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The Impact of Prefrontal Cortex “Warm Up” on Immediate Cognitive Reappraisal
Ability in Older Adolescents with Elevated Symptoms of Depression

A Dissertation

Presented to

The Faculty of Social Sciences

University of Denver

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

by

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August 2015

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Title: The Impact of Prefrontal Cortex “Warm Up” on Immediate Cognitive Reappraisal Ability in Older Adolescents with Elevated Symptoms of Depression

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Abstract

Cognitive Reappraisal (CR) is a central component of Cognitive Behavioral Therapy for adolescent depression. Yet, previous research indicates that a brain region highly associated with successful CR in adults, the Prefrontal Cortex (PFC), is not fully developed until early adulthood. Thus, there is growing concern that CBT interventions directed at building CR abilities in depressed teens might be constrained by PFC immaturity. However, CR is an effective strategy for regulating affect. The current study evaluated an intervention aimed at enhancing CR performance through PFC “warm up” with a working memory task. Additionally, the study examined moderators of intervention response, as well as cognitive correlates of self-reported CR use.

Participants included 48 older adolescents (mean age=19.1, 89% female) with elevated symptoms of depression who were randomly assigned to a lab-based WM or control activity followed by a CR task. Overall, results failed to support the effectiveness of “warm up” to augment CR performance. However, current level of depression predicted negative bias and sadness ratings after CR instructions, and this effect was qualified by an interaction with condition. The moderator analysis showed that depressive symptoms interacted with condition such that in the control condition, participants with higher depressive symptoms had significantly lower negative bias scores than individuals with lower depressive symptoms, but this pattern was not found in

the experimental condition. Contrary to hypotheses, history of depression did not moderate treatment response. Additional analyses explored alternative explanations for the lack of intervention effects. There was some evidence to suggest that the WM task was frustrating and cognitively taxing. However, irritation scores and overall WM task accuracy did not predict subsequent CR performance. Lastly, multiple cognitive variables emerged as correlates of self-reported CR use, with cognitive flexibility contributing unique variance to self-reported CR use. Results pointed to new directions for improving CR performance among youth with elevated symptoms of depression.

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Chapter One: Background and Significance

Decades of randomized controlled trials on psychosocial treatments for psychological disorders in youth have produced mixed results (Weisz, Chorpita, Palinkas, Schoenwald, Miranda, Bearman, et al., 2012). Current Evidence Based Therapy (EBT) approaches, though more effective than wait list and attention controls, fail to produce remission in approximately 40% of treated youth and leave many more with residual symptoms (Weersing & Brent, 2010). Results have been especially poor in effectiveness trials when researchers have aimed to transport EBTs from highly controlled research settings to real-world clinics (Southam-Gerow, Rodriguez, Chorpita, and Daleiden, 2012). Accordingly, there is ample room for improvement in current treatment protocols for youth disorders. One particularly promising avenue for enhancing existing treatment protocols is to draw on affective neuroscience findings to augment current CBT principles. The current study examines a core component of CBT for depression from a neuroscience perspective in order to develop a strategy for enhancing efficacy. The primary focus is on Cognitive Reappraisal (CR), a core emotion regulation skill taught in CBT. Based on developmental and neurocognitive research, a strategy for augmenting cognitive reappraisal was developed and tested in a lab-based analog study.

Emotion Regulation

Emotion Regulation (ER) refers to the processes by which individuals influence their experience and expression of emotions (Gross, 1998). Much of the contemporary work on emotion regulation stems from Gross's process model of emotion regulation (2001), which outlines the temporal sequence of emotion generation beginning with the selection of a situation and ending with an observable emotional response. According to this model, ER strategies fall into two categories: Antecedent-focused, those strategies that are implemented before an emotional response is generated and response-focused, which refers to the regulation of affect once an emotion has been generated.

There is great variability in ER techniques that individuals use to modulate their emotional experience. While some ER strategies serve a protective function and promote adaptive coping and adjustment, others exacerbate the symptoms of a variety of psychological disorders (Aldao, Nolen-Hoeksema, & Schweizer, 2010). Individuals with depression, for example, tend to have poor ER skills which contribute to reduced emotional response to positive stimuli and a heightened response to negative stimuli (Rottenberg, Gross, & Gotlib, 2005). One particular ER strategy, cognitive reappraisal (CR), has been especially studied in the context of depression and refers to the act of restructuring or reinterpreting a potentially negative situation in order to buffer its negative effects or lessen its severity (Gross, 1998). CR is an antecedent-focused strategy that falls under the umbrella of secondary control coping, meaning it involves an active shift in cognitions, expectations, or goals as opposed to changing the stimulus itself (Heckhausen & Schulz, 1995). By altering the interpretation of the event, one also alters

the trajectory of the emotional experience and response (Gross, 1998). Thus, successful CR can significantly reduce not only an individual's expression of negative emotions but also reduce their negative affective experience and physiological arousal (Gross, 1998). Further, Mauss and colleagues (2007) found that reappraisal can also lead to an increase in positive affect as well. As such, cognitive reappraisal represents an adaptive ER strategy. Unfortunately, research indicates that depressed individuals, both adults and adolescents, utilize this strategy less than their non-depressed counterparts and when they use CR it seems to be less effective (Connor-Smith, Compas, Wadsworth, Thomsen, & Saltzman, 2000; Joormann & Gotlib, 2009; Gotlib & Joormann, 2010; Rottenberg, Gross, & Gotlib, 2005; Silk, Steinberg, & Sheffield, 2003).

