Examining the temporal dynamics of emotion regulation via cognitive reappraisal

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ABSTRACT

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Regulating emotions effectively is an indispensable human task, essential for maintaining proper health and well-being. While the investigation of emotions and strategies for regulating them has been a timeless and irresistible activity, pursued by artists and philosophers throughout human history, recent decades have given rise to the controlled examination of emotion and emotion regulation by psychologists in the laboratory. While substantial progress has been made in describing, categorizing, and understanding the effectiveness of multiple strategies to regulate emotion in the laboratory, and while several long-term cognitive treatment modalities incorporating numerous regulation strategies are in practice in clinical psychology, there has been substantially less basic investigation into two overarching questions that form the basis of this dissertation: (1) how we can effectively prepare to regulate emotion using specific strategies? and (2) how can emotion regulation efficacy using particular strategies can change over time through repeated training? In this dissertation, I will focus on one promising type of cognitive change-based emotion regulation strategy, that of cognitive reappraisal. Cognitive reappraisal refers to reevaluating the meaning of an affective stimulus in a way that alters its emotional impact. In a series of four studies, I will address the two above questions using a combination of dependent measures, including questionnaire and task-based selfreported behavior, psychophysiology, and functional neuroimaging. In Study 1, I will provide evidence for the neural mechanisms that are conducive to reappraisal success and failure (measured via behavioral self-report) during anticipation of emotion regulation using whole-brain mediation and pattern expression analyses. Anticipatory activity in an area of rostrolateral prefrontal cortex (RLPFC) commonly associated with stimulusindependent mind-wandering was associated with poorer regulation outcomes, while anticipatory anterior insula activity implicated in internal affective integration was associated with better regulation outcomes. In Study 2, I will examine whether a short course of reappraisal training (in one of two reappraisal modalities: reinterpretation and psychological distancing, or a no-regulation control group) yields improvements in selfreported levels of negative affect during a laboratory task and in questionnaire reports of perceived stress in daily life. Results indicated that distancing shows promise as a trainable emotion regulation strategy, yielding decreasing reports of negative affect over time that were not attributable to habituation. Study 3 used the same experimental paradigm, adding psychophysiological data collection during the laboratory task (mean changes in heart rate). The combined results of Studies 2 and 3 indicated that while there was evidence of longitudinal decreases in negative affect for both distancing and reinterpretation, in distancing these effects were not attributable to habituation, and distancing was further uniquely associated with decreases in perceived stress in daily life among participants. Further, Study 3 indicated that mean changes in heart rate for distancing training yielded a pattern of increasing differentiability between regulated and unregulated trials over time, but this pattern was absent for reinterpretation training and the no-regulation control group. Finally, in Study 4, I examined the effects of a short

course of reappraisal massed practice, where one engages in repeated distancing episodes using the same stimuli. Specifically, I examined the behavioral and neural sustainability of responses to stimuli for which one has engaged in massed distancing practice versus simple repeated viewing, versus stimuli regulated but not practiced, and versus novel negative stimuli. Results indicated that distancing massed practice resulted in a sustained adaptive response pattern in a key subcortical appraisal region (amygdala) over time relative to other conditions. Overall, these studies elucidate the temporal dynamics involved in reappraisal response patterns, including evidence for adaptive anticipation mindsets, as well as evidence for the effectiveness of short courses of reappraisal training, particularly using psychological distancing.

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I'd like to dedicate this dissertation to my father, who showed me the way.

He looks on the bright side of everything, Including me. He thinks I'll be all right With doctoring. But it's not medicine— Lowe is the only doctor's dared to say so— It's rest I want—there, I have said it out— From cooking meals for hungry hired men And washing dishes after them—from doing Things over and over that just won't stay done. By good rights I ought not to have so much Put on me, but there seems no other way. Len says one steady pull more ought to do it. He says the best way out is always through.

- Robert Frost, "A Servant to Servants"

INTRODUCTION

Emotion regulation is as indispensable as emotions are ubiquitous. In the Western tradition, philosophers from Plato and Aristotle to later Kant and Hume have considered the proper role of reason is mollifying and challenging the passions and emotions we experience. Every student studying for a big exam and losing a grip on composure and perspective and every bar-room patron tempted with the urge to fight needlessly may similarly come to wrestle with the proper way to work through a negative experience. The question of how best to regulate emotion is both timeless and of enormous societal importance, given the tragic consequences that can arise when negative emotions in particular are allowed to spiral out of control.

Encouragingly, though the question of how best to regulate emotions is timeless, the past century has seen the rise of social and cognitive psychology, and with them the ability to gain more carefully-controlled, experimentally-grounded insights into the nature of emotional experience and of different classes of strategies that can be used to regulate that experience. William James put forth the view of emotions as behavioral and physiological response tendencies that may or may not be ultimately expressed (James, 1884, 1894). Thus, James promoted the idea that it may not be the features of a situation itself that determine one's response, but rather the interaction of the external world with the particular tendencies that are part of an individual.

These ideas led to the development of modern appraisal theory, as described by psychologists such as Richard Lazarus, which holds that the way in which a person construes a situation is of critical importance in determining one's response to it (Lazarus, 1966, 1991; Lazarus & Folkman, 1984). The idea that one's cognitive

interpretation of a situation was an essential ingredient in governing behavior was a crucial element of the cognitive revolution in psychology and related fields and stood in contrast to the prevailing behaviorist viewpoint that situational inputs and behavioral outputs were the only variables of interest in experimental psychology. The cognitive viewpoint was exemplified by other prominent psychologists such as Walter Mischel, who described how behavior could be explained by an interaction between variables pertaining to both person and situation (W. Mischel, 1973; W. Mischel & Shoda, 1995).

The concept of emotion regulation also fit well within the framework of appraisal theory. If one's cognitive appraisal of a situation is a critical factor in determining one's emotional response, then changing one's cognitive appraisal of a situation should theoretically be an effective regulation technique. Lazarus and Alfert (1964) demonstrated that this was in fact the case, as they observed that healthy adult participants who denied the reality and impact of aversive film clips demonstrated both lower self-reported stress levels of lower psychophysiological indicators of stress. Similarly, Mischel and Baker (1975) demonstrated this same cognitive transformation of appraisal phenomenon in children; children who focused on appraising an appetitive stimulus in a non-consummatory fashion (e.g. likening a marshmallow to a cloud) were able to delay gratification significantly longer than children who appraised the stimuli in consummatory ways.

This cognitive transformation of the appraisal process is what is meant by cognitive reappraisal (or, more simply, reappraisal). Reappraisal refers to re-imagining an affective stimulus in a way that alters its emotional impact (Gross, 1998b). James Gross situated reappraisal within an influential process model of emotion regulation as a

cognitive change-based strategy (Gross, 1998b). As with other appraisal theorists, Gross' formulation holds that emotional responses are governed by response tendencies that are behavioral, physiological, and experiential. While "affect" and "emotion" are sometimes used interchangeably, Gross defines emotion as response tendencies that occur over a relatively brief time period in response to situations and stimuli one experiences, whereas affect is a superordinate category that encompasses emotions and longer-lasting emotional episodes and moods, which lack a particular elicitor. Emotion regulation, then, can be seen as various ways to increase, decrease, or maintain one's emotion response tendencies using a variety of strategies. While this dissertation work will focus exclusively on down-regulation of negative emotion given its theoretical importance and translational relevance to clinical contexts, there are of course adaptive reasons that one might want to up-regulate negative emotion or down- or up-regulate positive emotion as well (Kim & Hamann, 2007; Ochsner & Gross, 2005).

Emotion regulation strategies may be divided into two classes. Gross' process model makes a distinction between antecedent and response-focused regulatory strategies. Antecedent-focused strategies take place before the emotion is generated, and response-focused strategies take place after emotion generation (Gross, 1998a, 1998b; Gross & Munoz, 1995). Thus, antecedent-focused strategies aim to ultimately alter which response tendencies are elicited, whereas response-focused strategies aim to alter the responses themselves. Antecedent-focused strategies include situation selection, situation modification, attentional deployment strategies (such as distraction), and cognitive change-based strategies. As discussed previously, reappraisal is situated within the cognitive change class of antecedent-focused regulatory strategies. An exemplar response-focused strategy, by contrast, is expressive suppression, where one attempts to have one's face and body reveal as little emotion as possible in response to a situation.

Given this framework, a natural question is to compare the effectiveness of various strategies in a controlled, laboratory context. A number of studies have now done so, often comparing antecedent (i.e. reappraisal) to response-focused strategies (i.e. suppression). There is evidence that while both reappraisal and suppression successfully decrease emotional behavior (facial and body movements) relative to no regulation in response to aversive stimuli, only reappraisal reduced self-reports of negative affect, and suppression was associated with increased physiological arousal (Gross, 1998a; Gross & Levenson, 1993). Importantly, when viewing the stimulus (aversive film clips), there was no difference in the degree to which participants covered their eyes across conditions, indicating that reappraisal effects in this paradigm are not simply driven instead by a modification of the situation as a whole (Gross, 1998a). Suppression has also been associated with poorer memory for emotional events (Richards & Gross, 2000a) and reduced well-being relative to reappraisal (Gross & John, 2003). More recently, reappraisal has been compared to distraction, an attentional deployment operationalized as keeping six letters in mind during the presentation of an emotional stimulus, and reappraisal led to reduced self-reports of negative emotion relative to distraction (McRae et al., 2010). Distraction has been shown to entail fewer cognitive costs and physiological arousal relative to reappraisal, but this has been shown to be true only when reappraisal is initiated relatively late (i.e. after the onset of emotional response tendencies) (Sheppes, Catran, & Meiran, 2009; Sheppes & Meiran, 2008). Thus, reappraisal has been shown to be a very promising emotion regulation strategy during single experimental sessions,

entailing relatively few cognitive, behavioral, or physiological costs, and has been associated with positive overall well-being.

Given this, reappraisal has received considerable interest and attention in the fields of emotion and emotion regulation. As described to this point, reappraisal could refer to a vast number of cognitive strategies by which one could re-imagine or reconstrue an affective stimulus. Ochsner and Gross describe a theoretically-meaningful partitioning among various classes of reappraisal that one could employ (Ochsner & Gross, 2008). One the one hand, one could *reinterpret* the meaning of an affective stimulus by telling oneself a story about the outcome (e.g. that it's not as bad as it first seemed or that help is on the way) (Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner et al., 2004). Alternatively, one could employ *psychological distancing* and impact the personal relevance of the emotional event to oneself. There are several ways that this could be accomplished. One is to appraise the event as a detached, objective, impartial observer (Gross, 1998a; Kross, Davidson, Weber, & Ochsner, 2009; Ochsner et al., 2004). Another method of varying psychological distance is one advanced by Yaacov Trope and colleagues, whereby one could cognitively vary the sense of spatial, temporal, or social closeness one has to a situation, among other strategies (Liberman, Trope, & Stephan, 2007; Trope, Liberman, & Wakslak, 2007). Both of these conceptualizations of psychological distancing (hereafter, simply "distancing") are theoretically meaningful and contributed to the operationalizations used in the current studies. Overall, regulating emotions via reappraisal (via either reinterpretation and/or distancing) has been shown to be an adaptive, flexible, effective regulatory strategy.

To this point, reappraisal has been considered from social (e.g. behavioral) and cognitive levels of analysis. Recent advances in cognitive neuroscience have made it possible to further examine the neural mechanisms that support reappraisal. The emerging field of social cognitive neuroscience is attempting to synthesize information acquired via behavioral, psychophysiological, and neuroscience methods in order to understand a cognitive construct like reappraisal through the integration of multiple levels of analysis (Ochsner, 2007; Ochsner & Lieberman, 2001). Viewed from this perspective, in addition to being effective in changing affective experience and psychophysiological arousal, reappraisal has been shown to modulate neural systems associated with emotion reactivity and regulation (Denny, Silvers, & Ochsner, 2009; Ochsner & Gross, 2005, 2007).

One brain area that has been closely linked to negative emotion reactivity is the amygdala, a bilateral almond-shaped structure located at the anterior portion of the medial temoporal lobe. Seminal rodent research helped establish the importance of this brain region for the acquisition of conditioned fear (Maren, Aharonov, & Fanselow, 1996; Quirk, Repa, & LeDoux, 1995). Human neuroimaging research has consistently noted the involvement of the amygdala in signaling salient information in the environment, particularly for negatively-valenced states like fear (Denny et al., 2009; Joseph E. LeDoux, 2000; Ochsner & Gross, 2004, 2007, 2008).

Further, when down-regulating negative emotion, reappraisal has been shown to engage regions in the prefrontal cortex (PFC) (e.g. medial and ventrolateral PFC) and other regions including dorsal anterior cingulate cortex (dACC), while at the same time attenuating neural responses in the amygdala (Denny et al., 2009; Ochsner & Gross,

2004, 2005, 2008). Indeed, a recent quantitative meta-analysis has shown that the activity of the amygdala is a frequent regulatory target of reappraisal (i.e. greater activity to negative stimuli without regulation relative to engaging in reappraisal) (Buhle et al., 2011).

This relationship between PFC activity and subcortical activity in the amygdala has been conceptualized as an interaction between bottom-up appraisal systems (including the amygdala) and top-down appraisal systems (including the lateral PFC and dACC) (Denny et al., 2009; Ochsner & Gross, 2007). Bottom-up appraisal systems are thought to subserve intrinsic, unconscious response tendencies, whereas top-down appraisal systems are thought to subserve conscious attention to and selection of various alternative response patterns that can directly influence both the bottom-up appraisal process and the ultimate behavioral response (Ochsner & Gross, 2007; Ochsner, Ray et al., 2009). Consistent with this view, activity from the amygdala has been shown to negatively correlate with activity from regions in the PFC including ventrolateral (Ochsner et al., 2002; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008) and ventromedial PFC (Urry et al., 2006). A recent mediation analysis found a functional pathway from ventrolateral PFC (vIPFC) through the amygdala leading to poorer regulation success during regulation of negative stimuli (defined as poorer ability to down-regulate negative affect), whereas a separate pathway from vIPFC through nucleus accumbens (associated with reward anticipation in other contexts (Knutson, Adams, Fong, & Hommer, 2001)) was associated with greater reappraisal success, defined as greater reductions in negative affect when reappraising versus responding naturally without explicit instructions to regulate.

As discussed previously, one important distinction in the current literature is that reappraisal has typically been operationalized in one of two distinct ways: either via reinterpretation or distancing. In addition to being a theoretically meaningful distinction, with one strategy emphasizing context-specific re-framing (reinterpretation) and the other involving cognitively altering proximity to the self (distancing), these two strategies have been shown to be subserved by distinct neural mechanisms. Most of the social cognitive neuroscience literature has operationalized reappraisal in one or the other way without a direct comparison of each. However, while one neuroimaging study reported no differences between the two strategies in terms of behavioral efficacy, a significant difference in neural recruitment was reported across the two forms of reappraisal (Ochsner et al., 2004). Reinterpretation was shown to recruit relatively more lateral PFC activity, whereas distancing was shown to recruit relatively more anterior medial PFC/ anterior cingulate activity. This result suggests that actively engaging in distancing may indeed depend on the neural mechanisms supporting conceptualizations of the self, given that medial PFC activity has been closely linked to self-related cognition (Denny, Kober, Wager, & Ochsner, in press; Northoff et al., 2006; Qin & Northoff, 2011; van der Meer, Costafreda, Aleman, & David, 2010).

Current Questions

Thus far, both the behavioral and neuroimaging reappraisal literature have been principally focused on examining the implementation of reappraisal during the presentation of a stimulus and during a single experimental session (Denny, Ochsner, Weber, & Wager, under review; Ochsner et al., 2005; Ochsner & Gross, 2008). One

recent study has shown that attenuation of amygdala activity that occurs during downregulation of negative emotion is sustained in a follow-up passive viewing scan that occurred 10 minutes after an active regulation scan (Walter et al., 2009). In addition, Raffael Kalisch has provided initial evidence that the neural substrates mediating reappraisal during negative stimulus presentation may be divided into implementation and maintenance phases, with the former involving relatively greater left lateral PFC recruitment and the latter involving relatively right-lateralized anterior PFC regions that have been implicated in working memory (Kalisch, 2009).

Overall, however, the temporal dynamics and trainability of reappraisal remain unclear. Thus, the current work encompasses four fundamental questions concerning the temporal dynamics of reappraisal: (1) How can we adaptively prepare to regulate emotion via reappraisal? Study 1 addresses this question using mediation effect parametric mapping (MEPM) (Atlas, Bolger, Lindquist, & Wager, 2010; Wager, Davidson et al., 2008) in order to determine what anticipatory neural mechanisms are associated with ultimately self-reported reappraisal success and failure. (2) Can we get better at reappraising over time? Specifically, can longitudinal training in reappraisal lead to improved reappraisal efficacy, as measured by self-reported emotional experience, questionnaire reports, and psychophysiology? (3) Are certain reappraisal strategies more effective over time? In other words, are there differences between reinterpretation and distancing in terms of their adaptive longitudinal impacts? Questions 2 and 3 are addressed by Studies 2 and 3. And finally, (4) Does repeated practice using reappraisal for the same stimuli lead to long-lasting, adapative consequences? This question addresses whether repeated, massed practice in reappraisal—rather than longitudinal,

distributed practice—yields adaptive changes in behavioral self-reports and in the reactivity of the neural architecture supporting reappraisal (i.e. particularly in the amygdala). This question is examined in Study 4.

<u>Study 1: Neural mechanisms of adaptive reappraisal anticipation (Denny et al.,</u> <u>under review)</u>

Introduction

Imagine that you receive some advance notice of imminent bad news—for example, pausing before entering a gravely ill family member in the hospital. You know that you will soon need to regulate your emotions, but you have a few moments to first anticipate beforehand. In that anticipation, you may have expectations about what you're able to experience that may be either helpful or unhelpful in your ultimate ability to regulate your emotions. Study 1 sought to examine how can we adaptively prepare to reappraise, even in the absence of specific instructions about how to go about it. Specifically, what neural mechanisms subserve ultimate self-reported regulation success or failure? Despite the relevance of understanding how best to prepare to regulate negative events, relatively little prior work has investigated the connection between anticipatory neural responses and subsequent self-reported reappraisal success or failure (Denny et al., under review).

Though this question has not been thoroughly examined, prior work has suggested three types of non-competing alternative hypotheses. The first of these is that PFC activity could be involved in setting adaptive anticipatory expectations that ultimately lead to reappraisal success. As reviewed previously, PFC activity—particularly in lateral PFC but also in posterior dorsomedial and ventromedial PFC, along with activity in the dACC—has been consistently associated with the application of reappraisal strategies when one is actually presented with the stimulus (Buhle et al., 2011; Goldin, Manber-Ball, Werner, Heimberg, & Gross, 2009; Kalisch et al., 2005; Kalisch, Wiech, Herrmann, & Dolan, 2006; McRae et al., 2010; McRae, Ochsner, Mauss, Gabrieli, & Gross, 2008; Ochsner et al., 2002; Ochsner, Hughes, Robertson, Cooper, & Gabrieli, 2009; Ochsner et al., 2004; Phan et al., 2005; van Reekum et al., 2007). Also, as reviewed previously, amygdala activity has been shown to drop during regulation (Ochsner & Gross, 2008).

