From Perception to Imagery

After conditioning was verified, generalization from perception to imagery must also be determined. Based on analyses done on data from studies 1 and 2, participants reported higher levels of fear and had larger SCRs when imagining CS+ in comparison to CS- providing support for the generalization of fear acquired to viewing CS+ to its mental imagery. Further, these findings were apparent even though participants correctly estimated the absence of shock during the imagined extinction phases across both studies. In study 2, however, generalization was not observed in brain activations within ROIs. Considering the elevations in self-reported fear and SCR, this lack of brain activations was likely a representation of incomplete neural overlaps between affective imagery and perception instead of absence of generalization. Indeed, the ROIs applied to extinction fMRI data were generated based on the meta-analysis result by Fullana et al. (2016) over perceptual fear conditioning. Our findings of self-reported fear and SCR were consistent with results reported by Greening et al. (2021) in which generalization of fear from viewing to imagining was also evident in brain regions including R-AIC, dorsolateral prefrontal cortex, and bilateral inferior parietal lobe. Here, the lack of significant contrasts in the brain could be a result of methodological differences. Specifically, in study 2, the CS+ was imagined after completion of perceptual conditioning while in Greening et al. (2021), imagery of CS+ was produced during conditioning. Further research is needed to locate the regions involved in generalized fear in imagery.

One concern was raised in study 1 regarding the possibility that the SCR elevations of CS+ during imagery extinction was the result of imagining being more effortful as CS+ was imagined while CS- was viewed. In study 2, both CS+ (i.e., CS+IV) and CS- was imagined

confirming that the contrast in SCR was not due to the difference in effort between the actions of active imagining and viewing.

5.3. Extinction of Fear Towards Viewed CS+ Following Imagery Exposure

Backed with successful conditioning and generalization, evaluations were made to determine whether learned fear towards the perception of CS+ went through extinction after repeated exposure to its imagery. Consistently across studies 1 and 2, no spontaneous recovery of differential fear was observed based on SCR descriptions indicating that, as hypothesized, extinction of fear took place via imagery exposure, consistent with the limited existing literature (Agren et al., 2017; Reddan et al., 2018). This was further confirmed by the findings in study 2 that unlike the CS+ that went through imagery exposure (i.e., CS+IV), the CS+ that was not imagined before re-exposure (i.e., CS+V) retained its differential SCR when it was viewed again despite a correct reporting of no accompanying shock.

Interestingly, while no discrimination was detected in physiological responses (i.e., SCR) when viewing the CS+ after imagery extinction, self-reported fear from participants in both studies still carried an impression of conditioned fear. This resistance of self-reported fear towards extinction was also observed by other researchers (Lau et al., 2008; Shechner et al., 2015) and can be interpreted as a reflection of stable declarative knowledge of CS+ and CS- identities. In study 2, R-AIC and dACC ROIs also exhibited such resistance. Future research examining the influence of declarative knowledge on expressions of conditioned fear is needed.

5.4. The Multi-Component Construct of Emotion

Outside of the main research question of imagery extinction, though still relevant, a pattern emerged through the examination of results from studies 1 and 2, that depending on the source of measurement, the derived description of fear varied. Specifically, the presence of

conditioning or extinction effects in one measurement may not necessarily guarantee the same pattern in another measure. So far, our investigations have employed subjective (i.e., self-reported fear), physiological (i.e., SCR), and neurological (i.e., fMRI) measures of fear and found consistent support for conditioning in all of these indicators. The picture for extinction, however, was less uniform with clear evidence only in the form of SCR expression. As mentioned previously, considering the subjective nature of self-report data and that participants were able to correctly detect CS-US contingencies, it is reasonable to attribute the persistence of self-reported fear to a stable knowledge of CS identities. Nevertheless, these findings are consistent with the literature where inconsistent levels of concordance have been reported across (Friedman et al., 2014; Mauss et al., 2005; Rosenberg & Ekman, 1994) and even within (Quigley & Barrett, 2014) these three categories. The need of employment of multiple measurements across subjective, physiological, and behavioral categories (Lang, 1968; Mauss & Robinson, 2009; Rachman, 1978) was made apparent. The missing piece in studies 1 and 2 was a behavioral measure. In an effort to complete the "triangulation" of fear, study 3 sought to determine the eligibility of a RT-based behavioral measure in the current conditioning paradigm.