Cognitive Reappraisal in CBT Protocols for Adolescent Depression

In multi-component, manualized therapy protocols such as Cognitive Behavioral Therapy (CBT), clients are taught specific cognitive skills, behavioral coping strategies, and management of affect-related processes (Reinecke, Ryan, & Dubois, 1998; Rossello & Bernal, 1999). CR is a cognitive skill that is a central component of many well-known manualized therapy protocols for adolescent depression (e.g. Primary and Secondary Control Enhancement Training: Weisz, Thurber, Sweeney, Proffitt, & LeGagnoux, 1997; ACTION: Stark, Schnoebelen, Simpson, Hargrave, Molnar & Glen, 2007; Group Therapy Manual for Cognitive-Behavioral Treatment of Depression: Rossello and Bernal, 1999). Though treatment protocols that include CR have been empirically supported through multiple efficacy trials (see Weisz, McCarty, & Valeri, 2006 for a review) the field still lacks adequate dismantling studies supporting a direct link between

cognitive reappraisal and symptom reduction in adolescents. Other treatment components, aside from CR, such as mood monitoring, problem-solving, or behavioral activation may be responsible for the positive change that is observed in these treatments. In fact, Shirk and colleagues (2013) found that changes in maladaptive cognitions predicted subsequent changes in depressive symptoms, but client involvement in cognitive restructuring components and homework did not predict changes in cognitions. One option for improving current CBT approaches might be to enhance CR training by focusing on some of its underlying components.

Cognitive Reappraisal in Adults

Despite the dearth of evidence supporting the direct effectiveness of CR training in CBT for adolescent depression, previous research using both self-report and behavioral methods has reliably identified it as an effective coping strategy for adult populations. Studies using self-report data indicate that individuals that report frequent use of CR also tend to report more positive affect, greater life-satisfaction, higher self-esteem and fewer symptoms of depression (Gross & John, 2003; John & Gross, 2004). CR may be particularly useful in the face of uncontrollable life events or circumstances. For example, Wadsworth and colleagues (2011) demonstrated that self-reported use of secondary control coping methods, including cognitive reappraisal, moderated the impact of poverty-related stress on internalizing symptoms in low-income parents. Studies that assess reappraisal *ability*, (successful reduction of negative affect in a laboratory setting) have yielded similar results. Troy and colleagues (2010) found that cognitive reappraisal ability moderated the impact of significant life stressors on depression symptoms.

Further, McRae and colleagues (2012) identified a link between reappraisal ability and overall life satisfaction and higher rates of positive emotion.

Additional work has indicated that CR is also an efficient use of cognitive resources because it occurs early in the emotion regulation process and thus reduces the subjective experience and behavioral expression of negative affect, both of which require substantial cognitive effort (Gross, 1998). Specifically, the use of CR has been shown to boost an individual's performance on recognition tasks and enthusiasm for engaging in future cognitive related activities (Leroy, Gregoire, Magen, Gross, & Mikolajczak, 2012). The use of CR during emotionally taxing situations is also associated with better performance on subsequent memory tasks (Richards & Gross, 2000; Steinberger, Payne, & Kensinger, 2011).

Neural and Cognitive Correlates of Cognitive Reappraisal

A recent review of imaging studies with adults indicated that successful CR is supported by substantial activation of the prefrontal region, the posterior parietal lobe, and the lateral temporal cortex as well as modulation of activity in the amygdala (Buhle, Silvers, Wager, Lopez, Onyemekwu, Kober, Weber, & Ochsner, 2014). Thus, these findings suggest that CR involves cognitive control, semantic and perceptual reasoning, and regulation of affect (Buhle et al., 2014), processes that involve generating, maintaining, and applying alternative ideas, while simultaneously evaluating current emotion states (Ochsner & Gross, 2008).

Many areas of the prefrontal cortex (PFC), including the dorsomedial (dmPFC), ventrolateral (vlPFC), and dorsolateral (dlPFC) areas contribute different components of

cognitive control over emotion (Goldin et al., 2008). For instance, the dmPFC likely supports semantic and self-reflective processing (Olsson & Ochsner, 2009), while the vlPFC contributes selection and inhibition of reappraisals (Simmonds et al., 2008). However, a number of previous studies have focused on the dlPFC and its specific impact on manipulating reappraisals in working memory and down-regulating negative emotion during cognitive reappraisal (Ochsner & Gross, 2005; Ray et al., 2005, Wager & Smith, 2003). A review by Smith and colleagues (1998) suggests that the dlPFC is particularly important for tasks in which an individual must store and then manipulate information to produce a new output. In the case of CR, researchers hypothesize that the dlPFC is critical in that it is involved in the generation and maintenance of alternative ways of thinking about emotional situations or evocative stimuli (Ray, et al.,2005).

Ochsner and Gross (2008) highlight a number of important ways that imaging findings extend behavioral research. First, it illuminates the distinct mechanisms of similar behavioral outcomes, like distraction and reappraisal, for instance. While both lead to a reduction of negative affect at the behavioral level in the short term, the underlying neural processes of each behavior are, in fact, quite distinct (McRae, Hughes, Chopra, Gabrieli, Gross, & Ochsner, 2010). Second, imaging work has shown that linguistic and cognitive processes, not typically thought to be relevant for emotion regulation, are implicated in CR (Ochsner & Gross, 2008). Further, by understanding the distinct neural processes, and therefore, the implicated brain regions, it enables the correct identification of the cognitive mechanisms that contribute to behavioral outcomes (Aue, Lavelle, & Cacioppo, 2009). This knowledge then enables the design of

neurobehavioral therapies that target these cognitive mechanisms which can lead to more effective interventions (Siegle, Ghinassi, & Thase, 2007). Finally, understanding the neural correlates of CR is particularly relevant to the current study as it provides insight into the challenges of CR for youth.