In addition, a few studies have examined the use of reappraisal-like strategies to regulate affective responses elicited during anticipation of a stimulus, with results mostly parallel to those described above. Three studies found that when anticipating the presentation of a negative stimulus, reappraisal can either increase (Delgado, Nearing, Ledoux, & Phelps, 2008; Herwig, Baumgartner et al., 2007) or decrease (Kalisch et al., 2005) activity in medial PFC regions associated with attention to and attributions about emotional states (Kober et al., 2008; Olsson & Ochsner, 2008), along with decreased activity in the amygdala (Delgado, Nearing et al., 2008; Herwig, Baumgartner et al., 2007) presumably reflecting regulation of anticipatory anxiety. A fourth study found that when participants imagined calming and distracting pleasant scenes while anticipating monetary rewards they increased lateral and medial PFC and decreased striatal activity (Delgado, Gillis, & Phelps, 2008). Critically, while all of these studies exmained regulation of affective responses elicited during the anticipation of an upcoming event, none was designed to directly relate anticipatory PFC activity to success at reducing selfreported affective responses to the subsequently experienced event itself.

Related work in the expectancy literature suggests that PFC activity supports expectations about an upcoming negative stimulus that may diminish negative affective responses when these expectations are preparatory and positive. This is exemplified by the placebo effect, where one has an expectation that a drug will reduce the aversive response to a stimulus (e.g. painful heat) (Price et al., 1999). Neuroimaging work has shown placebo analgesia significantly alters the neural correlates of pain anticipation and experience in pain-sensitive brain regions (Atlas et al., 2010; Wager, Atlas, Leotti, & Rilling, 2011; Wager, Rilling et al., 2004). In particular, increases in placebo analgesia have been shown to be predicted by increases in anticipatory activity in a frontoparietal network, including parts of anterior PFC (including Brodmann areas (BA) 9 and 10), and by decreases in activity in a posterior insula/temporal cortex network (Wager et al., 2011).

A second hypothesis, however, is that the PFC could be involved in setting maladaptive expectancies whereby PFC supports negative expectations that promote responses in affective appraisal-related regions like the amygdala. This hypothesis is supported by an extensive literature in human and non-human animals documenting the behavioral and physiological consequences of anticipating negative events predicted by presentation of a conditioned stimulus, including increased heart rate, startle potentiation, freezing, and stomach ulceration (Lang, Davis, & Ohman, 2000; Lang, Kozak, Miller, Levin, & McLean, 1980). This literature has identified the amygdala as a key mediator of such conditioned fear responses (Davis, 1992; J. E. LeDoux, 1996; Quirk et al., 1995; Walker & Davis, 1997). In like fashion, human studies have shown that anticipating negative events elicits self-report (G. Butler & Mathews, 1987; Savitsky, Epley, &

Gilovich, 2001) and psychophysiological (Grillon, Ameli, Woods, Merikangas, & Davis, 1991) markers of negative affect. Imaging studies have shown that anticipation of a clearly or potentially aversive event is associated with increased activation of both the amygdala (Herwig, Abler, Walter, & Erk, 2007; Herwig, Kaffenberger, Baumgartner, & Jancke, 2007; Kaffenberger, Bruhl, Baumgartner, Jancke, & Herwig, 2010) and, critically, the anterior and dorsomedial PFC and anterior cingulate cortex (Mechias, Etkin, & Kalisch, 2010; Ueda et al., 2003).

The relationship between negative anticipation and peripheral physiological reactivity has been shown to be mediated by particular portions of the medial PFC in the rostral dorsal and pregenual cingulate cortices (Wager et al., 2009). Activity in this area may be important for shaping affective processes in a number of ways. For example, activity in this area was associated with lower expectations of drug effectiveness and reduced responses to a placebo analgesic (Wager et al., 2011), which is striking given that dorsal portions of the medial and lateral PFC (including portions of BA 9 and 10) have been implicated in the top-down cognitive generation of negative emotion (Ochsner et al., 2004; Ochsner, Ray et al., 2009). This suggests that prefrontal cortex implements conceptual processes that support both generation and mitigation of negative emotion.

In addition, similar medial regions of rostral MPFC, including portions of BA 9 and 10, have been implicated in subserving mind-wandering (Christoff, Gordon, Smallwood, Smith, & Schooler, 2009; Mason et al., 2007), which is similar to anticipation in that the mind is engaged in thoughts that are not directly related to current stimulus presentation. Mind-wandering has been shown to recruit a similar network of regions as the brain's default mode, which involves regions that are relatively more active when at rest and not engaged in task performance (Gusnard, Akbudak, Shulman, & Raichle, 2001; Raichle et al., 2001). Interestingly, a recent experience-sampling study has shown that people mind-wander frequently regardless of current activities and are less happy when they do so, and that mind-wandering is often a cause, rather than a consequence, of unhappiness (Killingsworth & Gilbert, 2010). If one were to engage in mind-wandering during reappraisal anticipation, especially if you are unaware of the exact nature of the forthcoming stimulus presentation, it's possible that you would later be less prepared to successfully reappraise the stimulus. Taken together, these literatures on anticipation and mind-wandering demonstrate that not only is the type of expectation—negative or positive—about an upcoming affective stimulus important in determining its impact on subsequent affective responses, but that similar regions of anterior PFC have been associated with the maintainance of both types of expectations.

A third hypothesis is that regions involved in emotion-related processes may play key roles in setting adaptive or maladaptive expectancies. Here, prior work has suggested that the insula might play a key role. In addition to PFC, the insula has also been shown to be importantly involved in the anticipation and appraisal of emotional events, in addition to the integration of sensory and motor information (Augustine, 1996). Differences in anatomy (Mesulam & Mufson, 1982a, 1982b; Mufson & Mesulam, 1982, 1984) and resting-state functional connectivity (Deen, Pitskel, & Pelphrey, 2011) have been reported within the insula, with separate subregions for posterior, ventral anterior, and dorsal anterior insula, each of which have been shown to have slightly different functional specializations. In particular, posterior insula has been more strongly associated with primary interoceptive representations of sensations from the body, while increasingly anterior insula has been more associated with emotional and motivational states (Augustine, 1996; Craig, 2009; Nitschke, Sarinopoulos, Mackiewicz, Schaefer, & Davidson, 2006; Wager & Barrett, 2004). During implementation of reappraisal, insula activity—particularly posterior insula activity—has frequently been observed as being a regulatory target (i.e. showing greater activity during negative event appraisal relative to regulation) (Denny et al., 2009; Ochsner et al., 2002; Ochsner & Gross, 2008; Ochsner et al., 2004).

The anterior insula, by contrast, has been strongly linked to integration of affective information and internally-focused awareness. While some researchers have reported the involvement of both dorsal and ventral anterior insula in interoceptive awareness (Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004), Wager and Barrett (2004) have provided evidence for a ventral-dorsal distinction in the anterior insula, such that ventral anterior insula is more strongly associated with emotional awareness (Carlson, Greenberg, Rubin, & Mujica-Parodi, 2011), and dorsal anterior insula is more strongly associated with updating goal states and top-down executive control (Nee, Wager, & Jonides, 2007; Wager, Jonides, & Reading, 2004). Ventral anterior insula activity has been reported during the anticipation of aversive events (Carlson et al., 2011; Kalisch et al., 2006), though these effects weren't shown to be specifically attuned to negatively-valenced anticipation states (Carlson et al., 2011). The fact that anterior insula has been implicated broadly in both affective integration and cognitive control suggests that it has the potential to promote reappraisal success via integrating information about the body, one's current emotional state and current task goals.

To differentiate among these three hypotheses, we employed a variant of a wellstudied reappraisal task (Ochsner & Gross, 2008). This task presents participants with aversive images and asks them either to let themselves respond naturally (i.e. baseline Look trials) or to reinterpret the meaning of the image in a way that lessens its unpleasant impact (i.e. Reappraise trials). The present task modified the basic trial structure to insert an anticipatory gap between the presentation of the cue instructing participants that they would Look or Reappraise and the presentation of the aversive or neutral image.

Using this design we adopted a three-step analysis procedure to address the three hypotheses enumerated above concerning the way in which expectations of the need to reappraise influence subsequent neural and behavioral responses to affective events. We reasoned that the best way to determine how expectations influence ultimate reappraisal success was by first identifying a signature of successful reappraisal. To do this, our first step involved correlating reappraisal success (defined as the drop in self-reported negative affect on Reappraisal as opposed to Look trials) with activity in the amygdala, which is the affect-related region most commonly modulated by reappraisal of negative emotion (Ochsner & Gross, 2008). This identified a region of the left amygdala whose activity during reappraisal of an aversive image was negatively correlated with reappraisal success. In the second step, we used Mediation Effect Parametric Mapping (MEPM) to test for the hypothesized relationships among anticipatory neural activity, amygdala activity during reappraisal, and self-reports of negative affect (Atlas et al., 2010; Wager, Davidson et al., 2008). Here, we aimed to determine whether and how brain activity during anticipation of reappraisal (i.e. in the 6 s before the image to be reappraised was presented) is associated with subsequent reappraisal success, mediated

by stimulus-related activity in the functionally defined area of the left amygdala described above. On one hand, if anticipating reappraisal enhances regulatory success, then we should find that anticipatory activation of reappraisal-related regions leads to larger drops in negative affect via down-regulation of subsequent amygdala responses to aversive images. On the other hand, if anticipating reappraisal diminishes regulatory success, then we should find that anticipatory activation of reappraisal-related regions leads to aversive images in negative affect via down-regulation of subsequent amygdala responses to aversive images.

Finally, in the third step, we sought to determine how well our mediation results fit with prior work on related cognitive and affective phenomena (e.g. the default mode, various forms of cognitive control, expectancies, emotional responses and judgments of self and other). We deemed this important because it would help constrain the functional interpretation of our results by telling us how the regions we see active during anticipation are similar to or different than those implicated in other behaviors. To do this, we used pattern expression analyses to test the functional coherence between our mediation results and the results of related prior studies as approximated by Neurosynth software (Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011).

<u>Methods</u>

Participants

Thirty-six healthy participants (mean age=22.0 years; 13 female) were recruited in accordance with the human subjects regulations of Columbia University and were paid \$20/hour for their participation. All participants were right-handed as measured by the Edinburgh Handedness Inventory and were screened with questionnaires to ensure good

general health and fMRI scan eligibility. Six participants were excluded prior to analysis because they were not within movement, normalization, or timing-accuracy tolerances. Thus, the present analyses were performed on data from 30 participants.

Materials

The basic stimuli, task design, and procedures used in the current study have been detailed in a prior report focusing on activity solely during the presentation of aversive images (Wager, Davidson et al., 2008). In this prior report the anticipation period was not examined. The current study focuses on the relationship between activity during the cue and anticipation periods and subsequent activity during the picture presentation period.

Forty-eight aversive images were selected from the International Affective Picture Set (IAPS; Lang, Greenwald, Bradley, & Hamm, 1993); mean normative valence = 2.24, mean normative arousal = 6.28), comprising a subset of those used in Ochsner et al. (2004), plus twenty-four neutral images (valence = 5.27, arousal = 3.51), for a total of 72 test images. Each image subtended ~12° visual angle when viewed inside the scanner. An additional set of 18 similarly valenced and arousing aversive images and 7 neutral practice images was used during a training session conducted prior to scanning (and described below).

Task Design

Test images were presented in one of three conditions. For the LookNeu and LookNeg conditions, participants were shown either neutral or aversive images and were asked to look at the image, understand its content, and allow themselves to experience/feel any emotional response it might naturally elicit. By contrast, for the ReappNeg condition, participants viewed aversive images and were asked to reinterpret their meaning so that they felt less negative in response to them (cf. previous published work from our laboratory (Ochsner & Gross, 2008)). The assignment of negative images to conditions was randomized and counterbalanced across participants. Before presentation of each image, participants viewed a cue that signaled both the image type (aversive or neutral) and the instruction type (Look or Reappraise). Cues were white shapes—a circle, a square, and a triangle (~0.5° visual angle)—presented on a black background. The assignment of shape to condition was counterbalanced across participants.

Previous studies of reappraisal have not separated brain activity related to anticipation and instruction processing, stimulus viewing, and picture rating, and a goal of our task design was to provide the ability to separately estimate the magnitude of brain activation related to each of these three phases of the image viewing and rating procedure. To accomplish this, a partial trial design was employed (Ollinger, Corbetta, & Shulman, 2001; Stern, Wager, Egner, Hirsch, & Mangels, 2007). Three variants of each task condition (LookNeu, LookNeg, and ReappNeg) were used, with an equal distribution of each type of trial: full (AntStim) trials, anticipation-only (AntOnly) trials, and stimulus-only (StimOnly) trials. On full trials, a 2 s instruction cue was followed by a 4 s anticipatory interval during which a fixation cross was presented on the screen. An image was subsequently presented for 8 s, followed by a fixation cross for 4 or 7 s jittered interstimulus interval (ISI; uniform distribution of 4 and 7 s intervals). Following the ISI period, the words ''How negative do you feel?'' appeared onscreen for 2.1 s, and participants rated their current level of negative affect on a five-point scale by pressing a button with one of five fingers on a button-response unit (0 = "not at all negative," indicated by a thumb button press, up to 4 = "extremely negative," indicated by a fifth-finger button press). Following the rating, a 4 or 7 s jittered inter-trial-interval concluded the trial. This trial structure is shown in Figure 1 for a full trial. The AntOnly trials were identical to the Full trials, except that the picture presentation period was omitted. The StimOnly trials were identical to the full trials, except that the full trials, except that the 4 s anticipation interval was omitted.

This design allowed us to construct orthogonal predictors for Cue-, Anticipation-, and Image-related brain activity related to each trial type in the General Linear Model (GLM) that could provide efficient estimates of activation in each phase of the trial for each condition.

Procedure

A comprehensive pre-scanning training procedure was used to assure that participants understood the cue-task associations and the reappraisal strategy (see Wager et al., 2008 for details). During the task in the fMRI scanner, 108 total trials were presented (36 trials per condition), according to the trial structure above. Within each condition, 12 trials were presented for each trial type (LookNeu, LookNeg, and ReappNeg) X trial type (full trial, AntOnly, StimOnly) combination. Following scanning, participants completed a post-task questionnaire during which they confirmed that they reappraised as instructed prior to being debriefed and thanked for their participation.

Data Acquisition and Analysis

I. Behavioral

Behavioral data were analyzed using linear mixed models incorporating fixed effects estimates for trial type, condition, and their interaction, and a random effect consisting of an intercept for each participant.

II. fMRI

Whole-brain fMRI data were acquired on a 1.5T GE Signa Twin Speed Excite HD scanner (GE Medical Systems). Functional and anatomical images were acquired with a T2*-sensitive EPI BOLD sequence with a TR of 2000 ms, TE of 40 ms, flip angle of 60°, field of view of 22 cm, 24 slices, and 3.44 × 3.44 × 4.5 mm voxels. Stimulus presentation and data acquisition were controlled using E-Prime software (PST Inc.). Data from one behavioral trial from one participant had to be discarded due to technical problems. Functional images were subjected to standard preprocessing using FSL (FMRIB Centre, University of Oxford) and SPM2 (Wellcome Department of Cognitive Neurology, UCL) software, and first-level (within-participant) statistical analysis using SPM2. Separate regressors in the GLM were specified for fMRI responses to the cue, anticipation, stimulus viewing, and rating response periods.

II(a). Defining Amygdala Region-of-Interest

In order to address our first question of interest concerning how reappraisal expectations modulate subsequent behavioral and neural responses to affective events, we first subjected values for the [ReappNeg image viewing - LookNeg image viewing] contrast to second-level robust regression analysis (Wager, Keller, Lacey, & Jonides, 2005) to localize regions correlated with reappraisal success, defined as each participant's self-reported [LookNeg – ReappNeg] rating average. This reappraisal success regressor excluded ratings made during AntOnly trials, as those ratings were made on trials in

which no image was presented. We spatially limited this robust regression analysis to an a-priori region of interest, the amygdala, in order to define a seed region to be used in subsequent mediation analyses. Each participant's global MR signal during the picture presentation period was used as a covariate in this analysis. Because signal in the medial temporal lobe is subject to signal drop out, and given our a-priori interest in the amygdala, threshold for this analysis was set at p<0.01 (one-tailed).

II(b). Mediation Analysis

We then employed Mediation Effect Parametric Mapping (MEPM). The MEPM analysis is based on a standard three-variable path model (Baron & Kenny, 1986) where a predictor (X) is related to an outcome (Y) via a mediator (M). For a mediation result to be significant, M must be related to X (path a), M must be related to Y after controlling for X (path b), and the indirect relationship (a*b) must also be significant. MEPM analysis was conducted on [ReappNeg - LookNeg] contrast values using a bias-corrected, accelerated bootstrap test for the statistical significance of the product a*b (Efron & Tibshirani, 1993; Shrout & Bolger, 2002). In order to compute contrast values suitable for a mediation analysis including activation during the full pre-stimulus anticipation window (i.e. for the cue and anticipation periods), a weighted sum of the beta estimate maps for cue and anticipation was computed for each participant using the sum of each respective column in the design matrices as the weight. Thus, these contrast values represented the total area under the curve (AUC) of the predicted time course for each condition. Contrast values were then built by taking the difference of the Reapp Neg and Look Neg AUC maps.

MEPM analyses were then performed using the [ReappNeg – LookNeg] contrast values during the cue/anticipation period (the X or predictor variable), the stimulus presentation period (the M or mediator variable), and behavioral reappraisal success scores (the Y or outcome variable). We performed a MEPM analysis in which the mediator values were pre-defined as beta weights from the amygdala seed region, defined as described above, during the picture presentation period, and then the whole brain was searched for predictor (X) regions at cue/anticipation whose activity showed a relationship with reappraisal success (Y) that was mediated by the activity of the seed amygdala region (M) (Figure 2). In this analysis, by-participant average beta weights for global cue/anticipation activity (using the AUC images) and global stimulus presentation period activity were each entered as covariates.

Family-wise error thresholds for resulting mediation t-score (a*b) images were determined using AlphaSim (Ward, 2000). Significant clusters (FWE-corrected, p<0.05) were thresholded at p<0.05, uncorrected, with an extent of at least 50 voxels. For display purposes using NeuroElf software (neuroelf.net), mediaiton t-score images were then resliced to isometric voxels (2 x 2 x 2 mm), and family-wise error (FWE) multiple comparison correction thresholds were again determined using AlphaSim. Clusters were thresholded at p<0.05, uncorrected, with an extent of at least 333 voxels, resulting in a whole-brain corrected FWE rate of p<0.05.

III. Pattern Expression Analysis

Finally, we performed a pattern expression analysis between the present mediation results and each of 13 task set maps derived via Neurosynth mapping of the extant literature (neurosynth.org) (Yarkoni et al., 2011). As detailed by Yarkoni and colleagues, Neurosynth uses an HTML parser to search the continually evolving online database of thousands of recent neuroimaging studies for papers that contain distinct terms at sufficiently high frequencies (i.e. terms that occur in at least 20 studies). Neurosynth then extracts all coordinates from each paper associated with a given highfrequency term. While the automated extraction algorithm does not distinguish between contrasts within a paper or between activations and deactivations, meta-analytic comparisons have shown that Neurosynth maps are nonetheless valid and reliable as a rough estimation of the neural correlates of various psychological phenomena (Yarkoni et al., 2011). To minimize differences among varying thresholding methods, unthresholded maps were used.