One hurdle over choosing concurrent behavioral measures and perhaps part of the reason why behavioral descriptions are relatively scarce is that the addition of behavioral probes may cause interference to the conditioning process itself. While RT-based behavioral measures have been used in human conditioning research (Lewis et al., 2013; Meulders et al., 2011; Öhman et al., 2001; Silvers et al., 2016), none have looked into the possibility of interference. Based on results of study 3, a conclusion can be made that within the selected conditioning paradigm, the behavioral task generated a sensitive behavioral measure (i.e., RT) of differential fear learning without causing deterrence to conditioning expressions in self-reported fear and SCR. As such,

future fear conditioning research with similar experimental designs can extend data collection from self-report and SCR to RT providing a more comprehensive assessment of fear. Additionally, as the probe task performance during imagery trials relies on correct mental visualization, this particular task can also serve as a window to imagery when needed.

5.5. Conclusion

In summary, results from the series of studies presented here provided support for extinction of fear towards a perceptual stimulus via imagery exposure. We observed differential fear after conditioning procedures supported by self-reported fear, SCR, and brain activations. Following extinction through imagery, no recovery of conditioned fear was found as measured by SCR upon re-exposure. Directions for future research was also provided with an emphasis on multi-component assessments of emotional responses. In addition to fill in the gap within the experimental literature of emotion regulation through imagery and provide guidance for the clinical application of imagery-based treatments, future research with assorted outcome measures could also contribute to the understanding of underlying mechanisms of emotion (Gentsch, Grandjean, & Scherer, 2014; Sze, Gyurak, Yuan, & Levenson, 2010) and inform clinical diagnoses of affective conditions (Hastings et al., 2009; H. S. Schaefer et al., 2014).