Cognitive Reappraisal in Adolescents

Although CR is an adaptive ER strategy and an important target of intervention for adolescent depression, it is not clear that adolescents and even young adults have attained a level of neurological maturation that will support effective cognitive reappraisal. Adolescence marks a period of significant brain development, particularly in regions and systems that underlie emotion regulation (Steinberg, 2004). Specifically, there is significant maturation of the PFC during this time and also increased connectivity between the PFC and several areas of the limbic system (Bunge & Wright, 2007; Spear, 2000). For instance, Perlman and Pelphrey (2011) compared children to adults on an affect laden working memory task and found that connectivity between the amygdala (where the emotions were generated) and the PFC (region responsible for affect regulation) increased with age. These structural changes also coincide with memory and cognitive control functions (Sowell, Delis, Stiles & Jerigan, 2001; Rubia, Smith, Woolley, Nosarti, Heyman, Taylor, & Brammer, 2006). Importantly, however, this development extends well beyond adolescence into early adulthood (Sowell et al., 2001). In fact, emotion regulatory abilities are among the last executive function processes to develop (Prencipe, Kesek, Cohen, Lamm, Lewis, & Zelazo, 2011). Thus, it is likely that the PFC circuits involved in CR are relatively under-developed prior to early adulthood.

As a result, CR is likely to be less effective, more difficult to utilize, or both for adolescents. In fact, McRae and colleagues (2012) found that a linear increase in PFC activation accompanied a linear increase in CR abilities over the course of adolescence and early adulthood. The results of this study are consistent with self-report data that indicates adolescents tend to report using significantly fewer cognitive coping strategies than adults (Garnefski, et al., 2002) and that their self-reported use increases with age (Williams & McGillicuddy-De Lisi, 2000). However, there is still some evidence to indicate that self-reported use of cognitive coping strategies like cognitive reappraisal can protect against depression and anxiety in adolescents (Betts, Gullone, & Allen, 2009; Garnefski et al., 2003; Garnefski, Kraaij, & van Etten, 2005; Kraaij, Garnefski, de Wilde, Dijkstra, Gebhardt, Maes, & ter Doest, 2003) lending further support for boosting this skill during this developmental period.

Depression and Executive Function

Ineffective use of CR is likely to be exacerbated in adolescents with depression who tend to show poor regulatory functions in the PFC (Hilari, Simic, Pariante, Papadopoulos, Cleare, Brammer, et al., 2009). Siegle and colleagues (2007) proposed that depressed individuals chronically fail to recruit the PFC in the face of negative affect thereby causing the connections in this brain region to atrophy, making it less likely for its activation in the face of future emotional arousal. While many regions of the PFC are thought to play a role in the development and maintenance of depression (Drevets, 2000), Koenigs and Grafman (2009) hypothesized that dlPFC dysfunction in particular could largely contribute to depressive symptoms given the dlPFC's role in regulating negative

affect. More specifically, individuals with depression, both adults and children, tend to show a reduced emotional response to positive stimuli and a heightened response to negative stimuli (Gaffrey, Luby, Belden, Hirshberg, Volsch, & Barch, 2011; Rottenberg, Gross, & Gotlib, 2005). In turn, depressed adolescents may show significant EF deficits, especially in the dlPFC (Hilari et al., 2009), and thus have unique difficulty successfully using CR. Therefore, one potential consequence of chronic depressive episodes of long duration could be weak or highly under-developed neural networks that support executive function including CR.

Importantly, the dlPFC is largely involved in working memory (WM) functions, especially those related to verbal and spatial working memory (Barbey, Koenigs, & Grafman, 2013; Smith, Jonides, Marsheutz, & Koeppel, 1998). WM capacity is also associated with the ability to adaptively update emotional and cognitive material (Joormann, et al., 2011; Levens & Gotlib, 2010). Accordingly, enhanced WM capacity is thought to underlie more positive ER strategies like CR (McRae, Jacobs, Ray, John, & Gross, 2012; Schmeichel, Volokhov, & Demaree, 2010). It is perhaps not surprising then that previous work has demonstrated marked WM deficits in individuals with depression, which is thought to mediate the pattern of cognitive dysfunction in this population (Christopher & MacDonald, 2005; Gruber, Zilles, Kennel, Gruber, & Falkai, 2011; Joormann, Levens, & Gotlib, 2011; Rose & Ebmeier, 2006).

For instance, in a study by Levens and Gotlib (2010), depressed patients were compared to controls on an affect-laden working memory task. Compared to controls, depressed participants tended to show a bias towards accurately recalling negative stimuli

over positive ones. The finding indicated that depressed individuals tend to more fully integrate negative affect into WM than their non-depressed counterparts and thus have an easier time engaging in rumination about negative topics. In a related study, adults with depression exhibited difficulty ignoring irrelevant negative material while updating the contents of working memory thus leading to higher rates on rumination, than their non-depressed counterparts (Joormann & Gotlib, 2008).

Working memory deficits are apparent in children and adolescents with depression as well (Klimkeit, Tonge, Bradshaw, Melvin, & Gould, 2011). Owens and colleagues (2012) found that depressive symptoms were associated with working memory deficits in a sample of school aged children and these deficits mediated the relationship between depressive symptoms and poor school performance. In another study, Gunther and colleagues (2004) compared children and adolescents with depression to youth with anxiety disorders and healthy controls on a variety of neurocognitive measures. Results demonstrated that only youth with depression demonstrated deficits in the area of working memory.

Prefrontal Cortex “Warm Up”

Taken together, evidence indicates that CR involves activation of the dlPFC (Koenigs & Grafman, 2009). Specifically, theory and research suggest that the dlPFC contributes WM functions in the process of cognitive reappraisal (Schmeichel et al., 2010). However, the PFC is not fully developed in adolescence and does not attain full maturity until early adulthood (Bunge & Wright, 2007). There is also evidence that WM functions are impaired among depressed adolescents, thereby further compromising

underlying functions that support CR (Tavitian et al., 2013). It is not known if increased activation of the PFC, particularly the dlPFC, might enhance CR among youth with depressive symptoms. In the current study, it is hypothesized that activation of the dlPFC through a WM task could improve CR, at least temporarily, by “warming up” circuits that support its use. In fact, it is possible that repeated activation of PFC circuits, especially those involved in working memory, could lead to improvements in CR ability (Siegle et al., 2007).