Whole-brain cross products were calculated between mediation t-statistic images from the present results and effect images from the neurosynth maps, which were generated for the following 13 search conditions associated with diverse cognitive and emotional phenomena: Maps corresponding to "emotion" (324 studies, including studies of pain and empathy) and "emotion regulation" (29 studies, including reappraisal and suppression) were of particular a priori interest, and the additional terms were chosen to approximate the neural correlates of additional affective (reward, autonomic, aversion, pain), cognitive (semantic, executive, reasoning), and social cognitive-related phenomena (self, default, episodic, social).

<u>Results</u>

Behavioral Results

Figure 3 shows average negative affect ratings for each condition for AntStim and StimOnly trials and separately for anticipation only (AntOnly) trials. Negative affect
reports did not differ between AntStim and StimOnly trials (F(1,145)=.715, n.s.), nor was there a significant interaction between trial type and condition for AntStim and StimOnly trials (F(2,145)=1.733, n.s.), so data is shown collapsed across those two trial types. However, there was a main effect of condition (F(2,145)=428.36, p<0.001); negative affect ratings for both negative image viewing conditions (Reapp Neg and Look Neg) were significantly greater than those for the Look Neu condition (t(29)=12.59, p<0.001, and t(29)=22.62, p<0.001, respectively). Critically, among AntStim and StimOnly trials, reappraising negative images significantly modulated participants' self-reported negative affect relative to responding naturally to negative images (t(29)=8.10, p<0.001).

For AntOnly trials, there was a main effect of condition (F(2,58)=10.14, p<0.001), with Look Neu ratings significantly lower than Look Neg (t(29)=3.29, p<0.003) and Reapp Neg (t(29)=4.78, p<0.001) ratings, but no significant difference between Look Neg and Reapp Neg ratings (t(29)=0.15, n.s.).

I. Amygdala Region-of-Interest (ROI)

In order to address our primary question regarding potential amygdala-mediated relationships involving anticipatory brain activation that are correlated with reappraisal success, we first carried out a robust regression analysis to determine which voxels in the amygdala showed activation during the stimulus presentation period that was significantly correlated with reappraisal success. Three voxels in the left amygdala were significantly negatively correlated with reappraisal success at the search threshold (p<0.01, one-tailed). These voxels in the left amygdala (MNI: [-21, -3, -23],

[-14, -7, -23], and [-17, -7, -23]) represented our amygdala seed ROI for the subsequent mediation analysis.

II. Mediation Analysis

We found that a broad area of right rostrolateral PFC (RLPFC; BA 10) showed anticipatory activity prior to reappraisal that was negatively correlated with reappraisal success and significantly mediated by amygdala activity during the picture presentation period (Figures 2 & 4; Table 1). Increased anticipatory RLPFC activity was positively correlated with amygdala activation during the stimulus presentation period, and stimulus-related amygdala activity was negatively correlated with reappraisal success. In addition, a more dorsal medial PFC region (BA 8) also showed this negative mediated relationship, as did the posterior cingulate/precuneus, superior temporal gyrus/temporoparietal junction, and pre- and postcentral gyrus (Figure 4; Table 1). Several regions also showed a significant positively mediated relationship. We observed a significant positive mediation result in bilateral insula (Figure 4; Table 1). Left ventral anterior insula and right ventral mid-insula activity was positively correlated with reappraisal success, mediated by amygdala stimulus-related activity. Anticipatory insula activity in these ROI's was negatively correlated with stimulus-related amygdala activity. Two separate clusters in the anterior lobe of the cerebellum also exhibited this pattern. In order to examine individual differences in relative recruitment of anticipatory regions associated with reappraisal success and failure, we assessed correlations between extracted beta-weights in these ROI's. Anticipatory activity (Reapp Neg – Look Neg during cue/anticipation) from each insula cluster was positively correlated with activity from each PFC cluster (BA 8 and BA 10); right insula activity was correlated r=0.46, p < 0.02 with BA 8, and r = 0.60, p < 0.01 with BA 10, whereas left insula activity was correlated r=0.48, p<0.01 with BA 8, and r=0.52, p<0.01 with BA 10.

III. Pattern expression analysis

We then tested the functional coherence between the present results (i.e. anticipatory brain activity related to reappraisal success and mediated by amvgdala activity) and the existing neuroimaging literature for a variety of task sets, as approximated via Neurosynth software (Yarkoni et al., 2011). The mediation results showed by far the best match (and most opposite pattern of functional coherence) with the default mode map, indicating that the present pattern of anticipatory regions predicting reappraisal failure and success is relatively opposite of the results observed for default mode activation (that is, negative mediation results were associated with default mode activations and positive mediation results were associated with default mode deactivations). However, the mediation results showed the greatest functional coherence with aversion, emotion, and autonomic task sets. Neurosynth maps are displayed in Figure 5A for default mode, social/mentalizing, executive, and autonomic-related activity, for purposes of comparison with the present mediation results for the same slices (Figure 5A, bottom). Figure 5B shows results of the pattern expression analysis between the present results and all 13 Neurosynth images.

<u>Discussion</u>

The present results serve as the first investigation of mediated relationships among anticipatory brain activity and subsequent self-reported emotion regulation success. In this study we sought to identify regions of the brain that show anticipatory activity prior to the instruction to reappraise that predict changes in amygdala activity during reappraisal itself, which in turn predict changes in self-reported reappraisal success or failure. We found that anticipatory RLPFC activity, which is not typically observed in reappraisal studies (Buhle et al., 2011), predicted increased amygdala activity during the picture presentation period, which in turn predicted reappraisal failure. Dorsomedial PFC, superior temporal gyrus, posterior cingulate/precuneus, and pre- and postcentral gyrus activity also predicted reappraisal failure, mediated by stimulus-related amygdala activity. In addition, we found that anticipatory activity in left anterior and right mid-insula, as well as cerebellum, predicted decreased stimulus-related amygdala activity and in turn greater reappraisal success. Notably, as substantiated in the pattern expression analysis, the network of brain regions that were related to reappraisal failure and success during the anticipation period did not bear great similarity to the network of regions recruited during emotion regulation implementation itself (Buhle et al., 2011). *Implications for Neural Mechanisms of Expectancy x Regulatory Strategy Interactions I. Anticipatory Activity Associated with Less Regulatory Success*

In thinking about the meaning of anticipatory activations that predicted less reappraisal success it is important to emphasize that participants were not explicitly instructed to perform any regulation during the anticipation interval, in contrast to prior work (Delgado, Gillis et al., 2008; Delgado, Nearing et al., 2008; Herwig, Baumgartner et al., 2007; Kalisch et al., 2005). Rather, they were simply told to get ready for the upcoming picture and be ready to employ the cued strategy during the picture presentation.

In this context it is interesting that we observed activity in RLPFC and other areas that have been associated with executive control and mentalizing, like the temporoparietal junction (Denny et al., in press). RLPFC has been previously associated with emotional awareness and the self-generation of information - including intentions

for future actions (Burgess, Scott, & Frith, 2003; Christoff & Gabrieli, 2000; Costa et al., 2011; Gilbert et al., 2006; Ochsner, Hughes et al., 2009; Ray et al., 2005). This suggests that the anticipatory RLPFC activity observed here may reflect self-generation of negative expectancies on the part of the participant (Sawamoto et al., 2000) in advance of the need to regulate that ultimately exert influence over their reappraisal success. Indeed, a very similar region of RLPFC has shown positive correlations with state negative affect when viewing aversive pictures (Nitschke et al., 2006).

Additional regions that were negatively associated with reappraisal success have been associated with a network for mentalizing—i.e., thinking about one's own or another's mental state—including dorsomedial PFC, posterior cingulate/precuneus, and superior temporal gyrus/temporoparietal junction activity (Denny et al., in press; Gilbert et al., 2006; Qin & Northoff, 2011; van der Meer et al., 2010; Van Overwalle, 2009, 2011). In combination with RLPFC Activity, this suggests that participants may have been imagining how they might feel when the picture is presented, and were elaborating on it, which served to create a negative expectation that was ultimately confirmed and led to poorer regulation outcomes (Klaaren, Hodges, & Wilson, 1994; Wilson, Lisle, Kraft, & Wetzel, 1989).

This interpretation raises the question of whether participants were feeling negative during the anticipation interval as a result of developing the proposed negative expectation. Given that we did not observe significant differences in self-reported negative affect scores for anticipation-only Reappraise and Look Negative trials, however, the idea that participants felt especially "negative" during reappraisal anticipation in particular is not supported in the present work. That said, the lack of

behavioral evidence for anticipatory negative affect may be due to the facts that 1) multiple brain regions exhibited anticipatory activity that was both positively and negatively associated with reappraisal success via amygdala activity, and 2) activity from regions of interest that positively (i.e. insula) and negatively (i.e. RLPFC) mediated reappraisal success were positively correlated. Thus, it's possible that there are both benefits and costs of reappraisal anticipation, and this may have obscured a behavioral main effect on self-reported emotion (i.e. a general increase in anticipatory negative affect during reappraise trials).

II. Anticipatory Activity Associated with Increased Regulatory Success

In the present study, not all anticipatory activation was maladaptive, however. We observed a substantial area of left ventral anterior and right ventral mid-insula activation that predicted diminished amygdala activation during picture presentation and in turn ultimate reappraisal success. This result is consistent with prior work showing that the ventral anterior insula is importantly involved in integration of affective information, including meta-awareness of bodily states and awareness of emotional and motivational states more generally (Wager & Barrett, 2004), and that greater emotional awareness may yield better regulatory outcomes (Barrett, Gross, Christensen, & Benvenuto, 2001). Here, it is possible that greater insula activity reflects greater internal and emotional awareness, which in turn helps participants be ready to clearly identify their subsequent emotional responses to presented photos, which in turn helps them more easily pick effective reappraisals.

In addition to insula, anticipatory cerebellar activity promoted reappraisal success via stimulus period amygdala deactivation. This is consistent with work implicating similar deep cerebellar foci in arousal and affective valuation (Stoodley & Schmahmann, 2009; Wager et al., 2011; Wager, Barrett et al., 2008).

Relationships to Other Phenomena

The pattern expression analysis was designed to quantitatively assess the fit between the present results and meta-analytic maps corresponding to a variety of related phenomena, including across affective, cognitive, and social domains. The results of the pattern expression analysis support the conclusion that the regions that are negatively associated with reappraisal success are similar to those associated with the default mode (Gusnard et al., 2001; Raichle et al., 2001), as this was the overall best match. This result indicates that those regions that were negatively associated with reappraisal success in the mediation analyses are most closely linked to the positive activations associated with the default mode. As noted previously, important elements of the default mode network, including rostral MPFC, have been implicated in mind-wandering (Christoff et al., 2009; Mason et al., 2007). The pattern expression results described here bolster the interpretation that participants may have engaged in stimulus-independent thought, including mind-wandering, that was ultimately not productive or helpful.

Finally, the findings of the current study are further illuminated when viewed in the context of prior studies that examined emotion regulation during anticipation of emotional events (Delgado, Gillis et al., 2008; Delgado, Nearing et al., 2008; Erk, Abler, & Walter, 2006; Herwig, Baumgartner et al., 2007; Kalisch et al., 2005). In one study, Herwig and colleagues reported that anticipatory posterior medial and dorsolateral PFC activity may serve to attenuate negative emotional processing and down-regulate anticipatory activity in the amygdala when using a "reality checking" emotion regulation technique, similar to psychological distancing (Ochsner & Gross, 2008). By contrast, in the current experiment, participants were instructed to reinterpret stimuli by telling themselves a story about how the outcome is not as negative as it first seemed, and activation of a substantially more anterior MPFC region was associated with poorer regulation success. This region was also substantially more anterior relative to the regions associated with performing cognitive regulation (thinking safe, calming thoughts) in paradigms examining anticipation of physical pain (Delgado, Nearing et al., 2008; Kalisch et al., 2005) or rewarding outcomes (Delgado, Gillis et al., 2008). Prior to picture presentation, deliberating about what may be presented and how best to reinterpret it is premature, since there was no way to predict the content and themes of the upcoming picture (other than its global valence). We argue that this higher-order reasoning may have been subserved by RLPFC.

In some support of this notion, Erk and colleagues (2006) report that a cognitive load (n-back) manipulation during anticipation did not significantly affect subsequent amygdala activity when a negative stimulus was presented, though there was some evidence of a trend in left amygdala. However, a region of anterior MPFC similar to the RLPFC results reported in this study was activated during anticipation of negative stimuli under conditions where participants were relatively free to let their minds wander (i.e. very low cognitive load). This is consistent with the results of the current study and the mind-wandering implications discussion above, as well as the idea that this area of rostral MPFC may play a role in abstract conceptualizations of unpleasant experiences (Amodio & Frith, 2006).

Limitations and Future Directions

Inasmuch as Study 1 advances our understanding of the mechanisms underlying the anticipation of emotion regulation, future research may target at least four questions not addressed here. First, it is notable that we did not observe any significant direct relationships between anticipatory brain activity and reappraisal success in our mediation analysis (across entire whole-brain corrected clusters), even though the indirect mediation effects reported were significant. Future analyses may examine what accounts for this statistical suppression by examining additional third variables (including additional potential mediators) and may incorporate multilevel modeling, which would assess whether the reported effects hold within as well as between individuals.

Second, in our study the nature of the expectancy was open-ended, in the sense that participants did not know the characteristics of the forthcoming stimulus (beyond its overall valence and whether it would be reappraised), and our reappraisal strategy required a stimulus-specific reinterpretation. Thus, we may have set participants up for some degree of failure insofar as their expectations couldn't help but be incorrect and potentially unhelpful. Future work may unpack whether expectations about alternative types of reappraisal strategies may prove more adaptive. For example, one candidate is psychological distancing (Kross et al., 2009; Walter Mischel & Baker, 1975; Ochsner & Gross, 2008), which involves viewing a stimulus in a detached, objective, impartial manner. Such a strategy may invoke more of a task "mindset" that is not stimulus specific and relatively adaptive, even during anticipation.

Third, future studies could incorporate psychophysiological data, such as skin conductance response and heart rate variability. This would be useful to more completely establish the nature of participants' emotional states during anticipation of reappraisal

and provide additional measures of changes in emotional response that might be differentially impacted by anticipation (Gross, 1998a; Urry, 2010).

Finally, it would be very interesting to know whether individuals that vary within the normal or abnormal range of emotional responding and regulatory ability would show more or less RLPFC or insula activity during reappraisal anticipation. Among healthy individuals, future work may examine individual differences that may lead to greater or less RLPFC activity, including whether adaptive response patterns are more prevalent over time in aging. Regarding clinical implications, in one of the few neuroimaging studies to investigate the anticipation of emotional stimuli in a clinical population, Abler and colleagues (2007) reported elevated dorsolateral PFC (BA 9) activation in depressed patients for anticipation of negative vs. positive stimuli in the absence of explicit instructions to subsequently regulate during stimulus presentation, which is consistent with the results of the current study (Abler, Erk, Herwig, & Walter, 2007). It would be similarly interesting to know whether patients with different forms of psychopathology involving emotion dysregulation would show greater anticipatory RLPFC activity in our paradigm, coupled with diminished ability to subsequently down-regulate amygdala responses to aversive stimuli.

<u>Study 2: Behavioral Effects of Reappraisal Training (Denny & Ochsner, in prep.)</u> <u>Introduction</u>

In addition to knowing how to adaptively anticipate reappraisal, a second question motivating the present work was whether one can become better at reappraising over time

with repeated practice. In other words, we sought to determine if self-reports of negative affect, both inside and outside the context of a laboratory task, would be reduced over time through a relatively short course of training in reappraisal. This question, while highly relevant to basic and translational research, has not been fully addressed in the literature. Studies 2 and 3 represent the first investigation into the longitudinal trainability of reappraisal.

While this question has not been examined directly, prior work in clinical contexts has substantiated the effectiveness of cognitive therapies that contain elements of reappraisal in addition to other regulation techniques, such as cognitive behavioral therapy (CBT) (Hollon & Beck, 1994). CBT involves "reality checking" of current patterns of reasoning, emotion, and behavior, and is individually tailored to the needs of a patient based on their history and treatment goals (Sheldon, 2011). This training timecourse is also generally extensive; a typical course of CBT often lasts for three months (Dobson, 2010). A recent review of meta-analyses of the effectiveness of CBT for various clinical disorders indicates that it is particularly effective in reducing reports of negative affect and clinical symptomology for unipolar depression, generalized anxiety disorder, panic disorder, social phobia, and posttraumatic stress disorder (A. C. Butler, Chapman, Forman, & Beck, 2006). In addition, dialectical behavior therapy (DBT), a CBT-based therapy, has been shown to be an effective treatment for borderline personality disorder, though again it involves training in disparate cognitive and behavioral strategies (Linehan, 1993; Linehan, Armstrong, Suarez, Allmon, & Heard, 1991; Linehan et al., 1999).

The present study, by contrast, sought to address three knowledge gaps simultaneously: (1) Can healthy participants benefit from reappraisal training? (2) Can the strategy be focused to only include reappraisal (and more specifically, either reinterpretation or distancing)? And finally (3) can a relatively short course of training (two weeks) lead to longitudinal adaptive effects on self-reported negative affect, both inside and outside of the laboratory?

We hypothesized that reappraisal would be an effective strategy that would exert adaptive longitudinal effects. Further, there is reason to believe that the longitudinal training profiles of reinterpretation and distancing may be different. As described previously, reinterpretation refers to recontextualizing an affective stimulus in a way that reduces its negative impact. For example, one could imagine that the events depicted in a negative image are not as bad as they first seemed, or that help is on the way. Distancing, by contrast, involves appraising a stimulus as a detached, objective, impartial observer, and/or imagining that whatever the stimulus is depicting occurred far away from me or a long time ago. One important distinction between these two strategies was described in the discussion of Study 1; reinterpretation, as described here, is a very context-specific strategy. Thus, it may be harder to adopt a facilitative reinterpretation mindset over time if instructions are stimulus-specific, though it is possible that some benefits may generalize. Distancing, on the other hand, can more easily be conceptualized as "mindset" of being detached, and as such, one might expect distancing to not only exert effects for regulation trials, but also for trials in which no regulation was explicitly instructed. Thus, if adopting a distanced mindset becomes more intuitive, it may exert effects even when the explicit instruction is to "look and respond naturally," as is often

used in unregulated conditions in reappraisal work (Denny et al., under review; Ochsner & Gross, 2008).

Furthermore, when considering a reappraisal training paradigm, four conceptual factors need to be addressed: (1) the length of the training, (2) the specific strategy (or strategies) to be trained, (3) whether the training is distributed (over many days) or massed (repeated training exposures in a single day), (4) whether practice is with novel or repeated stimuli.