Appendix. Supplementary Material

A.1. Chapter 2

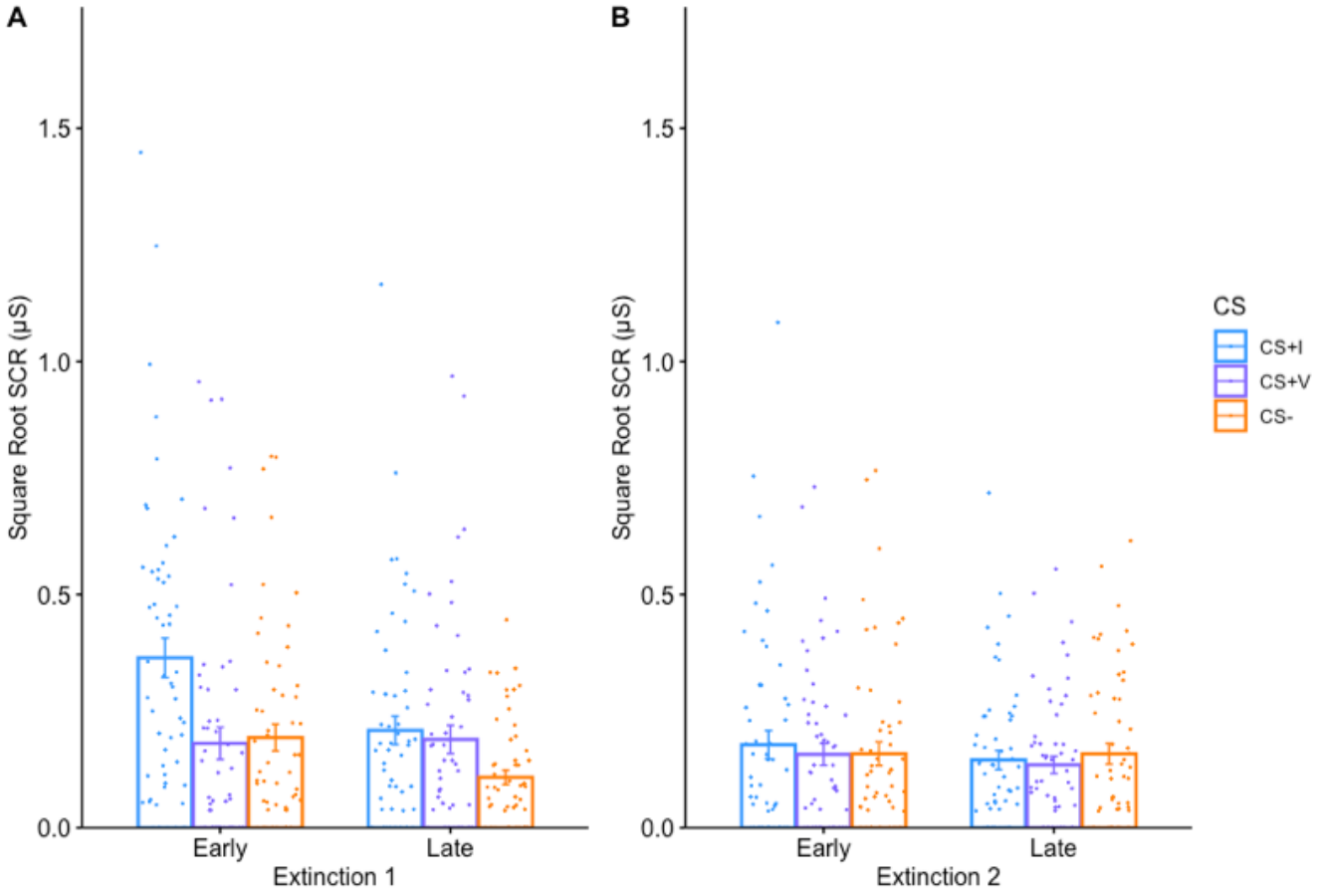

Figure 2.S1. Mean square-rooted SCR for each CS type during early and late Extinction Phase 1 (A) and Extinction Phase 2 (B). Error bars show ± 1 standard error. Each dot represents one subject.

A.2. Chapter 4

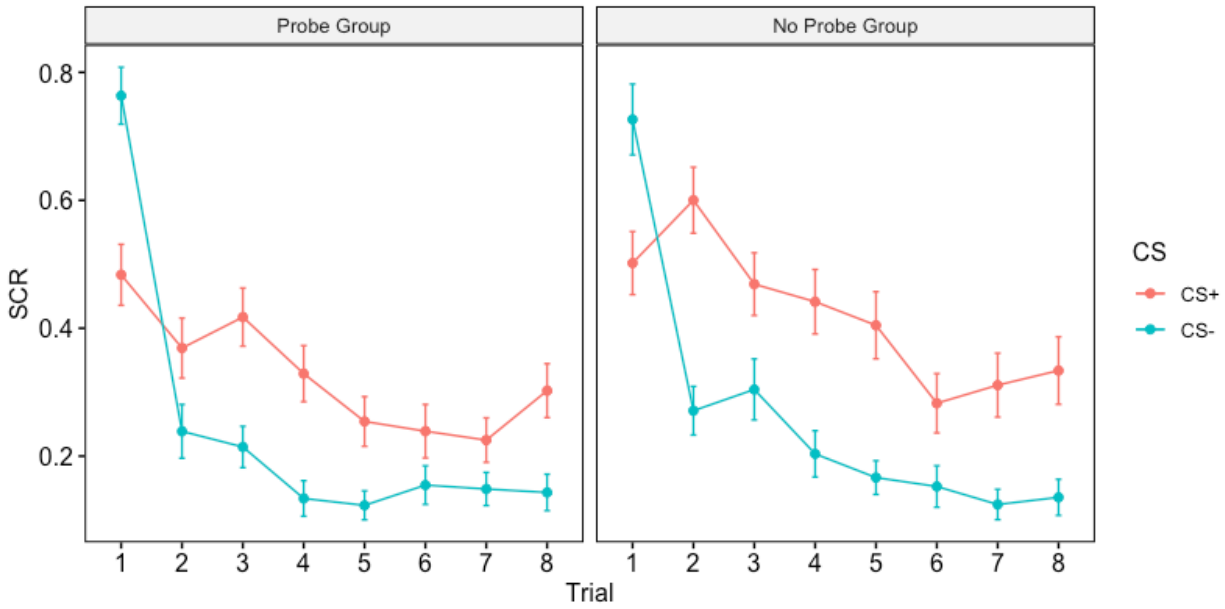

Figure 4.S1. Trial-by-trial SCR during acquisition in probe group and no probe group. First two trials (CS+ trial 1 and CS- trial 1) displayed here are not included in analyses. Error bars show ± 1 standard error.

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Vita

Xinrui Jiang received her Bachelor of Science in Psychology from East China Normal University, Shanghai, China and Colorado State University, Fort Collins, Colorado in 2014. She completed her master's degree in Clinical Psychology at Louisiana State University, Baton Rouge, Louisiana, and is anticipating to receive a Doctor of Philosophy Degree in Cognitive and Brain Sciences from Louisiana State University in August 2021.