Considering the dlPFC’s specific involvement in CR (Koenigs & Grafman, 2009), it is an ideal target for warm-up preceding a CR task. Previous imaging studies indicate that the dlPFC is necessary for verbal working memory tasks (Barbey et al., 2013). And while several cognitive-related tasks, in addition to working memory, are likely to involve the dlPFC, such as flexibility and planning (Barbey, Colom, & Grafman, 2013), a working memory task may be especially useful to individuals since individuals with depression show WM deficits and stronger WM capacity is thought to underlie successful CR (Schmeichel & Demaree, 2010). Thus in sum, engaging in a verbal working memory task not only has the potential to recruit a brain region necessary for successful CR but also targets a mechanism typically shown to be a deficit for adolescents with depression and a barrier to successful CR.

Neurobehavioral Therapies Targeting Working Memory

Traditional CBT is aimed at altering dysfunctional patterns of thinking and behaviors through ongoing discussion in session between the client and therapist and practice outside of session (Beck, Rush, Shaw, & Emery, 1979). Conversely,

neurobehavioral therapies are aimed at identifying and then modifying core cognitive mechanisms that contribute to and maintain key symptoms of psychiatric disorders (Siegler et al., 2007). Gaining understanding of the mechanisms through which interventions work helps to clarify how and for whom treatments will be effective thus reducing the need for excessive lengthy and costly clinical trials (Onken, 2015).

For instance, a growing research base supports Cognitive Bias Modification of Interpretations (CBM-I) training as an effective neurobehavioral therapy children and adolescents with anxiety (Lau & Pile, 2015). CBM-I training targets an individual's negative cognitive bias towards interpreting ambiguous stimuli as threatening, a significant underlying mechanism of anxiety (Mathews & MacLeod, 2005). Additional recent neurobehavioral trials have targeted emotion inhibition and its impact on rumination (Cohen, Mor, & Henik, 2015) and pupillary reactivity to negative feedback and its influence on depressive symptoms (Collier & Siegler, 2015).

Of particular relevance to CR and the current study, however, are neurobehavioral studies that targeted working memory. Specifically, working memory training programs have been implemented in samples of children and adolescents with ADHD and have produced improvements in motor activity level, inattention, and hyperactivity (Klingberg, Forssberg, & Westerberg, 2002; Klingberg, et al., 2005). An additional study examining a working memory training program, demonstrated improvements in anxiety symptoms and emotional and behavioral problems (Roughan & Hadwin, 2011). These programs, though yielding promising results, require extended practice over a period of several weeks.

Yet, previous studies have also indicated that boosting particular neural mechanisms in a single session can improve performance on subsequent affect-related tasks (Amir, Weber, Beard, Bomyea, & Taylor, 2008; Bomyea & Amir, 2011). Individuals showed improvements on a thought suppression task following a working memory program that required a high level of inhibitory control (Bomyea & Amir, 2011). Results suggest that activation of functions that underlie particular cognitive processes improve performance on other related tasks.

Further, in a recent meta-analysis, Melby-Lervag & Hulme (2013) found that across multiple studies of both child and adult samples, working memory training programs appear to produce short-term, specific training effects. Therefore, while brief working memory training may not produce long-term changes in dlPFC activity or working memory capacity, it may have the potential to boost CR in the short term. Consistent with the work of Amir and colleagues, it is hypothesized that WM training and the corresponding activation of the dlPFC will enhance immediate CR performance.

Summary

In summary, CR is an effective emotion regulation strategy among adults but appears to be less utilized by adolescents. This is likely due to the fact that the PFC, a critical brain region involved in CR is not fully developed until early adulthood. Additionally, even as the PFC reaches optimal development, under-utilization of CR by depressed adolescents could result in atrophied or stunted growth in networks underlying CR. Consequently, a potentially effective emotion regulation strategy is less effective among adolescents, especially those who have experienced depression.

The current study investigated the effect of PFC “warm up” on immediate CR ability in older adolescents with elevated depressive symptoms. It was hypothesized that PFC “warm up” would enhance CR performance. Specifically, WM was targeted because of its central role in CR. Though it will be important for future research to show that PFC “warm up” improves CR skill acquisition and produces long-term effects on cognitive coping, the goal of the current study was to demonstrate the impact of PFC “warm up” on immediate CR performance. It was hypothesized that individuals randomized to the PFC “warm up” condition would demonstrate significantly greater CR ability than those individuals randomized to the control condition.

A secondary aim of the study was to examine depression history and symptom characteristics that could potentially moderate the response to PFC enhanced CR. Based on the work of Siegle and colleagues (2007), youth with more severe or more chronic (earlier age of onset) depressive symptoms may have atrophied or stunted networks within the PFC. Thus, it was hypothesized that such youth might be less responsive to a single session of PFC activation than youth with less severe or chronic depressive symptoms.

A third aim of this study was to examine cognitive correlates of CR in order to identify additional potential targets for intervention. Given the fact that CR recruits the PFC (Goldin et al., 2008) and the PFC is linked to several executive functions implicated in CR (e.g. emotion inhibition, attention, shifting, working memory) (Monsell, 2003) it was hypothesized that greater executive functions would be associated with higher levels of reported CR use.

Chapter Two: Methods

Participants

Participants were invited to take part in the study through the Sona System (an undergraduate research participation recruitment system) at the University of Denver. Participants received extra credits for psychology classes in exchange for participation. Individuals were eligible to complete the initial online survey if they were between the ages of 18-22. For the online survey portion of the study, participants included 288 older adolescents and emerging adults (69% female; 74% Caucasian) between the ages of 18 and 22 (mean age=19.5, SD=1.2). The sample included 49 eighteen year-olds (17%), 61 nineteen year-olds (22%), 47 twenty year olds (16%), 29 twenty-one year-olds (10%), and 12 twenty-two year olds (4%).

Upon completing the online survey, a subset of participants were then invited to participate in the experimental phase of the study if they obtained scores above 9 (the mean score for a college-aged sample (Whisman et al., 2012)) on the Beck Depression Inventory-II (Beck, Steer, Ball, & Ranieri, 1996). Of the participants that completed the online survey, 135 were invited to participate in the lab session. Of invited participants, 60 completed the lab-based session (88% female; 65% Caucasian; mean age=19.2,

SD=1.2) all of whom had elevated depression scores on the BDI-II (mean score=13.4, SD=8.6).