In Studies 2-4, we sought to vary several of these factors in order to make initial inferences about the trainability of reappraisal, and future work will continue to vary these factors systematically. In Studies 2 and 3, we sought to use a relatively short course of training (two weeks) with training in either reinterpretation, distancing, or a control group that saw the same negative stimuli but were never cued to regulate and were always told to always look and respond naturally (the "Look Only" group). Further, we sought to examine training that is distributed in time (sessions every 2-5 days), with presentations of unique affective images during Sessions 1-3, and the same images from Session 1 presented at Session 4 to address test-retest reliability. In Studies 2 and 3 we sought to examine the duration of effects over the course of the two-week training period. *Methods*

Participants

As detailed below, to increase power and reliability (and given a lack of interaction with whether one completed the task with psychophysiological recording), participants' behavioral and questionnaire data was combined across Studies 2 and 3. 103 participants from the Columbia University community gave informed consent and

completed the 4-session training procedure and were paid \$20/hour for their participation. 2 participants' data were not analyzed due to too much elapsed time between sessions, 1 participant's data were not analyzed due to an inaccurate session number being entered into the computer program controlling the counterbalanced image display, and 1 participant's data were not analyzed due to being a behavioral outlier of more than 3.5 standard deviations from the mean, with additional comments from the experimenter that the subject was not properly attending to the task. Thus, the current self-reported negative affect results reflect data from 99 participants (N=33 in each of Reinterpretation [mean age = 23.9 years, 26 female], Distancing [mean age = 23.9 years, 22 female], and Look Only groups [mean age = 22.4 years, 19 female]). Questionnaire reports from 3 Distancing participants were not available due to technical difficulties with questionnaire data collection at Session 1. Participants reported no psychiatric history, no chronic pain or autoimmune disorders, no substance abuse, and no psychoactive medication use within the past 6 months.

Materials

99 aversive images were selected from the International Affective Picture System (IAPS) (Lang et al., 1993); mean normative valence = 2.39, mean normative arousal = 6.02), along with 9 additional negative images that have been used in prior reappraisal studies (Ochsner et al., 2002; Ochsner et al., 2004), for a total of 108 negative task images. 54 neutral images from the IAPS were also shown; mean normative valence = 5.33, mean normative arousal = 3.15. An additional set of 18 similarly valenced and arousing images and 6 similarly valenced and arousing neutral images were used during training and practice (and described below).

Procedure

During each of 4 sessions, each spaced 2-5 days apart, participants (1) completed questionnaires, (2) received training in either reappraisal (reinterpretation or distancing) or the control instructions (Look Only), and then (3) completed an image-based task that's very similar to the one reported in Study 1 and in prior work (Ochsner et al., 2002; Ochsner et al., 2004). Each of these 3 components is explained in more detail below.

I. Questionnaires

Participants completed questionnaires at the beginning of every session. Two longitudinal questionnaires were given at all 4 sessions: the Perceived Stress Scale (PSS; Cohen, Kamarck, & Mermelstein, 1983) and the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988). At Session 1, these questionnaire items were framed "In general", and at Sessions 2, 3, and 4, they were framed "In the past few days". The "in general" and "in the past few days" forms of the PSS are contained in Appendix A and B, respectively. During Session 1 only, participants also completed the Ruminative Responses Scale (RRS; Nolen-Hoeksema & Morrow, 1991).

II. Training

At each of the 4 sessions, participants then were randomly assigned to receive training in either Reinterpretation, Distancing, or Look Only. Training consisted of an approximately 6-10 minute interaction with an experimenter in which a standardized set of instructions were given (see Appendices C-E for the training script for Reinterpretation, Distancing, and Look Only, respectively). In the course of these instructions, participants were first given instructions about the two cues that they would see: LOOK and DECREASE. For images preceded by a LOOK cue, participants were instructed to simply look and respond naturally to the image. For images preceded by the DECREASE cue, participants were given standardized instructions in the appropriate strategy. Then, three "walk-through" images were presented. The first of these was a negative image to which participants were instructed to respond naturally. Then, two additional negative "walk-through" regulation training images were presented in which participants were asked to vocalize appropriate reappraisals (in the case of the Reinterpretation and Distancing groups) or to just look and respond naturally to the images (Look Only group). Participants were guided in their responses by the experimenter to focus on the appropriate strategy and were given examples following their self-generation in order to increase clarity. Experimenters were trained to spend more time explaining a strategy if participants could not self-generate an appropriate reappraisal. Walk-through images were unique for every session, and were counterbalanced across sessions. At Session 1 only, participants also completed 9 fixedpace practice trials that followed the timing of the actual image-based task, described below.

III. Image-Based Task

The image-based task used was very similar to the one used in Study 1; the primary difference is that there was no anticipation interval. The trial structure for the task for Studies 2 and 3 is shown in Figure 6. For each trial, a cue (either LOOK or DECREASE) was presented for 2 s, followed by a neutral or negative IAPS image for 8 s, followed by a fixation interval of either 2 or 4 s, then a rating period in which participants rated their current strength of negative affect on a scale of 1 (least) to 5 (most) for 4 s, and finally and inter-trial fixation interval of either 2 or 4 s.

As in Study 1, 3 different trial types (i.e. conditions) were presented at each session: "Look Neutral" (i.e. LOOK instruction paired with a neutral picture), "Look Negative" (i.e. LOOK instruction paired with a negative picture), and "Reapp Negative" (i.e. DECREASE instruction paired with a negative picture). 18 trials were presented per condition per session. The task was divided into 3 runs per session, with 6 trials per run per condition per session. Thus, 54 trials were presented per session total. Unique trials were presented at Sessions 1, 2, and 3. At Session 4, the task images from Session 1 were shown again (with conditions maintained) for test-retest purposes. Images were counterbalanced across sessions and conditions. Within runs, trials were presented in a randomized order. After Session 4, participants were thanked and reminded of their next session time. After Session 4, participants were thanked and debriefed.

Data Acquisition and Analysis

Behavioral and questionnaire data were analyzed using linear mixed models incorporating fixed effect estimates for group assignment, session, and condition, and their interactions, and a random effect consisting of an intercept for each participant. Planned paired and independent-sample t-tests were then performed to further investigate the effects.

The only difference between Study 2 and Study 3 was that Study 3 participants completed the above procedure with the addition of psychophysiological recording equipment (to record heart rate, as detailed in Study 3) during the image-based task portion of the experiment. Prior to pooling behavioral data across Study 2 and 3, a mixed model ANOVA was performed incorporating the factors above (group, session, and condition), as well as a binary factor for whether participants received psychophysiological recording or not. There was no main effect of receiving psychophysiological recording on negative affect reports, nor was there any two-way interaction with any of the other factors in the design. Therefore, to increase power and reliability, behavioral results were pooled across Studies 2 and 3 and reported below. *Results*

Self-Reported Negative Affect

Figures 7-9 show average negative affect reports by condition and session for the Reinterpretation, Distancing, and Look Only groups, respectively. Figure 10 shows results for Reapp Negative trials across all three groups. Figure 11 shows results for Look Negative trials across all three groups. Error bars reflect standard error of the mean. There were significant main effects of group, F(2,97)=4.24, p<0.02 (with Distancing group ratings being lower), session F(3,928)=9.33, p<0.001 (with a downward trend in ratings over time), and condition F(2,928)=2301.65, p<0.001 (with a robust differentiation between negative and neutral trials). In addition, there was a significant interaction between Group and Condition, F(3,928)=9.96, p<0.001.

For exploratory purposes, gender was also included in a separate analysis as a factor along with the other factors noted above in a full factorial linear mixed model. There was a significant interaction of Gender and Condition, F(2,899)=22.48, p<0.001. This interaction was further probed using independent-sample t-tests, indicating that reactivity (i.e. Look Negative – Look Neutral ratings) was significantly greater in females than males (p<0.001), and regulation capacity (i.e. Look Negative – Reapp Negative ratings) was also significantly greater in females than males (p<0.001), and that both of these effects were driven by significantly greater reports of negative affect in the Look Negative condition in females relative to males (p<0.001). There was no significant main effect of gender on negative affect reports, however, F(1,92)=2.36, n.s., and all other interactions with gender were not significant.

To further probe longitudinal changes, paired t-tests first examined change over time in each condition and each group. For Reinterpretation, there was a significant decrease in negative affect over time in all three conditions (p<0.01 for Look Negative and Reapp Negative, p<0.03 for Look Neutral). Likewise, Distancing led to drops in ratings for all three conditions (p<0.01 for Look Negative, Reapp Negative, and Look Neutral). For the Look Only group, there was a significant decrease over time in the Look Negative condition (p<0.01 for Look Negative, n.s. for Look Neutral).

To further probe between-group differences, additional ANOVAs and independent-sample t-tests were performed for Reapp Negative and Look Negative ratings across groups. Reapp Negative ratings for the Reinterpretation and Distancing groups (Figure 10) showed a main effect of group, F(1,64)=5.00, p<0.03, with ratings for the Distancing group being lower overall. A main effect for session was also present, F(3,192)=9.45, p<0.001, indicating downward movement in ratings overall over time. Ttests revealed a significant difference between groups at Session 1 (p<0.04) and Session 2 (p<0.02), and a marginal effect at Session 4 (p<0.08), with lower ratings for the Distancing group.

Look Negative ratings showed a pattern more typical of a group X session interaction, though this was not significant, F(6,288)=1.66, p=0.131, n.s. There were, however, main effects of group, F(2,96)=3.67, p<0.03 (with the Distancing group showing lower ratings) and session, F(3,288)=17.50, p<0.001, indicating a general

downward trend in ratings over time. T-tests revealed that Distancing group self-reports in the Look Negative condition were not significantly different from other groups at Session 1, but they were significantly lower than Look Only ratings at Session 2 (p<0.05), Session 3 (p<0.02), and Session 4 (p<0.01). Distancing ratings were also significantly lower than Reinterpretation ratings at Session 2 (p<0.02) and Session 4 (p<0.05), and marginally lower at Session 3 as well (p<0.08). Critically, the Distancing group showed a significantly larger drop over time than the Look Only group (p<0.05). This last analysis controlled for any baseline emotion differences by comparing longitudinal within-subject negative affect drops across groups.

Questionnaire Reports

There were no baseline (Session 1) differences between groups in PANAS reports of positive and negative affect (all p>0.24). In addition, ruminative responses scores (RRS) did not differ between groups (all p>0.50). Further, there were no baseline differences in perceived stress (PSS) (all p>0.41). There were, however, interesting longitudinal changes in perceived stress. Figure 12 shows drops over time in perceived stress by group (Session 4 – Session 1), and Figure 13 shows perceived stress reports in each group over time. A mixed model ANOVA shows that there is no main effect of group, but there is a main effect of session, F(3,279)=2.88, p<0.04, with lower reports over time overall. The interaction between group and session is n.s. However, the Distancing group shows a significant drop over time in perceived stress (p<0.03), whereas the other two groups do not (Figure 12). Figure 13 indicates that the reduction in perceived stress in the Distancing group occurs relatively quickly—between the first and second session—and is then maintained in subsequent sessions, in contrast to other groups. Independent-sample t-tests show that the change in perceived stress between Sessions 1 and 2 is significantly larger for the Distancing group relative to the Look Only group (p<0.02).

<u>Discussion</u>

The present results represent the first investigation of the longitudinal trainability specifically of reappraisal in healthy adults. Results showed that individuals can indeed improve in their ability to down-regulate negative affect over time using reappraisal. In fact, there was evidence for longitudinal trainability in both reinterpretation and distancing, in that negative affect reports were shown to decrease over time, both when one is instructed to regulate and during uninstructed negative stimulus trials where one is simply instructed to look and respond naturally.

Distancing, however, led to lower negative affect reports when reappraising negative stimuli overall, relative to reinterpretation. Further, only distancing was associated with drops in negative affect over time for uninstructed trials (i.e. "look and respond naturally" trials) relative to the Look Only control group. This result is intriguing and suggests that distancing may become more "natural" over time after repeated practice, inasmuch as unregulated negative affect reports drop over time in a manner beyond what is attributable to habituation. If distancing becomes more automatic, even when you aren't told to distance, it may show particular promise as a training strategy, and may show additional long-lasting adaptive consequences (some of which are explored in Study 4).

This interpretation was further bolstered by the results of the questionnaire analysis of perceived stress reports. Reports of perceived stress in daily life significantly

decreased over time for distancing, but not for reinterpretation or Look Only. Further, the perceived stress timecourse across groups (Figure 13) supports the idea that distancing yields a relatively large, sustained drop in stress in daily life that is not present in the other groups, despite good comparability between the groups in terms of demographic variables and similar levels of global positive and negative affect and rumination tendencies across groups. Though these results argue for the benefits of distancing training, the physiological mechanisms that accompany these benefits is currently unknown. Study 3 attempted to address this question.

<u>Study 3: Psychophysiological effects of reappraisal training (Denny & Ochsner, in</u> prep.)

Introduction

Study 2 suggested that we can improve over time in our ability to regulate negative emotions via reappraisal. However, does our physiological state reflect what our mind knows? Study 3 addressed this question by employing identical procedures to those used in Study 2, but added a continuous psychophysiological measurement—heart rate which has been shown to vary meaningfully in the context of affective appraisal (Bradley & Lang, 2007; Greenwald, Cook, & Lang, 1989; Hare, Wood, Britain, & Shadman, 1971; Lang et al., 1993) and reappraisal (Urry, 2010; Williams, Bargh, Nocera, & Gray, 2009).

Heart rate is influenced by both the sympathetic and parasympathetic nervous systems and has been shown to be an index of psychophysiological arousal (Vrana, Cuthbert, & Lang, 1989). Specifically during presentation of negative pictorial stimuli, heart rate has been shown to *decelerate* (Bradley & Lang, 2007; Greenwald et al., 1989; Hare et al., 1971; Lang et al., 1993).

In addition, Williams and colleagues (2009), Urry (2010), and Gross (1998a) investigated the impact of an instruction to reappraise on mean changes in heart rate when anticipating or experiencing negative events. Williams and colleagues found that regulating anticipatory anxiety (speech preparation) via reappraisal (distancing) led to decreases in mean heart rate responses relative to no regulation. However, there may be differences in the psychophysiological profiles of response between events like speech preparation in which you're anticipating the negative event (as in Study 1) and times when a negative external stimulus is being presented to you (e.g. negative pictures and films).

Two studies examined changes in heart rate and reappraisal during presentation of negative stimuli. Urry found that while heart decelerated for negative stimuli overall, and while the mean change in heart rate was lower during down-regulation of negative emotion via reappraisal (operationalized as reinterpretation) than during an unregulated look condition, this difference between reappraisal and the look negative condition was not significant. Gross similarly did not detect heart rate change differences between a reappraisal group (operationalized as distancing) and a separate group that did not perform regulation when looking at negative films. Gross notes that while this null finding is difficult to interpret, there are several possible alternative explanations. One possibility is that reappraisal does not influence heart rate physiology. However, another possibility, suggested by Gross among other alternatives, is that more detailed reappraisal instructions might engender a difference in heart rate response, with the hypothesis being that reappraisal would then lead to greater heart rate deceleration relative to an unregulated control condition. This hypothesis was tested in Study 3.

<u>Methods</u>

Participants

Study 2 gave recruitment details that also apply to Study 3. Of the 103 participants who were recruited to participate in Studies 2 and 3, 52 were recruited for Study 3. As noted above, 1 participant's data were not analyzed due to being a behavioral outlier of more than 3.5 standard deviations from the mean, with additional notes from the experimenter that the subject was not properly attending to the task. Thus, 51 participants for Study 3 were distributed across the three groups: Reinterpretation, N=17 (mean age = 22.9 years, 13 female); Distancing, N=17 (mean age = 23.6 years, 12 female); and Look Only, N=17 (mean age = 23.2 years, 11 female). During heart rate analysis, 7 out of 51 participants were found to have excessively noisy physiological data and were excluded from the heart rate analysis. Thus, the reported heart rate averages are derived from 14 Reinterpretation participants (mean age = 23.6 years, 10 female), 16 Distancing participants (mean age = 23.6 years, 11 female), and 14 Look Only participants (mean age = 23.1 years, 10 female).

Materials

Materials were the same as in Study 2.

Procedure and Data Acquisition

The procedure was identical to Study 2, with the exception that participants also underwent concurrent physiological recording. When participants entered the testing room to receive training and complete the image-based task, they were connected to a Biopac ECG module (Biopac Systems, Goleta, CA) via two disposable circular electrodes. One electrode was placed on the right side of the participant's neck, and the second electrode was placed above the hip and below the rib cage on the participant's left side. Heart rate responses were then checked by the experimenter to ensure appropriate signal discrimination, and after this verification the physiological recording monitor was turned off for the duration of the image-based task. ECG was acquired continuously at 1,000 Hz. Following connection to physiological recording, the participant completed the training and image-based task as described in Study 2.

Data analysis

After data collection, heart rate data were first low-pass filtered twice using a 0.025 s kernel and subsequently filtered using the squared first derivative of the ECG signal. R-spikes were then detected using Neuroelf software (neuroelf.net). The timecourse was then visually inspected. Areas flagged to contain imperfect spike detection were examined by the experimenter, and the experimenter added and/or deleted beat detection in these areas by hand in order to minimize any artifactual intervals between beats (Urry, 2010). Data were then resampled first to 100 Hz, and then a continuous beats per minute (BPM) function was constructed for each participant at 10 Hz. Heart rate responses were then averaged by conditon for each participant at each session with the subtraction of a baseline heart rate occurring 0.1 s prior to the onset of the trial phase of interest. For the heart rate change timecourses shown in the results, this baseline was 0.1 s prior to the cue period onset, in order to show heart rate change associated with the cue and stimulus periods, as well as the first 2 s of post-stimulus fixation, for visualization purposes. For the heart rate change averages during the

stimulus period described in the results, this baseline was 0.1 s prior to stimulus period onset, with the averaging period being the 8 s stimulus period. Thus, this heart rate measure indicates accelerations or decelerations (in BPM) relative to the baseline BPM immediately preceding the onset of the trial phase of interest.

<u>Results</u>

Figures 14-16 show mean heart rate change timecourses for each condition at each session for the Reinterpretation, Distancing, and Look Only groups, respectively. 1 participant in the Reinterpretation group and 3 participants in the Look Only group had excessively noisy physiological signal in one or more intervening sessions (Sessions 2-3) and were excluded from these timecourse plots, though their usable data was still included in the average stimulus period plots described below.

Figures 17-19 show average heart rate change during the stimulus period for each group (Reinterpretation, Distancing, and Look Only, respectively). A mixed model ANOVA indicated main effects of session [F(3,393)=6.93, p<0.001], with general upward trends in heart rate change, and condition [F(2,390)=39.48, p<0.001], with Look Neutral heart rate changes being greatest overall. There was also a marginal interaction between group and condition, F(3,390)=2.48, p<0.07. To probe this interaction further, paired and independent-sample t-tests were performed. Look Neutral responses significantly increased over time in the Distancing group (p<0.01), while Reapp Neg responses significantly increased over time in the Reinterpretation group (p<0.02). No other conditions showed significant change over time. In the Reinterpretation group, while Reapp Neg heart rate change was lower than Look Neutral heart rate change at every session (all p<0.03), Reapp Neg heart rate change was never significantly different

from Look Neg heart rate change at any session. In the Look Only group, Look Negative and Look Neutral responses were only significantly different at Session 3, where Look Neutral was significantly greater (p<0.04). At Session 4, there was a trend toward lower heart rate change for Look Negative trials in the Look Only group (p<0.14).

With respect to the marginal group*condition interaction, while most conditions in each group showed upward trends in heart rate change over time, Reapp Neg responses in the Distancing group decreased over time, though this change over time was not significant. While there were no baseline (Session 1) differences across conditions for Distancing, Look Negative and Reapp Negative responses were increasingly differentiable over time. In particular, by Session 4, there is a significant difference between Look Negative and Reapp Negative heart rate change in the Distancing group (p<0.02). Further, comparing the within-subject differences between Look Negative and Reapp Negative heart rate changes over time reveals significant differentiation; the difference between Look Negative and Reapp Negative is significantly greater at Session 4 than at Session 1 in the Distancing group (p<0.03). The same comparison is not significant for the Reinterpretation group (p=0.76, n.s.).

Discussion

In this study, we have provided the first evidence of increasing differentiability over time between heart rate responses for reappraised versus unregulated negative pictorial stimuli. This differentiation tracks with having received increasing training in reappraisal (and getting better at reappraising as a result), with heart rate change lower for reappraisal than for an unregulated negative condition, a possibility that was suggested by Gross (1998a). We further replicated prior work showing that, in general, heart rate decelerates when appraising negative stimuli relative to neutral stimuli (Bradley & Lang, 2007; Greenwald et al., 1989; Hare et al., 1971; Lang et al., 1993).

This increasing differentiation of reappraised and unreappraised negative items in the Distancing group may reflect additional ability to effectively orient attention to the task when distancing at later sessions relative to earlier sessions, given that heart rate deceleration in general has been linked with this process in the context of appraising negative information (Hare et al., 1971). Effective instruction in reappraisal can be thought of as a process of attentional reorienting, with attention disengaging from the initial appraisal of an affective stimulus and toward the cognitive re-construal of it (Garland, Gaylord, & Park, 2009). Thus, one consequence of our training manipulation may have been to increase the specificity of this orienting process for reappraisal.

In this regard, it makes sense that such a finding would be observed for distancing, considering that the results of Study 2 suggested that distancing training yields significant improvements in affect both inside and outside of the laboratory. One question that might be posed relates to why we did not see the same pattern of effects in Look Negative trials as compared to Reappraise Negative trials in terms of heart rate change, given the results of Study 2 that showed that there are significant decreases over time in negative affect for both Look Negative and Reappraise Negative trials. One explanation is that, while Look Negative ratings do drop over time in Distancing (and in Reinterpretation and Look Only, though significantly greater than Look Only in the case of Distancing), negative affect reported during Look Negative trials is still always higher than negative affect reported during Reappraise Negative trials, at all sessions. Thus, the increasing differentiation that we have observed here for distancing may help confer the additional negative affect drop (via explicit regulation) that is observed when reappraising negative stimuli.

Study 4: Behavioral and neural mechanisms of reappraisal massed practice Introduction

To this point, I have examined the temporal dynamics of reappraisal by assessing the most adaptive patterns of looking forward (i.e. anticipation; Study 1) and the benefits of reappraisal training during the training period (Studies 2 and 3). Study 4 sought to extend this framework by looking backward; what are the long-term consequences of reappraisal training, even after the training period has ended? Addressing this question could elaborate on the promise of reappraisal training and suggest future avenues of research.

As reviewed earlier, while numerous studies have established that reappraisal involves engagement of lateral and medial prefrontal cortex activity coupled with attenuation of amygdala activity (Buhle et al., 2011; Denny et al., under review; Ochsner & Gross, 2008), these studies have almost all been designed to examine the neural mechanisms subserving active reappraisal implementation when a novel affective stimulus is presented. One study has recently been published examining the extent to which amygdala activity remains attenuated during passive viewing that occurs 10 minutes after active reappraisal, and results showed that reappraisal (via distancing) does involve a sustained drop in amygdala activity relative to an unregulated condition (Walter et al., 2009). Further, an additional study from this group of authors extended this same dataset to examine the neural correlates of recognition memory for reappraised versus unreappraised items one year after encoding, and has found that previously reappraised items were associated with less amygdala activity than unregulated items that are correctly remembered, although interestingly unregulated items that were not correctly remembered did not show significant amygdala activation relative to baseline (Erk, von Kalckreuth, & Walter, 2010). Thus, there is some evidence that regulation responses are maintained (at least in the short term and in the long term when making an explicit memory judgment), but there is a knowledge gap as to whether repeated practice confers a benefit over one-time reappraisals in terms of long-term neural reactivity in areas of *a priori* interest such as the amygdala.

Thus, the present study aimed to address: (1) the long-term sustainability of reappraisal-related amygdala attenuation during passive re-presentations of reappraised and non-reappraised stimuli, and (2) whether having had additional practice reappraising certain negative stimuli would lead to greater endurance of amygdala attenuation for those stimuli in particular. We aimed to simultaneously address both of these questions. We predicted that, one week following reappraisal, there will still be significant attenuation of amygdala activity for stimuli that one has reappraised repeatedly relative to stimuli that were previously seen and not reappraised (and relative to new negative stimuli).

Our plan for addressing these questions involved considerations of the reappraisal training design factors reviewed in Study 2. Specifically, with respect to the four factors (training duration, strategy, distributed versus massed training, and novel versus repeated stimuli), we chose to investigate the long-term (one week) effects of massed practice in reappraisal with the same stimuli (performed over the course of one training day) relative

to appraisals and reappraisals of comparable unregulated stimuli. In light of the results of Studies 2 and 3, we chose to employ the distancing strategy, given that distancing training has shown promise in terms of its adaptive impacts on behavior and psychophysiology.

<u>Methods</u>

Participants

Twenty-two healthy participants were recruited in accordance with the human subjects regulations of New York University and were paid approximately \$120 for the entire experiment (\$50 for each of two scanning sessions plus \$10/hour for the initial behavior-only reappraisal training session). Five exclusions were made for the following reasons: one participant had incorrect images shown at the final scanning session; one participant was a behavioral outlier (>3 standard deviations from the mean for negative affect reports during the training session), and there was evidence that the participant had not been engaged in performing the task; due to a technical problem, one participant had an unbalanced number of regulation versus no regulation training blocks; one participant showed unacceptably large functional image distortions due in part to repeated repositioning in the scanner. Thus, the present results reflect data from 17 healthy participants.

Materials

180 aversive images were drawn from the International Affective Picture System (Lang et al., 1993) (mean normative valence = 2.42, mean normative arousal = 5.75) along with 36 neutral images (mean normative valence = 5.51, mean normative arousal = 3.29). An additional set of 12 similarly valenced and arousing negative images were used during training and practice (described below).

Procedure

Participants completed 3 sessions over the course of 9 days, which included a behavior-only training session (Day 1), and two fMRI scanning days (Days 2 and 9). The task design is summarized in Figure 20.

I. Day 1

On the first day ("T1"), participants first received training in distancing using an instruction script and procedure that was very similar to the one described in Studies 2 and 3 (and Appendix D). As before, participants were told that they would see a number of images during the experiment. They were told that, for the first type of task that they would perform, they would see a number of trials, each beginning with a cue word presented in the center of a computer screen: either LOOK or DECREASE. For LOOK trials, participants were asked to look and respond naturally to the forthcoming image. For DECREASE trials, participants were walked through how to view the forthcoming image as a detached, objective impartial observer, and/or imagine that the pictured events occurred far away or a long time ago. The same walk-through procedure (with participant self-generation of appropriate reappraisals) as in Studies 2 and 3 was employed, with 1 LOOK and 2 DECREASE walk-through trials being performed. Participants then completed a fixed-timing practice with 3 LOOK and 3 DECREASE trials.

Participants then completed the image-based task described in Studies 2 and 3 at a computer. In contrast to Studies 2 and 3, participants completed 6 runs of trials that were blocked by condition, and images were repeated in like blocks. Specifically, participants

completed 3 runs of DECREASE trials and 3 runs of LOOK trials. Each run contained 36 negative image trials, and the blocks were repeated such that each LOOK and DECREASE trial was presented 3 separate times. The block presentation order always alternated between LOOK and DECREASE blocks, and whether the first block was LOOK or DECREASE was counterbalanced across participants. Within each run, trials were presented in randomized order. Further, negative images were separately randomly assigned to condition prior to generating the task scripts for each participant, for this and all subsequent conditions in the experiment, with the stipulation that the randomized condition assignments could not result in any pair-wise significant or marginal (p<0.10) differences between normative valences and arousals across all conditions in the experiment. The trial structure was very similar to the one used in Studies 2 and 3: the cue slide was presented for 2 s, followed by presentation of the image for 8 s, followed by a fixation interval of between 3 and 7 s (average = 4 s), followed by a negative affect rating period for 3 s, followed by an inter-stimulus fixation interval of between 3 and 7 s (average = 4 s). Following the completion of the sixth task block, the participant was reminded of the next session.

II. Day 2

Participants returned for an fMRI scan one day later on Day 2. Participants were first given an additional walk-through training of the distancing instructions (with unique walk-through images that were counterbalanced with those given at T1 across participants). Next, participants entered the fMRI scanner and completed an 8 minute resting state scan during which they were instructed to have whatever thoughts and feelings they naturally have, to keep their eyes closed, but to remain awake. Data from this and subsequent resting state scans were not examined in the present analyses. Then, participants completed the active regulation task ("T2") using the same trial structure and same two cues (LOOK or DECREASE) as T1. At T2, 180 total image trials were shown. The 36 Look Negative and 36 Distance Negative massed practice images from T1 were presented along with 36 novel Look Negative and 36 novel Distance Negative trials, and 36 novel Look Neutral trials. These 180 trials were evenly distributed into 6 functional runs, with 6 trials/condition/run. Within a run, trials were presented in randomized order.

Immediately following T2, participants completed another 8 minute resting scan. Immediately following the resting scan, participants completed a passive viewing scan ("T3") in which half of the images presented during T2 plus 18 novel negative images were presented for 2 s each with instructions to simply view the images (Walter et al., 2009). No cues were presented. The trial structure consisted of image presentation for 2 s, followed by an inter-stimulus fixation interval of between 3 and 7 s (average = 4 s). All 108 images were presented in a single run, in randomized order.

III. Day 9

One week after T2/T3, participants returned for an fMRI scan on Day 9. Participants first underwent an 8 minute resting state scan, followed by a passive viewing scan ("T4") in which the other half of images from T2 were shown, along with 18 novel negative images using the same trial structure as T3. As in T3, all 108 images were presented in a single run, in randomized order. Following T4, a final 8 minute resting state scan was performed.

Data Acquisition and Analysis

I. Behavioral

Behavioral data were analyzed using linear mixed models incorporating fixed effect estimates for condition (Look Neutral, Look Negative, and Distance Negative) and novelty (practiced versus un-practiced images), and a random effect consisting of an intercept for each participant.

II. fMRI

Whole-brain fMRI data were acquired on a 3.0T Siemens Allegra MRI system. Anatomical and functional images were acquired with a T2*-sensitive EPI BOLD sequence with a TR of 2000 ms, TE of 15 ms, flip angle of 82°, 34 slices, with 3mm isometric voxels, no interslice gap. Stimulus presentation and behavioral data acquisition were controlled using E-Prime software (PST Inc.). Functional images were subject to standard preprocessing using SPM8 software (Wellcome Department of Cognitive Neurology, UCL). A random-effects GLM was then run using Neuroelf v0.9c software (neuroelf.net) incorporating task regressors for T2, T3, and T4. For T2, separate regressors for fMRI responses to cue (differentiated by whether the cue was LOOK or DECREASE), stimulus presentation (differentiated by 5 conditions: Look Neutral, Look Negative - NEW, Look Negative - PRACTICED, Distance Negative - NEW, and Distance Negative – PRACTICED), and rating period (undifferentiated by conditon) were specified. For T3 and T4 separately, regressors for each stimulus presentation period were specified (i.e. for T3: Look Neutral, Look Negative – NEW, Look Negative - PRACTICED, Distance Negative - NEW, Distance Negative - PRACTICED, and Novel Negative. Separate regressors for the analogous trials shown at T4 were also specified). Regressors were convolved with a canonical hemodynamic response function (HRF). Motion estimates for each participant were also entered into the GLM. Beta

estimates underwent a percent signal change transformation. The GLM was computed using ordinary least squares regression and random effects modeling. Contrasts were then performed on the beta estimates for planned comparisons of reactivity (Look Negative > Look Neutral) and regulation (Distance Negative > Look Negative) at T2, and comparisons across conditions at T3 and T4. Data were visualized and thresholded (see Results) using Neuroelf, and beta estimates were extracted for *a priori* regions of interest (i.e. the amygdala and prefrontal cortex).

<u>Results</u>

Behavioral Results

Figures 21 and 22 show behavioral results for T1 and T2, respectively. Significant reductions in negative affect ratings over the course of the three blocks were observed in both Look Negative (p<0.01) and Distance Negative (p<0.01) practice. There was no significant drop between blocks 2 and 3 for Look Negative practice, however, while this drop was significant for Distance Negative practice.

At T2 (Figure 22), there was a significant main effect of condition,

F(2,64)=112.98, p<0.01. Further, there were significant differences between negative affect ratings between practiced and unpracticed stimuli for both Look Negative practice (p<0.02) and Distance Neg practice (p<0.01).

fMRI Results

For fMRI analyses, there were two *a priori* regions of interest: the amygdala and the prefrontal cortex. At T2, significant amygdala reactivity was observed for a contrast of novel Look Negative images versus Look Neutral images. Figure 23 (left) shows masked right amygdala reactivity for this contrast, thresholded at p<0.05 (Family-wise
error [FWE]-corrected, with thresholds of p<0.05, uncorrected, and an extent threshold of 93 voxels, determined using AlphaSim (Ward, 2000)). The displayed region-of-interest (ROI) represents a 32 voxel sub-cluster of an FWE-corrected region of activation as defined above, with peak voxel of [21, -3, -21] (MNI). Figure 23 (right) shows beta estimates for each condition at T2 averaged across the 32 ROI voxels for each participant. In addition to the significant reactivity effect, this ROI also showed a significant effect of regulation for novel stimuli; NEW Distance Neg activity was significantly attenuated relative to NEW Look Neg activity (p<0.02). This same comparison for practiced stimuli was not significant, despite a trend toward lower activity for practiced distance stimuli (p=0.13, n.s.). In this ROI at T3, practiced distance stimuli showed lower activity than novel negative stimuli (p<0.01) and NEW Look Negative stimuli (p<0.03). At T4, practiced distance stimuli showed lower activity than practiced Look Neg stimuli (p<0.03). In this ROI, practiced Look Neg stimuli showed significantly *increased* activity from T3 to T4 (p<0.05).

The second *a priori* ROI was prefrontal cortex. Figure 24 (left) shows left ventrolateral prefrontal cortex (VLPFC) activity for a contrast of NEW Distance Neg versus NEW Look Neg stimuli. Data were FWE-corrected (p<0.05) using thresholds of p<0.05 (uncorrected) and extent = 93 voxels. The ROI displayed in Figure 24 represents a cluster of 454 voxels active for this contrast, with peak activation at [-42, 45, 9] (MNI). Figure 24 (right) shows beta estimates in this ROI during the task at T2. All beta estimates were significantly different from each other pair-wise (p<0.05) with the exception of Look Neutral and NEW Look Negative. In this ROI, at both T3 and T4, there are no significant differences between practiced Distance Neg activity and other conditions, with the exception of novel negative stimuli (each p<0.03), which show less activity.

At T4, a slightly more posterior right amygdala ROI showed significant response sustainability for distance massed practice relative to all other negative image conditions (Figure 25). This ROI was defined from a contrast of practiced look versus practiced distance stimuli, taking a spherical of 1mm radius around [25, -9, -21] (7 voxels), given our a priori interest in amygdala activity and our explicit hypothesis that distancing would lead to sustained decreases in activity in the amygdala. This ROI is illustrated in Figure 25 (left). In this ROI, activity for practiced distancing stimuli is significantly lower than all other conditions (p<0.05), with the exception of Look Neutral (Figure 25, right).

<u>Discussion</u>

Study 4 was designed to address whether reappraisal massed practice yields longterm adaptive consequences. We first validated that massed practice leads to reductions in self-reported negative affect, which we observed, though we also observed this effect for look practice with negative images (i.e. a within-subject habituation control). However, later fMRI data differentiated the pattern of responses for distance practice versus look practice.

Our a priori hypothesis was that reappraisal training using distancing would modulate long-term reactivity in neural appraisal systems, in particular in the amygdala (Erk et al., 2010; Gross, 1998a; Walter et al., 2009). Indeed, this is what we observed using a targeted region of interest analysis focusing on the amygdala and an area of the VLPFC that has been commonly linked to implementation of reappraisal strategies (Buhle et al., 2011; Ochsner & Gross, 2008). Replicating prior work, the right amygdala showed significant reactivity to novel negative versus neutral stimuli during an active regulation task (as used in Studies 1-3), and was significantly attenuated for when distancing from novel stimuli relative to looking at novel stimuli. Amygdala reactivity to look and distance practiced stimuli was initially comparable, however, suggesting that training effects may be attributable to habituation.

These and prior data suggest three lines of argument for why the observed effects are unlikely to be solely attributable to habituation. First, it's not surprising that we observed a suppression of activity for look practiced stimuli at T2. Some habituation would be expected (cf. Study 2), but Studies 2 and 3 indicate that, during active receipt of distancing training, there is a significant transference of the distancing strategy to unregulated stimuli that is significantly greater than what is attributable solely to habituation. Given the amount of practice and instruction that one has had with distancing by T2 (two training sessions on two consecutive days, and 108 task regulation trials by the start of T2), it's not surprising that there could be carry-over.

Second, the neural correlates of regulation (i.e. Distance Neg > Look Neg) at T2 provide further support for this notion. We observed an increasing step-wise pattern of response in VLPFC, a brain area previously importantly linked to reappraisal maintenance and success (Wager, Davidson et al., 2008), such that practiced distance stimuli showed the highest level of activity, but also that practiced look stimuli showed more VLPFC activity at T2 than unregulated look negative stimuli (and more than look neutral stimuli). This suggests that participants may indeed be implicitly bringing regulatory resources to bear on the stimuli to which they have been repeatedly exposed but which they have not been told to regulate while at the same time receiving regulation training for other stimuli.

The third reason that the massed practice present effects are unlikely to be attributable to habituation is that, by the second passive viewing scan, reactivity in a slightly more posterior amygdala region differentiates between stimuli for which one has received massed practice in distancing versus massed practice in looking and responding naturally. In particular, amygdala reactivity at T4 is significantly lower for distancing massed practice than for every other condition, with the exception of look neutral. One question that may be raised is why we did not observe continued transference of the distancing pattern to the formerly unregulated trials even at T4. One reason may lie in the fact that in both Studies 2-3 and Study 4, transference was able to occur during relatively long stimulus presentation periods for each condition (8 s). In the two passive viewing scans in this experiment, stimuli were presented for only 2 s each, which may have not allowed sufficient time for the transference to fully occur. Alternatively, as discussed in Study 3, while transference was observed in the prior training studies, it did not carry all of the adaptive effects of regulation (cf. Study 3). Relatedly, stimuli for which one has had only one opportunity to distance may not be a sufficient amount of time or practice for effective consolidation into a less reactive representation when one encounters the stimulus again.