Measures

Cognitive, emotion, and personality characteristics.

Depressive symptoms. Depressive symptoms were measured using the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Ball, & Ranieri, 1996). The BDI-II is a 21-item self-report measure that includes items assessing a wide range of depression symptoms. The BDI-II is the most widely used dimensional measure of depression with adults and demonstrates good psychometric properties (Beck et al., 1996). A significant body of research supports the use of the BDI with adolescents (see Roberts, Lewinsohn, & Seeley, 1991). The average BDI score in a college aged sample is 9.3 (Whisman, Judd, Whiteford, & Gelhorn, 2012). The BDI was administered as a screening procedure and at the beginning of the lab session. Item # 9, which assesses suicidal ideation, was removed from the BDI-II during the screening procedures due to the fact that participants completed the questionnaire outside of the lab and immediate risk assessment and follow-up were not possible. Item # 9 was included on the BDI when administered during the lab session and risk assessment and safety planning followed when appropriate.

History of depression. A series of questions, adapted from items of the Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL; Kaufman, Birmaher, Brent, Rao, & Ryan, 1996), was added to the end of the BDI-II as part of the online survey to obtain a history of depression from participants. The K-SADS-PL is a semi-structured interview that assesses for the presence, duration,

and lifetime occurrence of a variety of disorders. Accordingly, questions were modified into a self-report format. Items on this measure assessed the duration of the current depressive period (i.e. Have you been having these feelings for longer than two weeks?), age at first onset (i.e. How old were you when you began feeling down/sad/irritable or lost interest in things?), and chronicity of depression (i.e. How many separate times in your life have you felt down/sad/irritable or lost interest in things?).

Cognitive reappraisal. Self-reported use of cognitive reappraisal was measured with the Emotion Regulation Questionnaire (ERQ; Gross & John, 2003). The ERQ is a 10-item self-report questionnaire that measures two distinct emotion regulation strategies: cognitive reappraisal and emotional suppression. Items measuring cognitive reappraisal assess an individual's ability to cognitively alter the potentially negative impact of a situation (e.g. I control my emotions by changing the way I think about the situation I'm in). Items measuring emotional suppression measure an individual's use of inhibiting emotional expression (e.g. I keep my emotions to myself). The ERQ demonstrates good validity and reliability (Gross & John, 2003) and was administered as a part of the online survey.

Cognitive flexibility. Cognitive flexibility was measured with the Cognitive Flexibility Scale (CFS; Martin & Rubin, 1995). The CFS is a 12-item self-report scale, in which individuals rate items on a likert scale ranging from 1 (strongly disagree) to 6 (strongly agree). Items assess an individual's awareness that multiple options exist in any given situation, willingness to adapt to situations, and self-efficacy in being flexible (e.g. I can communicate an idea in many different ways). High scores on the CFS indicate high

levels of cognitive flexibility. Previous work has demonstrated the CFS to be a psychometrically sound instrument (Martin & Rubin, 1995). The CFS was administered as a part of the online survey.

Emotional reactivity/physiological arousal. Emotional reactivity and physiological arousal were assessed with selected items from the Responses to Stress Questionnaire (RSQ; Connor-Smith et al., 2000). The RSQ is a 57-item self-report measure that assesses a broad range of cognitive and behavioral coping strategies employed by individuals when adapting to stress. The RSQ is comprised of 19 subscales and five factors. Each factor signifies a particular coping strategy. For the current study, only items that comprise the physiological arousal, emotional arousal, and involuntary action subscales (Connor-Smith, et al., 2000; Wadsworth, Rieckmann, Benson, & Compas, 2004), were used. High scores on these RSQ subscales indicate high levels of physiological arousal and emotional reactivity in response to stressful situations. This measure was administered to participants as a part of the online survey.

Executive function. In order to measure executive function, 24 items were selected from the Behavior Rating Inventory of Executive Function - Adult Version (BRIEF-A; Roth, Isquith, Fischer & Gioia, 2006). The BRIEF-A is a 75-item (9 subscale) self-report measure that assesses an individual's ability to perform a variety of executive functions and self-regulation tasks encountered in everyday life. In the current study, items from the Emotional Control, Shift and Working Memory subscales were used. The measure demonstrates valid psychometric properties (Roth et al., 2013) and was administered as a part of the online survey.

Experimental mood induction task & measures of mood.

Two film clips were used to induce sad moods during the experiment. A large research base supports the use of film clips to induce particular moods and is considered to be more ecologically valid than still pictures (Rottenberg, Ray, & Gross, 2007). Prior work in this area indicates that in order to obtain valid measures of emotion from viewers, clips should be under three minutes and measures of mood should follow immediately after the completion of the clip (Rottenberg, et al., 2007). Following Troy and colleagues (2010), clips from *Fatal Attraction* and *Kramer vs. Kramer* were shown to participants. Each clip was approximately two minutes long and has been shown to reliably induce comparable levels of sadness in viewers (Troy et al., 2010). All participants viewed both clips: the first without CR instructions and the second with CR instructions. Consistent with Troy et al. (2010), the two film clips yielded similar levels of sadness at the first viewing (*Kramer vs. Kramer* mean Sadness increase=2.1, SD=1.3; *Fatal Attraction* mean increase: 2.6, SD=1.7; $t(46)=-1.19, p=.24$). The order of presentation of the film clips was counterbalanced so that an equal number of participants in each experimental condition viewed the same order of clips. Participants were also asked to indicate whether they had previously seen the film from which the clip was taken. No participants reported previous viewings of the films.