Further, these data suggest a mechanism whereby responses to distance stimuli for which one has received mass practice may be "neutralized" over time. Amygdala reactivity to massed distancing practice stimuli starts fairly low and remains that way. However, VLPFC activity is initially high (highest of all conditions) for massed

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distancing practice stimuli, but a week later VLPFC is not particularly recruited for these stimuli at the same time that the amygdala is continuing to show low reactivity for them. In addition, reactivity to look practiced stimuli actually increases over time in the amygdala, driving some of the reactivity differences between T2 and T4. This may reflect the fact that whatever reactivity attenuation is present for these look practiced stimuli (due to whatever factor), the suppression of amygdala activity for such stimuli is fleeting without the added focus of distancing practice, which may improve long-term memory consolidation (McGaugh, 2000).

While we did observe sustained reductions in amygdala activity one week after regulation, we did not observe this pattern as reported by Walter and colleagues (2009) eight minutes after regulation for negative stimuli that were regulated at all versus negative stimuli that were not regulated. While this null result may stem from a variety of factors, beta estimates at T3 in the amygdala ROI's reported here did show the general trend reported by Walter and colleagues (i.e. negative regulated<negative unregulated), but the inter-subject error was too great to substantiate effects at this time point. Walter and colleagues did report having participants wait approximately 10 minutes after regulation to passively view, whereas our interval was closer to 8 minutes. Future work may indicate whether this time discrepancy was significant with respect to the amount of time necessary for consolidation effects to emerge in this reappraisal paradigm.

Further, future work may further investigate how massed reappraisal practice affects declarative memory in addition to passive reactivity, and whether effects of reappraisal training persist for even longer than a week. Doing so would continue to put the results of the present study in context, as the long-term consequences of reappraisal training are beginning to be explored.

General Discussion

This dissertation has sought to elucidate the temporal dynamics of reappraisal, a cognitive emotion regulation strategy that has been shown to be effective in down-regulating negative affect in single experimental sessions without maladaptive impacts on psychophysiology or other cognitive costs that have been associated with response-focused emotion regulation strategies like expressive suppression (Gross, 1998a, 1998b; Gross & John, 2003; Gross & Munoz, 1995; Jackson, Malmstadt, Larson, & Davidson, 2000; Ochsner & Gross, 2005, 2007; Richards & Gross, 2000b). However, as reviewed in this dissertation, several key questions regarding reappraisal have been relatively understudied: how can we effectively look forward to reappraisal (Question 1), how can we get better at reappraising over time through training, and are certain reappraisal strategies better than other (Questions 2 and 3), and what adaptive long-term consequences does reappraisal training have (Question 4)?

These four questions have been addressed through a series of four experiments that have argued for the usefulness of reappraisal as a training strategy. In Study 1, we observed that engaging brain areas previously associated with mind-wandering and stimulus-independent thought during anticipation of reappraisal was associated with less ultimate self-reported reappraisal success, mediated during the reappraisal itself by the activity of the amygdala, a brain area closely linked to negative affective reactivity that represented an a priori region of interest in Studies 1 and 4 (Denny et al., 2009; Ochsner & Gross, 2007, 2008). By contrast, engaging ventral anterior insula, previously associated with affective integration and interoceptive awareness (Augustine, 1996; Wager & Barrett, 2004) during anticipation was associated with greater reappraisal success, again mediated by amygdala activity. These results are interesting given that our reappraisal strategy for when stimuli were actually presented was reinterpretation, a context-driven strategy that may not have given participants enough information to prepare effective reappraisals for upcoming regulation trials, and may have led some participants to engage in unproductive mind wandering.

The results of Study 1 suggested that there might be meaningful differences between two types of reappraisal strategies: reinterpretation and psychological distancing. When down-regulating negative emotion, reinterpretation involves recontextualizing an affective stimulus so that events are not as bad as they first seemed (Ochsner et al., 2002; Ochsner & Gross, 2008; Ochsner et al., 2004). Distancing, by contrast, involves adopting a detached, objective, impartial mindset (Gross, 1998a; Kross et al., 2009; Ochsner et al., 2004) or imagining that negative events occurred far away from you or a long time ago (Liberman et al., 2007; Trope et al., 2007).

Thus, one interesting distinction between the two reappraisal strategies, borne out of the current pattern of results in Studies 2 and 3, is that distancing may invoke more of a global "mind-set" whereas reinterpretation may be geared more toward individual context-dependent affective instances, as least as it has been typically operationalized to this point. Studies 2 and 3 were motivated by the idea that while many clinical treatment modalities exist that employ elements of reappraisal (Hollon & Beck, 1994; Sheldon, 2011), reappraisal itself has not been examined for its effectiveness as a longitudinal

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training strategy in healthy adults. We found that a relatively short (two week) course of reappraisal training in either reinterpretation or distancing involved longitudinal decreases in negative affect during an image-based regulation task. However, negative affect was lower for distancing participants, despite a lack of baseline differences in affective responsivity prior to training onset (Watson et al., 1988). Further, distancing was uniquely associated with drops in negative affect that were larger than what could be attributed to habituation (via a control group that saw the same stimuli but with no training in regulation and no instruction to regulate). These drops in negative affect over time came even for *unregulated* trials in addition to regulated trials, suggesting that there may be some carry-over of the effects of distancing training to instances in which one is not instructed to regulate and is instead simply instructed to respond naturally. Thus, distancing may become more natural over time. Distancing was further uniquely associated with longitudinal drops in perceived stress in daily life (Cohen et al., 1983; Appendices A and B). Finally, in Study 3, distancing was uniquely associated with longitudinal differentiation of heart rate responses to regulated versus unregulated negative stimuli. Despite prior null effects in single experimental sessions, the hypothesis that reappraisal training may differentiate mean changes in heart rate, with heart rate changes lowest for reappraised stimuli, has been considered previously (Gross, 1998a), and this is in fact what we observed. These changes may reflect greater attentional orienting that one is employing when performing reappraisal by distancing (Garland et al., 2009; Hare et al., 1971). Further work may continue to probe the connection between the self-reported behavior and psychophysiological response patterns when receiving training in distancing.

Finally, in addition to this evidence that there are adaptive effects of distancing training during the period of time when it is trained, a final important question concerned whether there were adaptive effects of training that persisted even after the training period (Study 4). Given the results of Studies 2 and 3, we used distancing as our training strategy. In addition, as discussed in Study 2, any training paradigm must make decisions with respect to the length of training, whether the training is distributed or massed, and whether training and practice occur with novel or repeated stimuli. Given that these variables have not been systematically manipulated previously, we chose to focus on the effects of massed practice in distancing with the same stimuli in order to compare to the distributed practice employed in Studies 2 and 3. Study 4 was particularly designed to assess the neural mechanisms of adaptive or maladaptive patterns of response. Specifically, two regions of interest were targeted: the amygdala and the (particularly lateral) prefrontal cortex, given their extensive prior association with reappraisal reactivity and regulation, respectively (Buhle et al., 2011; Denny et al., 2009; Ochsner & Gross, 2007, 2008). We observed that distancing massed practice was uniquely associated with sustained decreases in amygdala activity during passive re-encounters with negative stimuli one week after the end of training. Thus, the present results have implications for the ability of healthy adults to benefit from reappraisal training, and elucidates some of the basic mechanisms by which these benefits may occur.

Further, these results suggest future avenues of research examining whether various clinical populations may similarly benefit from reappraisal training courses. I am currently engaged in research at the Mount Sinai School of Medicine in a longitudinal examination of the effectiveness of reappraisal training (by distancing) in borderline

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personality disorder, a population that exhibits characteristic and pronounced emotion dysregulation (Koenigsberg et al., 2009; Koenigsberg et al., 2002; Linehan, 1993; Linehan et al., 1991). Understanding whether courses of training in distancing (or other cognitive change strategies) are effective in clinical populations could ultimately lead to the development of more targeted translational therapies that could increase and improve treatment options for various populations that could benefit. As alluded to in the Frost quote given at the beginning, cognitive transformations and re-construals have the potential to powerfully and adaptively re-shape our affective experiences across a variety of domains and situations in life; oftentimes the best way out is through.

REFERENCES

Abler, B., Erk, S., Herwig, U., & Walter, H. (2007). Anticipation of aversive stimuli activates extended amygdala in unipolar depression. *J Psychiatr Res*, *41*(6), 511-522.

Amodio, D. M., & Frith, C. D. (2006). Meeting of minds: the medial frontal cortex and social cognition. *Nat Rev Neurosci,* 7(4), 268-277.

Atlas, L. Y., Bolger, N., Lindquist, M. A., & Wager, T. D. (2010). Brain mediators of predictive cue effects on perceived pain. *J Neurosci*, *30*(39), 12964-12977.

Augustine, J. R. (1996). Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Res Brain Res Rev, 22*(3), 229-244.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol*, *51*(6), 1173-1182.

Barrett, L. F., Gross, J., Christensen, T. C., & Benvenuto, M. (2001). Knowing what you're feeling and knowing what to do about it: Mapping the relation between emotion differentiation and emotion regulation. *Cognition and Emotion*, *15*(6), 713-724.

Bradley, M. M., & Lang, P. J. (2007). Emotion and motivation. In J. T. Cacioppo, L. G. Tassinary & G. G. Berntson (Eds.), *Handbook of psychophysiology* (3rd ed., pp. 581-607). Cambridge, UK: Cambridge University Press.

Buhle, J., Wager, T. D., Lopez, R., Onyemekwu, C., Silvers, J. A., & Ochsner, K. N. (2011). Cognitive reappraisal of emotion: A meta-analysis of human neuroimaging studies, *Poster presented at 2011 Annual Meeting of Society for Neuroscience*. Washington, D.C.

Burgess, P. W., Scott, S. K., & Frith, C. D. (2003). The role of the rostral frontal cortex (area 10) in prospective memory: a lateral versus medial dissociation. *Neuropsychologia*, *41*(8), 906-918.

Butler, A. C., Chapman, J. E., Forman, E. M., & Beck, A. T. (2006). The empirical status of cognitive-behavioral therapy: a review of meta-analyses. *Clin Psychol Rev, 26*(1), 17-31.

Butler, G., & Mathews, A. (1987). Anticipatory anxiety and risk perception. Oct 1987. *Cognitive Therapy and Research*, .11(5), pp.

Carlson, J. M., Greenberg, T., Rubin, D., & Mujica-Parodi, L. R. (2011). Feeling anxious: anticipatory amygdalo-insular response predicts the feeling of anxious anticipation. *Soc Cogn Affect Neurosci, 6*(1), 74-81.

Christoff, K., & Gabrieli, J. D. (2000). The frontopolar cortex and human cognition: Evidence for a rostrocaudal hierarchical organization within the human prefrontal cortex. *Psychobiology*, 28(2), 168-186.

Christoff, K., Gordon, A. M., Smallwood, J., Smith, R., & Schooler, J. W. (2009). Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. *Proc Natl Acad Sci U S A*, *106*(21), 8719-8724.

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *J Health Soc Behav, 24*(4), 385-396.

Costa, A., Oliveri, M., Barban, F., Torriero, S., Salerno, S., Lo Gerfo, E., et al. (2011). Keeping Memory for Intentions: A cTBS Investigation of the Frontopolar Cortex. *Cereb Cortex, 21*(12), 2696-2703.

Craig, A. D. (2009). How do you feel--now? The anterior insula and human awareness. *Nat Rev Neurosci, 10*(1), 59-70.

Critchley, H. D., Wiens, S., Rotshtein, P., Ohman, A., & Dolan, R. J. (2004). Neural systems supporting interoceptive awareness. *Nat Neurosci*, 7(2), 189-195.

Davis, M. (1992). The role of the amygdala in fear and anxiety. *Annu Rev Neurosci, 15*, 353-375.

Deen, B., Pitskel, N. B., & Pelphrey, K. A. (2011). Three systems of insular functional connectivity identified with cluster analysis. *Cereb Cortex*, 21(7), 1498-1506.

Delgado, M. R., Gillis, M. M., & Phelps, E. A. (2008). Regulating the expectation of reward via cognitive strategies. *Nat Neurosci, 11*(8), 880-881.

Delgado, M. R., Nearing, K. I., Ledoux, J. E., & Phelps, E. A. (2008). Neural circuitry underlying the regulation of conditioned fear and its relation to extinction. *Neuron*, 59(5), 829-838.

Denny, B. T., Kober, H., Wager, T. D., & Ochsner, K. N. (in press). A meta-analysis of functional neuroimaging studies of self and other judgments reveals a spatial gradient for mentalizing in medial prefrontal cortex. *J Cogn Neurosci*.

Denny, B. T., & Ochsner, K. N. (in prep.). Examining the temporal dynamics of emotion regulation: Evidence from longitudinal reappraisal practice.

Denny, B. T., Ochsner, K. N., Weber, J., & Wager, T. D. (under review). Anticipatory brain activity predicts the success of subsequent emotion regulation.

Denny, B. T., Silvers, J. A., & Ochsner, K. N. (2009). How we heal what we don't want to feel: The functional neural architecture of emotion regulation. In A. M. K. D. M. Sloan (Ed.), *Emotion regulation and psychopathology: A transdiagnostic approach to etiology and treatment* (pp. 59-87). New York: Guilford Press.

Dobson, K. S. (Ed.). (2010). *Handbook of cognitive-behavioral therapies* (3rd ed.). New York: Guilford Press.

Efron, B., & Tibshirani, R. (1993). *An introduction to the bootstrap*. New York: Chapman & Hall/CRC.

Erk, S., Abler, B., & Walter, H. (2006). Cognitive modulation of emotion anticipation. *Eur J Neurosci, 24*(4), 1227-1236.

Erk, S., von Kalckreuth, A., & Walter, H. (2010). Neural long-term effects of emotion regulation on episodic memory processes. *Neuropsychologia*, 48(4), 989-996.

Frost, R. (1915). A Servant to Servants. In *North of Boston*. New York: Henry Holt and Company.

Garland, E., Gaylord, S., & Park, J. (2009). The role of mindfulness in positive reappraisal. *Explore (NY)*, *5*(1), 37-44.

Gilbert, S. J., Spengler, S., Simons, J. S., Steele, J. D., Lawrie, S. M., Frith, C. D., et al. (2006). Functional specialization within rostral prefrontal cortex (area 10): a metaanalysis. *J Cogn Neurosci, 18*(6), 932-948.

Goldin, P. R., Manber-Ball, T., Werner, K., Heimberg, R., & Gross, J. J. (2009). Neural mechanisms of cognitive reappraisal of negative self-beliefs in social anxiety disorder. *Biol Psychiatry*, *66*(12), 1091-1099.

Greenwald, M. K., Cook, E. W., & Lang, P. J. (1989). Affective judgment and psychophysiological response: Dimensional covariation in the evaluation of pictorial stimuli. 1989. *Journal of Psychophysiology*, *3*(1), 51-64.

Grillon, C., Ameli, R., Woods, S. W., Merikangas, K., & Davis, M. (1991). Fearpotentiated startle in humans: effects of anticipatory anxiety on the acoustic blink reflex. *Psychophysiology*, 28(5), 588-595.

Gross, J. J. (1998a). Antecedent- and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. *J Pers Soc Psychol*, 74(1), 224-237.

Gross, J. J. (1998b). The emerging field of emotion regulation: An integrative review. *Review of General Psychology*, 2(3), 271-299.

Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being. *J Pers Soc Psychol*, 85(2), 348-362.

Gross, J. J., & Levenson, R. W. (1993). Emotional suppression: physiology, self-report, and expressive behavior. *J Pers Soc Psychol*, 64(6), 970-986.

Gross, J. J., & Munoz, R. F. (1995). Emotion regulation and mental health. *Clinical Psychology: Science and Practice*, 2(2), 151-164.

Gusnard, D. A., Akbudak, E., Shulman, G. L., & Raichle, M. E. (2001). Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proc Natl Acad Sci U S A*, *98*(7), 4259-4264.

Hare, R., Wood, K., Britain, S., & Shadman, J. (1971). Autonomic responses to affective visual stimulation. *Psychophysiology*, 7(3), 408-417.

Herwig, U., Abler, B., Walter, H., & Erk, S. (2007). Expecting unpleasant stimuli--an fMRI study. *Psychiatry Res*, 154(1), 1-12.

Herwig, U., Baumgartner, T., Kaffenberger, T., Bruhl, A., Kottlow, M., Schreiter-Gasser, U., et al. (2007). Modulation of anticipatory emotion and perception processing by cognitive control. *Neuroimage*, *37*(2), 652-662.

Herwig, U., Kaffenberger, T., Baumgartner, T., & Jancke, L. (2007). Neural correlates of a 'pessimistic' attitude when anticipating events of unknown emotional valence. *Neuroimage*, *34*(2), 848-858.

Hollon, S. D., & Beck, A. T. (1994). Cognitive and cognitive-behavioral therapies. In A. E. Bergin & S. L. Garfield (Eds.), *Handbook of psychotherapy and behavior change* (4th ed., pp. 428-466). Oxford: John Wiley & Sons.

Jackson, D. C., Malmstadt, J. R., Larson, C. L., & Davidson, R. J. (2000). Suppression and enhancement of emotional responses to unpleasant pictures. *Psychophysiology*, *37*(4), 515-522.

James, W. (1884). What is an emotion? Mind, 9, 188-205.

James, W. (1894). The physical basis of emotion. Psychological Review, 101, 205-210.

Kaffenberger, T., Bruhl, A. B., Baumgartner, T., Jancke, L., & Herwig, U. (2010). Negative bias of processing ambiguously cued emotional stimuli. *Neuroreport, 21*(9), 601-605.

Kalisch, R. (2009). The functional neuroanatomy of reappraisal: time matters. *Neurosci Biobehav Rev, 33*(8), 1215-1226.

Kalisch, R., Wiech, K., Critchley, H. D., Seymour, B., O'Doherty, J. P., Oakley, D. A., et al. (2005). Anxiety reduction through detachment: subjective, physiological, and neural effects. *J Cogn Neurosci*, *17*(6), 874-883.

Kalisch, R., Wiech, K., Herrmann, K., & Dolan, R. J. (2006). Neural correlates of selfdistraction from anxiety and a process model of cognitive emotion regulation. *J Cogn Neurosci, 18*(8), 1266-1276. Killingsworth, M. A., & Gilbert, D. T. (2010). A wandering mind is an unhappy mind. *Science*, *330*(6006), 932.

Kim, S. H., & Hamann, S. (2007). Neural correlates of positive and negative emotion regulation. *J Cogn Neurosci, 19*(5), 776-798.

Klaaren, K. J., Hodges, S. D., & Wilson, T. D. (1994). The role of affective expectations in subjective experience and decision-making. *Social Cognition*, *12*(2), 77-101.

Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *J Neurosci*, *21*(16), RC159.

Kober, H., Barrett, L. F., Joseph, J., Bliss-Moreau, E., Lindquist, K., & Wager, T. D. (2008). Functional grouping and cortical-subcortical interactions in emotion: a metaanalysis of neuroimaging studies. *Neuroimage*, *42*(2), 998-1031.

Koenigsberg, H. W., Fan, J., Ochsner, K. N., Liu, X., Guise, K. G., Pizzarello, S., et al. (2009). Neural correlates of the use of psychological distancing to regulate responses to negative social cues: a study of patients with borderline personality disorder. *Biol Psychiatry*, *66*(9), 854-863.

Koenigsberg, H. W., Harvey, P. D., Mitropoulou, V., Schmeidler, J., New, A. S., Goodman, M., et al. (2002). Characterizing affective instability in borderline personality disorder. *Am J Psychiatry*, *159*(5), 784-788.

Kross, E., Davidson, M., Weber, J., & Ochsner, K. (2009). Coping with emotions past: the neural bases of regulating affect associated with negative autobiographical memories. *Biol Psychiatry*, *65*(5), 361-366.

Lang, P. J., Davis, M., & Ohman, A. (2000). Fear and anxiety: animal models and human cognitive psychophysiology. *J Affect Disord*, *61*(3), 137-159.

Lang, P. J., Greenwald, M. K., Bradley, M. M., & Hamm, A. O. (1993). Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology*, *30*(3), 261-273.

Lang, P. J., Kozak, M. J., Miller, G. A., Levin, D. N., & McLean, A., Jr. (1980). Emotional imagery: conceptual structure and pattern of somato-visceral response. *Psychophysiology*, *17*(2), 179-192.

Lazarus, R. S. (1966). *Psychological stress and the coping process*. New York: McGraw-Hill.

Lazarus, R. S. (1991). Progress on a cognitive-motivational-relational theory of emotion. *Am Psychol*, *46*(8), 819-834.

Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal, and coping*. New York: Springer Publishing Company.

LeDoux, J. E. (2000). Emotion circuits in the brain. *Annual Review of Neuroscience*. Vol 23 2000, 155-184.

LeDoux, J. E. (Ed.). (1996). The emotional brain. New York: Simon & Schuster.

Liberman, N., Trope, Y., & Stephan, E. (2007). Psychological distance. In A. W. Kruglanski & E. T. Higgins (Eds.), *Social psychology: Handbook of basic principles* (2nd ed., pp. 353-381). New York: Guilford Press.

Linehan, M. M. (1993). Cognitive-behavioral treatment of Borderline Personality Disorder. In. New York: Guilford Press.

Linehan, M. M., Armstrong, H. E., Suarez, A., Allmon, D., & Heard, H. L. (1991). Cognitive-behavioral treatment of chronically parasuicidal borderline patients. *Arch Gen Psychiatry*, 48(12), 1060-1064.

Linehan, M. M., Schmidt, H., 3rd, Dimeff, L. A., Craft, J. C., Kanter, J., & Comtois, K. A. (1999). Dialectical behavior therapy for patients with borderline personality disorder and drug-dependence. *Am J Addict*, 8(4), 279-292.

Maren, S., Aharonov, G., & Fanselow, M. S. (1996). Retrograde abolition of conditional fear after excitotoxic lesions in the basolateral amygdala of rats: absence of a temporal gradient. *Behav Neurosci, 110*(4), 718-726.

Mason, M. F., Norton, M. I., Van Horn, J. D., Wegner, D. M., Grafton, S. T., & Macrae, C. N. (2007). Wandering minds: the default network and stimulus-independent thought. *Science*, *315*(5810), 393-395.

McGaugh, J. L. (2000). Memory--a century of consolidation. *Science*, 287(5451), 248-251.

McRae, K., Hughes, B., Chopra, S., Gabrieli, J. D., Gross, J. J., & Ochsner, K. N. (2010). The neural bases of distraction and reappraisal. *J Cogn Neurosci, 22*(2), 248-262.

McRae, K., Ochsner, K. N., Mauss, I. B., Gabrieli, J. D. E., & Gross, J. J. (2008). Gender differences in emotion regulation: An fMRI study of cognitive reappraisal. *Group Processes & Intergroup Relations*, .11(2), pp.

Mechias, M. L., Etkin, A., & Kalisch, R. (2010). A meta-analysis of instructed fear studies: implications for conscious appraisal of threat. *Neuroimage*, 49(2), 1760-1768.

Mesulam, M. M., & Mufson, E. J. (1982a). Insula of the old world monkey. I. Architectonics in the insulo-orbito-temporal component of the paralimbic brain. *J Comp Neurol*, *212*(1), 1-22.

Mesulam, M. M., & Mufson, E. J. (1982b). Insula of the old world monkey. III: Efferent cortical output and comments on function. *J Comp Neurol*, 212(1), 38-52.

Mischel, W. (1973). Toward a cognitive social learning reconceptualization of personality. *Psychological Review*, 80(4), 252-283.

Mischel, W., & Baker, N. (1975). Cognitive appraisals and transformations in delay behavior. *Journal of Personality and Social Psychology*, .31(2), pp.

Mischel, W., & Shoda, Y. (1995). A cognitive-affective system theory of personality: Reconceptualizing situations, dispositions, dynamics, and invariance in personality structure. *Psychological Review*, *102*(2), 246-268.

Mufson, E. J., & Mesulam, M. M. (1982). Insula of the old world monkey. II: Afferent cortical input and comments on the claustrum. *J Comp Neurol*, *212*(1), 23-37.

Mufson, E. J., & Mesulam, M. M. (1984). Thalamic connections of the insula in the rhesus monkey and comments on the paralimbic connectivity of the medial pulvinar nucleus. *J Comp Neurol*, 227(1), 109-120.

Nee, D. E., Wager, T. D., & Jonides, J. (2007). Interference resolution: insights from a meta-analysis of neuroimaging tasks. *Cogn Affect Behav Neurosci*, 7(1), 1-17.

Nitschke, J. B., Sarinopoulos, I., Mackiewicz, K. L., Schaefer, H. S., & Davidson, R. J. (2006). Functional neuroanatomy of aversion and its anticipation. *Neuroimage*, 29(1), 106-116.

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster: the 1989 Loma Prieta Earthquake. *J Pers Soc Psychol*, *61*(1), 115-121.

Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., & Panksepp, J. (2006). Self-referential processing in our brain--a meta-analysis of imaging studies on the self. *Neuroimage*, *31*(1), 440-457.

Ochsner, K. N. (2007). Social cognitive neuroscience: Historical development, core principles, and future promise. In A. Kruglanksi & E. T. Higgins (Eds.), *Social Psychology: A Handbook of Basic Principles* (2nd ed., pp. 39-66). New York: Guilford Press.

Ochsner, K. N., Beer, J. S., Robertson, E. R., Cooper, J. C., Gabrieli, J. D., Kihsltrom, J. F., et al. (2005). The neural correlates of direct and reflected self-knowledge. *Neuroimage*, *28*(4), 797-814.

Ochsner, K. N., Bunge, S. A., Gross, J. J., & Gabrieli, J. D. (2002). Rethinking feelings: an FMRI study of the cognitive regulation of emotion. *J Cogn Neurosci*, *14*(8), 1215-1229.

Ochsner, K. N., & Gross, J. J. (2004). Thinking makes it so: A social cognitive neuroscience approach to emotion regulation. In R. Baumeister & K. Vohs (Eds.), *The handbook of self-regulation* (pp. 221-255). New York: Guilford Press.

Ochsner, K. N., & Gross, J. J. (2005). The cognitive control of emotion. *Trends Cogn Sci*, 9(5), 242-249.

Ochsner, K. N., & Gross, J. J. (2007). The neural architecture of emotion regulation. In J. J. Gross (Ed.), *Handbook of emotion regulation* (pp. 87-109). New York: Guilford Press.

Ochsner, K. N., & Gross, J. J. (2008). Cognitive emotion regulation: Insights from social cognitive and affective neuroscience. *Current Directions in Psychological Science*, 17(2), 153-158.

Ochsner, K. N., Hughes, B., Robertson, E. R., Cooper, J. C., & Gabrieli, J. D. (2009). Neural systems supporting the control of affective and cognitive conflicts. *J Cogn Neurosci, 21*(9), 1842-1855.

Ochsner, K. N., & Lieberman, M. D. (2001). The emergence of social cognitive neuroscience. *Am Psychol*, *56*, 717-734.

Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D., et al. (2004). For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage*, 23(2), 483-499.

Ochsner, K. N., Ray, R. R., Hughes, B., McRae, K., Cooper, J. C., Weber, J., et al. (2009). Bottom-up and top-down processes in emotion generation: common and distinct neural mechanisms. *Psychol Sci, 20*(11), 1322-1331.

Ollinger, J. M., Corbetta, M., & Shulman, G. L. (2001). Separating processes within a trial in event-related functional MRI. *Neuroimage*, 13(1), 218-229.

Olsson, A., & Ochsner, K. N. (2008). The role of social cognition in emotion. *Trends Cogn Sci*, *12*(2), 65-71.

Phan, K. L., Fitzgerald, D. A., Nathan, P. J., Moore, G. J., Uhde, T. W., & Tancer, M. E. (2005). Neural substrates for voluntary suppression of negative affect: a functional magnetic resonance imaging study. *Biol Psychiatry*, *57*(3), 210-219.

Price, D. D., Milling, L. S., Kirsch, I., Duff, A., Montgomery, G. H., & Nicholls, S. S. (1999). An analysis of factors that contribute to the magnitude of placebo analgesia in an experimental paradigm. *Pain*, *83*(2), 147-156.

Qin, P., & Northoff, G. (2011). How is our self related to midline regions and the defaultmode network? *Neuroimage*, 57(3), 1221-1233. Quirk, G. J., Repa, C., & LeDoux, J. E. (1995). Fear conditioning enhances short-latency auditory responses of lateral amygdala neurons: parallel recordings in the freely behaving rat. *Neuron*, *15*(5), 1029-1039.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proc Natl Acad Sci U S A*, *98*(2), 676-682.

Ray, R. D., Ochsner, K. N., Cooper, J. C., Robertson, E. R., Gabrieli, J. D., & Gross, J. J. (2005). Individual differences in trait rumination and the neural systems supporting cognitive reappraisal. *Cogn Affect Behav Neurosci*, *5*(2), 156-168.

Richards, J. M., & Gross, J. J. (2000a). Emotion regulation and memory: the cognitive costs of keeping one's cool. *J Pers Soc Psychol*, 79(3), 410-424.

Richards, J. M., & Gross, J. J. (2000b). Emotion regulation and memory: The cognitive costs of keeping one's cool. Year of Publication 2000. *Journal of Personality and Social Psychology*, *79*(3), 410-424.

Savitsky, K., Epley, N., & Gilovich, T. (2001). Do others judge us as harshly as we think? Overestimating the impact of our failures, shortcomings, and mishaps. *J Pers Soc Psychol*, *81*(1), 44-56.

Sawamoto, N., Honda, M., Okada, T., Hanakawa, T., Kanda, M., Fukuyama, H., et al. (2000). Expectation of pain enhances responses to nonpainful somatosensory stimulation in the anterior cingulate cortex and parietal operculum/posterior insula: an event-related functional magnetic resonance imaging study. *J Neurosci, 20*(19), 7438-7445.

Sheldon, B. (2011). *Cognitive-behavioural therapy: Research and practice in health and social care* (2nd ed.). New York: Routledge.

Sheppes, G., Catran, E., & Meiran, N. (2009). Reappraisal (but not distraction) is going to make you sweat: physiological evidence for self-control effort. *Int J Psychophysiol*, 71(2), 91-96.

Sheppes, G., & Meiran, N. (2008). Divergent cognitive costs for online forms of reappraisal and distraction. *Emotion*, *8*(6), 870-874.

Shrout, P. E., & Bolger, N. (2002). Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychol Methods*, 7(4), 422-445.

Stern, E. R., Wager, T. D., Egner, T., Hirsch, J., & Mangels, J. A. (2007). Preparatory neural activity predicts performance on a conflict task. *Brain Res, 1176*, 92-102.

Stoodley, C. J., & Schmahmann, J. D. (2009). Functional topography in the human cerebellum: a meta-analysis of neuroimaging studies. *Neuroimage*, 44(2), 489-501.

Trope, Y., Liberman, N., & Wakslak, C. (2007). Construal Levels and Psychological Distance: Effects on Representation, Prediction, Evaluation, and Behavior. *J Consum Psychol*, *17*(2), 83-95.

Ueda, K., Okamoto, Y., Okada, G., Yamashita, H., Hori, T., & Yamawaki, S. (2003). Brain activity during expectancy of emotional stimuli: an fMRI study. *Neuroreport*, *14*(1), 51-55.

Urry, H. L. (2010). Seeing, thinking, and feeling: emotion-regulating effects of gazedirected cognitive reappraisal. *Emotion*, 10(1), 125-135.

Urry, H. L., van Reekum, C. M., Johnstone, T., Kalin, N. H., Thurow, M. E., Schaefer, H. S., et al. (2006). Amygdala and ventromedial prefrontal cortex are inversely coupled during regulation of negative affect and predict the diurnal pattern of cortisol secretion among older adults. *J Neurosci, 26*(16), 4415-4425.

van der Meer, L., Costafreda, S., Aleman, A., & David, A. S. (2010). Self-reflection and the brain: a theoretical review and meta-analysis of neuroimaging studies with implications for schizophrenia. *Neurosci Biobehav Rev, 34*(6), 935-946.

Van Overwalle, F. (2009). Social cognition and the brain: a meta-analysis. *Hum Brain Mapp*, *30*(3), 829-858.

Van Overwalle, F. (2011). A dissociation between social mentalizing and general reasoning. *Neuroimage*, *54*(2), 1589-1599.

van Reekum, C. M., Johnstone, T., Urry, H. L., Thurow, M. E., Schaefer, H. S., Alexander, A. L., et al. (2007). Gaze fixations predict brain activation during the voluntary regulation of picture-induced negative affect. *Neuroimage*, *36*(3), 1041-1055.

Vrana, S. R., Cuthbert, B. N., & Lang, P. J. (1989). Processing fearful and neutral sentences: Memory and heart rate change. *Cognition and Emotion*, *3*(3), 179-195.

Wager, T. D., Atlas, L. Y., Leotti, L. A., & Rilling, J. K. (2011). Predicting individual differences in placebo analgesia: contributions of brain activity during anticipation and pain experience. *J Neurosci*, *31*(2), 439-452.

Wager, T. D., & Barrett, L. F. (2004). From affect to control: Functional specialization of the insula in motivation and regulation. PsycExtra. Retrieved July 5, 2011, from http://psych-www.colorado.edu/~tor/Papers/Wager_Feldman_Barrett_2004_Insula_meta-analysis.pdf

Wager, T. D., Barrett, L. F., Bliss-Moreau, E., Lindquist, K., Duncan, S., Kober, H., et al. (2008). The neuroimaging of emotion. In M. Lewis, J. M. Haviland-Jones & L. F. Barrett (Eds.), *Handbook of emotions* (3rd ed., pp. 249-271). New York: Guilford Press.

Wager, T. D., Davidson, M. L., Hughes, B. L., Lindquist, M. A., & Ochsner, K. N. (2008). Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron*, *59*(6), 1037-1050.

Wager, T. D., Jonides, J., & Reading, S. (2004). Neuroimaging studies of shifting attention: a meta-analysis. *Neuroimage*, 22(4), 1679-1693.

Wager, T. D., Keller, M. C., Lacey, S. C., & Jonides, J. (2005). Increased sensitivity in neuroimaging analyses using robust regression. *Neuroimage*, *26*(1), 99-113.

Wager, T. D., Rilling, J. K., Smith, E. E., Sokolik, A., Casey, K. L., Davidson, R. J., et al. (2004). Placebo-induced changes in FMRI in the anticipation and experience of pain. *Science*, *303*(5661), 1162-1167.

Wager, T. D., van Ast, V. A., Hughes, B. L., Davidson, M. L., Lindquist, M. A., & Ochsner, K. N. (2009). Brain mediators of cardiovascular responses to social threat, part II: Prefrontal-subcortical pathways and relationship with anxiety. *Neuroimage*, *47*(3), 836-851.

Walker, D. L., & Davis, M. (1997). Double dissociation between the involvement of the bed nucleus of the stria terminalis and the central nucleus of the amygdala in startle increases produced by conditioned versus unconditioned fear. *J Neurosci*, *17*(23), 9375-9383.

Walter, H., von Kalckreuth, A., Schardt, D., Stephan, A., Goschke, T., & Erk, S. (2009). The temporal dynamics of voluntary emotion regulation. *PLoS ONE*, *4*(8), e6726.

Ward, B. D. (2000). *Simultaneous inference for FMRI data*. Retrieved July 3, 2011, from <u>http://afni.nimh.nih.gov/pub/dist/doc/manual/AlphaSim.pdf</u>

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*, *54*(6), 1063-1070.

Williams, L. E., Bargh, J. A., Nocera, C. C., & Gray, J. R. (2009). The unconscious regulation of emotion: nonconscious reappraisal goals modulate emotional reactivity. *Emotion*, *9*(6), 847-854.

Wilson, T. D., Lisle, D. J., Kraft, D., & Wetzel, C. G. (1989). Preferences as expectationdriven inferences: effects of affective expectations on affective experience. *J Pers Soc Psychol*, *56*(4), 519-530.

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nat Methods*, *8*(8), 665-670.



Figure 1. Trial structure for a full (AntStim) trial.



Figure 2. Mediation path diagram showing the predictor search variable (Reapp Neg – Look Neg brain activity during cue/anticipation), *a priori* mediator variable (amygdala activation during the picture presentation period), and outcome variable (reappraisal success self-reports). *a* and *b* are indirect paths, *c* is the total relationship, and *c'* is the direct path (controlling for the mediator).



Figure 3. Negative affect ratings. Black bars represent negative affect ratings from trials containing a picture presentation (i.e. full AntStim trials and StimOnly trials) and gray bars represent negative affect ratings from anticipation only (AntOnly) trials.



Figure 4. Brain activity during cue/anticipation that satisfies the mediated relationship depicted in Figure 2. Orange-to-yellow regions show a positive mediated relationship, such that increases are associated with greater reappraisal success, mediated by amygdala activity during picture presentation. Blue-to-green regions show a negative mediated relationship, such that more activity in these regions at cue/anticipation is associated with less reappraisal success, mediated by amygdala activity during picture presentation.



Figure 5. Pattern expression analysis results. *A, Top four rows:* Brain maps derived from Neurosynth depicting activations (yellow) and deactivations (blue) for various mental task sets. *A, bottom row:* Present mediation results, showing anticipatory activity associated with reappraisal success via positive (yellow) and negative (blue) mediation pathways, with FWE-corrected results outlined in dark yellow and purple, respectively. *B:* Pattern expression analysis results comparing current mediation results to various Neurosynth-derived task maps. A larger positive number along the x-axis reflects greater coherence between the Neurosynth map and the present mediation results, whereas a larger negative number reflects an increasingly opposite patterns of results across the compared tasks.