To obtain a self-report of mood, a shortened version of the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988) was administered. In the current study, the PANAS consisted of 6 self-reported items. Individuals rated the extent to which they felt six different emotions (e.g. interested, irritated, sad, afraid, proud,

happy) on a scale of 1 (very slightly or not at all) to 9 (extremely). In the current study, ratings of sadness and happiness were used for subsequent analyses. The PANAS is a reliable measure of current state (at the present moment) affect (Watson et al., 1988) and has been validated for use with adolescents (Huebner & Dew, 1995). The PANAS was administered immediately before and after each film clip.¹ Use of the PANAS as opposed to single emotion ratings avoided certain demand characteristics as it asked about several emotions. Therefore, participants did not know that sadness and happiness were the emotions of interest for the current study. CR ability was based on the calculation of residual change scores of happiness and sadness ratings between the uninstructed mood induction and the instructed mood induction.

Individuals' self-reported mood ratings are not always highly correlated with other measures of mood (e.g. skin conductance) (Shiota and Levenson, 2009). Accordingly, participants completed a laboratory task to complement their self-reported mood ratings. Due to the overlapping network of brain regions associated with mood and cognition, deficits in emotion-related cognitive processes, specifically attentional biases, have been observed in individuals in a sad mood (Chepenik, Cornew, & Farah, 2007, Isaac, Vrijssen, Eling, van Oostrom, Speckens, & Becker, 2012; Schmid & Mast, 2010). In the current study, participants completed an emotion recognition task following Schmid & Mast (2010). In this task, 60 different stimuli (30 depicting happy facial expressions and 30 depicting sad facial expressions) from the Facial Expressions of

¹ Due to an administrator error, the PANAS was not administered immediately before the second film clip for 33 participants. Thus, final analyses using self-report data were limited to a sample of 15 participants.

Emotion: Stimuli and Tests (FEEST: Young et al., 2002) were displayed to participants on a screen. The intensity of the emotion displayed on the faces was manipulated by morphing the happy and sad faces into neutral faces. These morphed faces expressed 25, 50, or 75% of the full happiness or sadness expressions and were shown for 2 seconds each. Immediately after the face was shown, participants indicated whether the facial expression was negative or positive. Based on previous work, individuals with a negative bias, which would be consistent with sad mood, demonstrate significantly higher recognition rates for negative faces than positive ones (i.e. percent correct for negative faces divided by the overall percent correct). In the current study, the correlation between self-reported sad mood following the first film presentation and negative bias was $r = .18$ ($p = .21$).

Conditions

Prior to the lab session, participants were blocked by gender and then randomized into two conditions using a random number generator: Working Memory (experimental) condition or the control condition. When a zero was generated, participants were randomized to the control group and when a one was generated, participants were randomized to the working memory condition.

Working memory condition.

Participants in this condition completed a modified Reading Span (Rspan) task, a working memory task, which has demonstrated improvements in performance on subsequent affect related tasks (Bomyea & Amir, 2011). During the Rspan, participants viewed single letters followed by whole sentences presented in blocks of two to six. As

the sentences appeared on the screen, participants verified their semantic accuracy (e.g. “The boy there was when the sun arose,” correct answer: no). Upon completion of the block, participants viewed a screen with multiple letters and selected the letters they previously saw in between the sentences in the correct order. Participants completed three repetitions of each span size presented in a random order or completed trials until 12 minutes had passed, whichever occurred first. On average, participants engaged in the Rspan task for 10.14 minutes (SD=1.6 minutes) and achieved an average recall accuracy of 49 percent (SD=22%). Upon completion of the Rspan task, participants were given the following reappraisal instructions from Troy et al. (2010):

Please watch the following film clip carefully. This time, as you watch, try to think about the situation you see in a positive light. You can achieve this in several different ways. For example, try to imagine advice that you could give to the characters in the film clip to make them feel better. This could be advice that would help them think about the positive bearing this event could have on their lives. Or, think about the good things they might learn from this experience. Keep in mind that even though a situation may be painful in the moment, in the long run, it could make one’s life better, or have unexpected good outcomes. In other words, try to think about the situation in as positive terms as you possibly can. This can be difficult at times, so it is very important that you try your best. Do you have any questions? It is very important that you carefully watch the film clip, but think about it from a positive perspective.

Control condition.

Participants in the control condition viewed the same sentences that the experimental condition viewed during the Rspan task. However, unlike the experimental condition, participants did not see or need to remember letters while evaluating the sentences, thus removing the working memory aspect of the task. Following the control task, participants received the same CR instructions as the experimental condition.

Procedure

All methods and procedures were approved by the University of Denver Institutional Review Board prior to the start of the study (IRB protocol # 2013-2472).

Phase 1: Screening.

Undergraduate participants were directed to an online survey website where they completed consent procedures and a set of measures (BDI-II, History of Depression, ERQ, CFS, RSQ, and BRIEF-A). Those with elevations in depressive symptoms (BDI score >9) were invited to participate in the lab-based portion of the study through email correspondence from the primary investigator. The email invitation included a hyperlink to an online calendar where participants could select a participation timeslot. All participants were given information about psychological services at the university counseling center regardless of BDI-II scores.

Phase 2: Lab session.

Participants who volunteered to take part in the lab session came to a university lab setting where they completed a new set of consent procedures for the second portion of the study. Following consent, participants completed the BDI-II and the abbreviated PANAS. Next, participants watched one of the two film clips in a counterbalanced order with the following instructions: *Please watch the following film clip carefully.* Upon completion of the film clip, participants self-reported their mood using the PANAS (described above). As a performance (behavioral) measure of mood, participants also completed the facial recognition task (FEEST).

Participants then completed procedures specific to their assigned condition. Before the participants in each condition were given the reappraisal instructions, they completed the PANAS and watched the second film clip. At the end of the final film clip, participants again completed the PANAS and the FEEST. Finally, participants were debriefed and given referrals to university-based counseling services if they showed distress or requested services.

Chapter Three: Results

Preliminary Analyses

Examination of outliers/frequency distributions of variables.

All study variables within the larger survey sample and the lab sample were examined for outliers and abnormal frequency distributions. Means, standard deviations, skew and kurtosis values for all variables are presented in Appendix A: Table 1..

Within the survey sample, outliers were detected for BDI scores (n=17), cognitive reappraisal (n=10), involuntary arousal (n=7), and cognitive flexibility (n=2). Of note, some participants were outliers across multiple variables (n=4). Outliers were removed from further analyses. Within the lab sample, outliers were detected for BDI scores (N=1) and cognitive flexibility (N=1), however given the smaller sample size for the lab session, outliers were adjusted to fit within 2.5 standard deviations of the mean rather than removed. With outliers removed or adjusted, all variables were normally distributed.

Missing data.

Within scales, missing items were imputed using the mean substitution method. The participant's mean score for the overall measure from which the item was missing was computed and substituted for any missing data point within that measure.

Self-reported mood data at time 3 (immediately before the second film clip) were missing for participants (n=33) due to a procedural error. Given that these data were not missing at random and constituted a large portion of the sample, imputation was not completed. FEEST negative bias scores were missing for one participant due to task instruction confusion and subsequent inability to complete the task. No other data were missing.

Recoded variables.

Due to the skewed distributions for several categorical variables, such as those related to history of depression, variables were recoded into two groups to signify presence or absence of depressive history—duration: current episode of depression lasting for the last month vs. current episode of depression lasting longer; number of episodes: current episode of depression only vs. multiple previous episodes; age of depression onset: onset before age 15 vs. onset after age 15. Ethnicity was recoded into two groups: Caucasian and non-Caucasian.

Manipulation check: Sadness induction.

In order to confirm that the movie clips induced comparable levels of sadness in participants regardless of the order in which the film clips were viewed, a repeated measures ANOVA was computed to examine changes in mood ratings from baseline (pre-clip) to the mood ratings reported post-clip.² There was a significant effect of time [$F(1,46)=124.9, p<.001$] but no main effect of film clip order [$F(1,46)=.7, p=.40$] or interaction between time and film clip order [$F(1,46)=1.4, p=.24$] thus confirming that

² All Participants denied previously seeing either of the films from which the clips were taken.

each film clip induced comparable and significant levels of sadness. Participants were excluded from further analyses if they failed to show increases in sadness following the initial film clips (N=12). Thus, the final sample of participants included 48 older adolescents (89% female; 71% Caucasian; mean age=19.1, SD=1.2) with elevated depression scores on the BDI-II (mean score=18.6, SD=8.8).³

Randomization check.

In order to determine if randomization was successful, a series of chi-square tests were computed to ensure that each condition was comparable in terms of categorical variables including gender, ethnicity, duration of depression (both current and past episodes), and chronicity of depression (presence of multiple depressive periods). Additionally, a series of independent t-tests were computed to ensure each condition was comparable in terms of continuous variables including depression scores, cognitive flexibility, use of CR and emotional arousal (descriptive data by treatment condition are presented in Appendix A:Table 2). Three significant differences between groups emerged including BDI scores (as measured during the online survey [$t(46)=-2.9, p=.01$] and during the lab session [$t(46)=-2.4, p=.02$]), and self-reported cognitive reappraisal [$t(46)=2.0, p=.05$].

Since BDI scores during the screening and lab phase of the project were highly correlated ($r=.79, p<.001$), it was determined that only BDI scores reported at the lab session would be controlled in subsequent analyses. BDI scores at the lab session were

³ Additional analyses were run using the entire sample of 60 participants but did not change the pattern of results.

deemed to be more relevant to the primary aims of the study and thus were entered as a covariate in subsequent analyses. CR scores were also entered as a covariate in subsequent analyses.

Primary Analyses

In order to evaluate the effects of PFC activation on CR performance (**Aim 1**), a 2-way mixed ANCOVA (between-subjects variable=experimental condition; within-subjects variable= time) was computed for each of the dependent variables (the FEEST and the PANAS). Main effects of condition, time, and the interaction of condition and time were examined. Given the significant difference in depression scores and self-reported cognitive reappraisal between the two conditions, these variables were entered as covariates for each ANCOVA. Since there were only two levels of the within-subjects variable (time), the assumption of sphericity was met.

For negative bias scores on the FEEST, no significant effects were observed for time [$F(1,43)=.3, p=.61$], condition [$F(1,43)=.2, p=.66$], or the interaction of time and CR [$F(1,43)=.7, p=.39$]. The primary test of intervention effect, the time by condition interaction was not significant [$F(1,43)=2.0, p=.16$] but was plotted for clarification and appears in Appendix B: Figure 1. To construct the plot, mean negative bias scores were computed at time 1 and time 2 separately for the control and working memory group. Although the plot suggests some reduction in bias following CR instructions for both groups, this pattern was not significant.

A significant interaction between time and current depression level was found. [$F(1,43)=4.41, p=.04$] (see Appendix B: Figure 2). To construct the plot, the sample was

divided into two groups (low depression (below the sample mean BDI score) and high depression (at or above the sample mean BDI score)) and mean FEEST negative bias scores were computed for each group at time 1 and time 2 and plotted. In order to further examine the interaction, a series of paired sample and independent-sample t-tests were conducted. Results indicated that for individuals with high depression, negative bias scores significantly differed from time 1 to time 2 [$t(17)=2.8, p=.02$] but this was not the case for individuals with low depression [$t(28)=1.3, p=.21$]. Further, negative bias scores did not differ between high and low depression groups at time 1 [$t(45)=-.3, p=.79$] or time 2 [$t(45)=.6, p=.53$].

For PANAS ratings, separate analyses were computed for sadness and happiness. For these analyses, initial changes in sadness and happiness ratings during the first film clip viewing were entered as covariates to account for initial reactivity. Depression scores and self-reported cognitive reappraisal were also entered as covariates.