Figure 6. Trial structure for Studies 2 and 3



Figure 7. Reinterpretation training negative affect ratings



Figure 8. Distancing training negative affect ratings



Figure 9. Look Only negative affect ratings



Figure 10. Reapp negative ratings for Reinterpretation and Distancing groups



Figure 11. Look Negative ratings for Reinterpretation, Distancing, and Look Only groups



Figure 12. Drops in perceived stress by group


Figure 13. Perceived stress reports over time across groups



Figure 14. Reinterpretation timecourses for mean heart rate change by session and condition. Condition bands reflect standard error of the mean.



Figure 15. Distancing timecourses for mean heart rate change by session and condition. Condition bands reflect standard error of the mean.



Figure 16. Look Only timecourses for mean heart rate change by session and condition. Condition bands reflect standard error of the mean.



Figure 17. Mean change in heart rate during the stimulus period for Reinterpretation



Figure 18. Mean change in heart rate during the stimulus period for Distancing



Figure 19. Mean change in heart rate during the stimulus period for Look Only



Figure 20. Task design for Study 4



Figure 21. Behavioral results from T1 massed practice



Figure 22. Behavioral results from the active regulation task (T2)



Figure 23. Right amygdala ROI (left) for a contrast of New Look Negative versus Look Neutral stimuli at T2 and extracted beta estimates across T2 conditions (right).



Figure 24. Left VLPFC ROI (left) for a contrast of New Distance Negative versus New Look Negative stimuli at T2 and extracted beta estimates across T2 conditions (right).



Figure 25. Right amygdala ROI (left) and extracted beta estimates across T4 conditions (right).

Mediation						a*b			а			b			c'			c	
	x	v	z	k	eff	1	D	eff	t	D	eff	t	D	eff	t	0	eff	Ť	D
Negative Mediated							F			F			-		10	-		•	-
RH Sup Frontal																			
(BA 10)	24	62	18	94	-1.22	-2.35	0.03	2.46	2.79	0.01	-0.48	-2.64	0.01	-0.25	-0.22	0.83	-1.48	-1.27	0.22
RH Sup Frontal Gyrus (BA 8) RH Sup	34	21	54	96	-1.48	-2.34	0.03	2.40	2.47	0.02	-0.61	-3.11	0.00	1.04	0.92	0.37	-0.44	-0.40	0.69
Temporal Gyrus (BA 40)	48	-48	23	174	-1.84	-2.33	0.03	2.99	2.58	0.02	-0.62	-2.96	0.01	1.37	1.02	0.32	-0.47	-0.40	0.69
LH Precentral Gyrus (BA 4) RH Post	-21	-21	54	74	-2.82	-2.27	0.03	5.78	2.62	0.01	-0.49	-2.54	0.02	-0.64	-0.12	0.91	-3.47	-1.44	0.16
Cingulate Gyrus (BA 31)	17	-41	32	105	-1.06	-2.25	0.03	2.20	2.59	0.02	-0.48	-2.67	0.01	-0.31	-0.22	0.83	-1.37	-1.26	0.22
RH Postcentral Gyrus (BA 3)	31	-34	50	50	-1.58	-2.25	0.03	3.10	2.79	0.01	-0.51	-2.47	0.02	0.03	0.00	1.00	-1.55	-1.49	0.15
Positive																	-		
Mediated Relationship																			
13)	41	0	-5	71	1.83	2.37	0.03	-2.78	-2.78	0.01	-0.66	-2.82	0.01	-1.79	-1.09	0.28	0.04	0.04	0.97
13) RH Anterior	-48	10	-5	59	1.40	2.35	0.03	-2.36	-2.78	0.01	-0.58	-2.79	0.01	-0.80	-0.74	0.47	0.60	0.73	0.47
Lobe Cerebellum RH Anterior	3	-69	-36	126	1.18	2.36	0.03	-2.18	-2.63	0.01	-0.54	-2.76	0.01	-0.48	-0.51	0.62	0.70	0.72	0.48
Lobe Cerebellum	14	-48	-41	56	1.39	2.31	0.03	-2.34	-2.57	0.02	-0.60	-2.76	0.01	-0.95	-0.86	0.40	0.44	0.43	0.67

Table 1. Brain activity during cue/anticipation that shows a significant amygdalamediated relationship with reappraisal success (a*b mediation path). Regions are wholebrain FWE-corrected at p<0.05 with thresholds of p<0.05 and $k \ge 50$ voxels. Coordinates are in MNI space. For each cluster, path coefficients, t-scores, and significance levels are shown for each mediation path.

Appendix A

The questions in this scale ask you about your feelings and thoughts *in general*. In each case, please indicate how often you generally feel or think a certain way.

1. In general, ho	ow often do you become u	pset because of something that happens unexpectedly?							
0=never	1=almost never	2=sometimes3=fairly often4=very often							
2. In general, ho 0=never	ow often do you feel that y 1=almost never	you are unable to control the important things in your life? 2=sometimes3=fairly often4=very often							
3. In general, ho	w often do you feel nervo	ous and "stressed"?							
0=never	1=almost never	2=sometimes3=fairly often4=very often							
4. In general, ho 0=never	ow often do you feel confi 1=almost never	dent about your ability to handle your personal problems? 2=sometimes3=fairly often4=very often							
5. In general, ho	ow often do you feel that t	hings are going your way?							
0=never	l=almost never	2=sometimes3=fairly often4=very often							
6. In general, how often do you find that you cannot cope with all the things that you have to do?									
0=never	1=almost never	2=sometimes3=fairly often4=very often							
7. In general, how often are you able to control irritations in your life?									
0=never	1=almost never	2=sometimes3=fairly often4=very often							
8. In general, ho	ow often do you feel that y	you are on top of things?							
0=never	1=almost never	2=sometimes3=fairly often4=very often							
9. In general, how often are you angered because of things that are outside of your control?									
0=never	1=almost never	2=sometimes3=fairly often4=very often							

 10. In general, how often do you feel difficulties are piling up so high that you cannot overcome them?

 __0=never
 __1=almost never
 __2=sometimes
 __3=fairly often
 __4=very often

Appendix B

The questions in this scale ask you about your feelings and thoughts *in the past few days*. In each case, please indicate how often you felt or thought a certain way.

1. In the past few	days, how often have you	been upset because of	f something that h	appened unexpectedly?
0=never	1=almost never	2=sometimes	_3=fairly often	_4=very often
2. In the past few life?	days, how often have you	felt that you were una	ble to control the	important things in your
0=never	1=almost never	2=sometimes	_3=fairly often	_4=very often
3. In the past few	days, how often have you	felt nervous and "stre	ssed"?	
0=never	1=almost never	2=sometimes	_3=fairly often	_4=very often
4. In the past few problems?	days, how often have you	felt confident about y	our ability to hand	ile your personal
0=never	1=almost never	2=sometimes	_3=fairly often	_4=very often
5. In the past few	days, how often have you	felt that things were g	going your way?	
0=never	1=almost never	2=sometimes	_3=fairly often	_4=very often
6. In the past few to do?	days, how often have you	found that you could	not cope with all t	the things that you had
0=never	1=almost never	2=sometimes	_3=fairly often	_4=very often
7. In the past few	days, how often have you	been able to control in	rritations in your l	ife?
0=never	1=almost never	2=sometimes	_3=fairly often	_4=very often
8. In the past few	days, how often have you	felt that you were on	top of things?	
0=never	1=almost never	2=sometimes	_3=fairly often	_4=very often
9. In the past few control?	days, how often have you	been angered because	e of things that we	re outside of your
0=never	1=almost never	2=sometimes	_3=fairly often	_4=very often
10. In the past few overcome them? 0=never	w days, how often have yo 1=almost never	u felt difficulties were 2=sometimes	piling up so high 3=fairly often	that you could not 4=very often

Instructions for Emotion Regulation task

Intro screen

In this task, what we are really interested in is people's ability to change how they are feeling. And the way we are going to ask you to change how you are feeling is by changing the way you think about something that we show you. So what's going to happen is that you will see a series of pictures, and some of them are going to make you feel somewhat negative or very negative, and some pictures might not make you feel very negative at all.

"Look" instruction

Before each picture, you are going to see one of two instructions that tells you what you are going to do while the picture is on the screen. The first instruction you might see is the *"look"* instruction. When you see the instruction to *look*, we want you to look at the picture, keep your eyes on it the whole time, and allow yourself to respond naturally to it. So have whatever thoughts and feelings you would naturally have in response to that picture.

"Decrease" instruction

The other instruction you will see is to "*decrease*". When you see the instruction to *decrease* we want you to think of something to tell yourself that helps you to feel less negative about the picture. So for example, you could tell yourself something about the outcome, so that whatever is going on will soon be resolved, or that help is on the way. You could also focus on a detail or aspect of the situation that isn't quite as bad as it first seemed. But we want you to stay focused on the picture, **not mentally distance yourself from the content of the picture**, and not think of random things that make you feel better, but rather to change something about the picture that helps you to feel less negative about it. Does that make sense? We'll do some practice in a few seconds so you can do it for yourself.

Rating screen

So after the picture is on the screen you will see a scale like this which will ask you to indicate how negative you feel. It goes from **1 to 5**, where 1 means that you don't feel negative at all, and **5** means that you feel very strongly negative. **2**, **3**, and **4 are in between**. We realize that sometimes you won't feel negative at all, sometimes you might have started to feel negative and then tried to decrease how negative you felt and that worked really well, and sometimes you attempt to decrease how negative you feel but couldn't think of something in time or it didn't really work that well. So no matter what happened through the course of looking at the picture, try to rate at the end how negative you feel when all is said and done, so where you ended up after all you tried to do. Does that make sense? Try to be as honest as you can about how you feel.

Here are how the trials will actually go when you are doing the task. First you'll see a fixation cross in the center of the screen. When you see it, just relax, stay focused on the screen, and get ready for the next part of the trial or for a new trial to begin. [NOW have subject hit a sample rating between 1-5 to advance the slide]

Look Cue screen

Since the instruction is *look*, do you remember what you are supposed to do?

Keep looking at the picture the whole time, pay attention to the picture and respond as you naturally would. [always restate this - some people say to just 'stare at it', but we want them to take it in and pay attention]

Look Picture screen, Rating screen

So that's one of the pictures you might see, then honestly rate about how negative you feel.

Decrease1 Cue screen

So then when you see the instruction to *decrease*, do you remember what you are supposed to do?

Right, try to think of the picture in a way that helps you to feel less negative. [always restate this in these words]

Decrease1 Picture screen

So for this picture, what might you tell yourself to feel less negative?

Great, so perhaps [give sample reinterpretation]. That's a great way to think about it differently to help you feel less negative. So the whole time the picture is up, once you think of something that helps you feel less negative, really try to convince yourself of that and really believe it so that you decrease how negative you feel as much as you can while the picture is on the screen. Hopefully that will come to you fairly quickly.

Just to give you an idea of the range of things that some other people have said in response to this picture [give another sample reinterpretation]. Any of those kinds of things could work.

You might end up reusing some of the kinds of things that you tell yourself, so there might be other pictures where it also works to tell yourself, "oh it looks like they're getting help and they'll be better soon". And that's ok, you can reuse those general categories of things to tell yourself, but every time a picture comes on the screen take a moment to think of the very best thing to tell yourself for that particular picture. We just don't want you to get to the point where you are applying the exact same change to every picture when the instruction is "Decrease". We really want you to actively think of the best way to change how you're feeling without mentally distancing yourself from the content of the picture. In other words, stay engaged in the content of the photo, but tell yourself of that for the rest of the time that the picture is on the screen when the instruction is to "Decrease".

Rating screen

So again, when you see the **1 to 5** scale, indicate how negative you feel when all is said and done and you've tried as hard as you can to convince yourself the way you were thinking about it was true.

Decrease2 Picture screen

So now here's another example of *decrease*. So what could you tell yourself to feel less negative?

Right, exactly. Just to give you other ideas, [give sample reinterpretations].

Once you've come up with a way to feel less negative, keep repeating it to yourself when the instruction is to "Decrease". Then be honest about how negative you feel when you make your rating.

Get Ready screen

Now what will happen is we will go through some trials exactly as they will appear in the actual task. So they will move along at a fixed pace. The two things to keep in mind are 1) that the rating scale will only be on the screen for a certain amount of time. So be sure to press the button when you actually see the scale from **1 to 5** on the screen. If you press it slightly before or after we might night get your response. Then the other thing to keep in mind is 2) that the pictures are up there for a good amount of time but not forever. So again you really want to try to think of something relatively quickly that is the best fit for that picture and then apply it for the rest of the time. And sometimes when the instruction is "decrease" you might not be able to think of something in time, some of them might just be a little bit overwhelming, and we understand that. Just be honest when the rating scale comes up.

Any questions?

Intro screen

In this task, what we are really interested in is people's ability to change how they are feeling. And the way we are going to ask you to change how you are feeling is by **altering the way you think about the personal relevance of a situation**. Specifically, we are interested in what happens when people try to <u>decrease</u> *negative* emotional responses by *changing their personal connection* to what is happening. So what's going to happen is that you will see a series of pictures, and some of them are going to make you feel somewhat negative or very negative, and some pictures might not make you feel very negative at all.

"Look" instruction

Before each picture, you are going to see one of two instructions that tells you what you are going to do while the picture is on the screen. The first instruction you might see is the *"look"* instruction. When you see the instruction to *look*, we want you to look at the picture, keep your eyes on it the whole time, and allow yourself to respond naturally to it. So have whatever thoughts and feelings you would naturally have in response to that picture.

"Decrease" instruction

When you see the instruction *Decrease*, we would like you to mentally distance yourself from the pictured events in such a way that your emotional response is decreased or attenuated. To do this, you should view the photos with a *detached*, *objective*, *impartial*, *and scientific mindset*, and/or *imagine that the pictured events happened far away or a long time ago*. As you view each pictured event, *what is critical is that you cut all personal ties to the event* in a way that any negative emotional reaction is decreased or attenuated as much as possible.

Rating screen

So after the picture is on the screen you will see a scale like this which will ask you to indicate how negative you feel. It goes from 1 to 5, where 1 means that you don't feel negative at all, and 5 means that you feel very strongly negative. 2, 3, and 4 are in between. We realize that sometimes you won't feel negative at all, sometimes you might have started to feel negative and then tried to decrease how negative you felt and that worked really well, and sometimes you attempt to decrease how negative you feel but couldn't think of something in time or it didn't really work that well. So no matter what happened through the course of looking at the picture, try to rate at the end how negative you feel when all is said and done, so where you ended up after all you tried to do. Does that make sense? Try to be as honest as you can about how you feel.

Here are how the trials will actually go when you are doing the task. First you'll see a fixation cross in the center of the screen. When you see it, just relax, stay focused on the screen, and get ready for the next part of the trial or for a new trial to begin. [NOW have subject hit a sample rating between 1-5 to advance the slide]

Look Cue screen

Since the instruction is *look*, do you remember what you are supposed to do?

Keep looking at the picture the whole time, pay attention to the picture and respond as you naturally would. [always restate this - some people say to just 'stare at it', but we want them to take it in and pay attention]

Look Picture screen, Rating screen

So that's one of the pictures you might see, then honestly rate about how negative you feel.

Decrease1 Cue screen

So then when you see the instruction to *decrease*, do you remember what you are supposed to do?

Right, try to think of the picture in a distanced way that helps you to feel less negative by viewing the photos with a detached mindset or imagining that the event occurred far away or a long time ago. [always restate this in these words]

Decrease1 Picture screen

So for this picture, what might you tell yourself to feel less negative?

Great, so perhaps [give sample distancing interpretation]. That's a great way to distance yourself from it to help you feel less negative. So the whole time the picture is up, once you think of something that helps you feel less negative, really try to convince yourself of that and really believe it so that you decrease how negative you feel as much as you can while the picture is on the screen. Hopefully that will come to you fairly quickly.

Just to give you an idea of the range of things that some other people have said in response to this picture [give another sample distancing interpretation]. Any of those kinds of things could work.

You might end up reusing some of the kinds of things that you tell yourself, so there might be other pictures where it also works to tell yourself, "it happened a long time ago or it's happening far away from me". And that's ok, you can reuse those general categories of things to tell yourself, but every time a picture comes on the screen take a moment to think of the very best thing to tell yourself for that particular picture. We just don't want you to get to the point where you are applying the exact same change to every picture when the instruction is "Decrease". We really want you to actively think of the the picture is on the screen when the instruction is to "Decrease".

Rating screen

So again, when you see the **1 to 5** scale, indicate how negative you feel when all is said and done and you've tried as hard as you can to convince yourself the way you were thinking about it was true.

Decrease2 Picture screen

So now here's another example of *decrease*. So what could you tell yourself to feel less negative?

Right, exactly. Just to give you other ideas, [give sample distancing interpretation].

Once you've come up with a way to feel less negative, keep repeating it to yourself when the instruction is to "Decrease". Then be honest about how negative you feel when you make your rating.

Get Ready screen

Now what will happen is we will go through some trials exactly as they will appear in the actual task. So they will move along at a fixed pace. The two things to keep in mind are 1) that the rating scale will only be on the screen for a certain amount of time. So be sure to press the button when you actually see the scale from 1 to 5 on the screen. If you press it slightly before or after we might night get your response. Then the other thing to keep in mind is 2) that the pictures are up there for a good amount of time but not forever. So again you really want to try to think of something relatively quickly that is the best fit for that picture and then apply it for the rest of the time. And sometimes when the instruction is "decrease" you might not be able to think of something in time, some of them might just be a little bit overwhelming, and we understand that. Just be honest when the rating scale comes up.

Any questions?

Appendix E

In this task, what we are really interested in is people's feelings as they look at pictures showing scenes of different emotional strength. What's going to happen is that you will see a series of pictures, and some of them are going to make you feel somewhat negative or very negative, and some pictures might not make you feel very negative at all.

"Look" instruction

Before each picture, you are going to see an instruction that tells you what you are going to do while the picture is on the screen. Specifically, you'll see the *"look"* instruction. When you see the instruction to *look*, we want you to look at the picture, keep your eyes on it the whole time, and allow yourself to respond naturally to it. So have whatever thoughts and feelings you would naturally have in response to that picture.

Rating screen

So after the picture is on the screen you will see a scale like this which will ask you to indicate how negative you feel. It goes from **1 to 5**, where 1 means that you don't feel negative at all, and **5** means that you feel very strongly negative. **2, 3, and 4 are in between**. We realize that sometimes you won't feel negative at all, and sometimes you might feel very negative. Try to be as honest as you can about how you feel. [NOW have subject hit a sample rating between **1-5** to advance the slide]

Ok, so now we'll complete some practice trials.

Look Cue screen

Since the instruction is *look*, do you remember what you are supposed to do? [That's right], keep looking at the picture the whole time, pay attention to the picture and respond as you naturally would. [always restate this - some people say to just 'stare at it', but we want them to take it in and pay attention]

Look Picture screen, Rating screen

So that's one of the pictures you might see, then honestly rate about how negative you feel.

Next you'll see a fixation cross in the center of the screen. When you see it, just relax, stay focused on the screen, and get ready for a new trial to begin.

Instruction screen

Now what will happen is we will go through some trials exactly as they will appear in the actual task. So they will move along at a fixed pace. One thing to keep in mind is that the rating scale will only be on the screen for a certain amount of time. So be sure to press the button when you actually see the scale from **1 to 5** on the screen. If you press it slightly before or after we might not get your response. Any questions?