For sadness ratings on the PANAS, there was no main effect of time [$F(1, 10)=2.5, p=.15$], condition [$F(1,10)=.02, p=.91$] or significant interactions between time and condition [$F(1,10)=.6, p=.46$], time and CR [$F(1, 10)=.4, p=.54$], or covariate effect of initial reactivity (change in sadness scores during first film clip) [$F(1,10)=.04, p=.85$]. However, a significant interaction between time and depression [$F(1,11)=8.9, p=.01$] emerged. To construct the plot, the sample was divided into two groups (low depression (below the sample mean BDI score) and high depression (at or above the sample mean BDI score)) and mean PANAS sadness scores were computed for each group at time 3 (before the second film clip) and time 4 (following the second film clip) and plotted (see

Appendix B: Figure 3). In order to further examine the interaction, a series of paired sample and independent-sample t-tests were conducted. Results indicated that for individuals with low depression, sadness scores significantly differed from time 3 to time 4 [$t(6)=-6.3, p=.001$] but this was not the case for individuals with high depression [$t(7)=1.4, p=.21$]. Sadness scores did not differ between high and low depression groups at time 3 [$t(13)=-1.5, p=.16$] or time 4 [$t(46)=-.6, p=.54$].⁴

Finally, for happiness ratings on the PANAS, no significant effects of time [$F(1,10)=.03, p=.87$], condition [$F(1,10)=2.1, p=.18$], or interactions between time and condition [$F(1,10)=.02, p=.91$], time and depression [$F(1, 10)=.1, p=.77$], time and CR [$F(1, 10)=.03, p=.88$], or covariate effect of initial reactivity [$F(1,10)=.01, p=.93$] emerged.

In addition, a four time point repeated measures analysis was conducted to clarify the overall pattern of change in self-reported affect. For sadness ratings across all four time points, no significant effects of time [$F(1,9)=1.4, p=.33$], condition [$F(1,9)=1.0, p=.34$], or interaction between time and condition [$F(1,9)=.9, p=.49$] emerged. Mauchly's Test of Sphericity indicated that the assumption of sphericity had not been violated, $\chi^2(5)=4.7, p=.46$. Visual representation of self-reported sadness across all four study time points are presented in Appendix B: Figure 4. The lack of a main effect for time is likely due to the fact these analyses included a small number of participants ($n=15$) and were thus underpowered. Additionally, variability in ratings existed at each time point for the

⁴ Analyses were also conducted by plotting the residuals of sadness scores and the pattern of results remained the same. Thus for ease of interpretation, mean scores at time 3 and 4 were plotted.

control condition (Time 1 mean=2.4, SD=1.9, Time 2 mean=5.1, SD=2.0, Time 3 mean=2.4, SD=1.1, Time 4 mean=3.58, SD=1.4) and the working memory condition (Time 1 mean=3.4, SD=2.2, Time 2 mean=5.4, SD=2.1, Time 3 mean=2.1, SD=1.1, Time 4 mean=4.0, SD=1.8).

For happiness ratings across all four time points, no significant effects of time [$F(1,9)=.2, p=.93$], condition [$F(1,9)=1.5, p=.24$], or interaction between time and condition [$F(1,9)=.6, p=.61$] emerged. Mauchly's Test of Sphericity indicated that the assumption of sphericity had not been violated, $\chi^2(5)=2.4, p=.79$. Visual representation of self-reported happiness across all four study time points are presented in Appendix B: Figure 5.

In order to examine depression variables as potential moderators of condition (**Aim 2**), a series of hierarchical regressions were computed with Time 2 FEEST negative bias scores as the dependent variable⁵. Time 1 FEEST negative bias was entered in step one; condition was entered in step two as a dummy variable; one of the depression predictor variables in step three; and the interaction between condition and the predictor variables in step four. Interaction effects were plotted.

First, current depressive symptoms were examined as a potential moderator. In step one, Time 1 FEEST negative bias scores significantly predicted Time 2 FEEST negative bias scores ($\beta=.55, t(46)=4.4, p<.001$) and accounted for a significant amount of the variance ($R^2=.30, F(1, 45)=19.4, p<.001$). In step 2, condition was not a significant

⁵ Regression analyses using PANAS ratings as the dependent variable were not computed due to the small sample size.

predictor of negative bias scores ($\beta=.04$, $t(46)=-.3$, $p=.78$), nor did its inclusion in the model account for a significant amount of the variance ($R^2=.30$, $\Delta R^2=.00$ $F(1, 44)=9.5$, $\Delta F(1, 44)=.1$, $p=.78$). Next, current BDI scores were entered in step three, which accounted for a significant amount of the variance ($\Delta R^2 = .08$, $\Delta F(1,43)=5.7$, $p=.02$, $\beta=-.31$, $t(43)=-2.4$, $p=.02$). In the final step of the regression analysis, the interaction of centered BDI scores and condition accounted for a significant proportion of the variance in FEEST negative bias scores ($\Delta R^2=.11$, $\Delta F(1,42)=8.7$, $p=.01$, $\beta=.58$, $t(42)=2.9$, $p=.01$). Therefore, a test of simple effects (Aiken & West, 1991) was calculated. In order to construct the plot, a separate linear regression was computed for participants with low BDI scores (below the sample mean) and high BDI scores (at or above the sample mean) with time 2 FEEST negative bias scores entered as the dependent variable, time 1 negative bias scores entered in step one and condition entered in step two. Standardized residuals and fitted lines were plotted for each group. As shown in Appendix B: Figure 6, the slopes were significantly greater than zero for both the low depression group [$t(45)=2.7$, $p=.01$] and the high depression group [$t(45)=3.2$, $p=.002$]. In the control condition, participants with high depression had significantly lower negative bias scores than individuals with lower depression [$t(45)=-4.0$, $p<.001$]. Depression groups did not differ in the working memory condition [$t(45)=-.5$, $p=.64$].

Additional hierarchical regression analyses were conducted to examine history of depression variables as moderators. Again, Time 1 FEEST negative bias scores were entered in step one and condition was entered in step two. In step three, length of current depressive episode (previous month vs. longer than previous month) accounted for a

significant amount of the variance ($\Delta R^2 = .06$, $\Delta F(1,43)=4.4$, $p=.04$, $\beta=-.28$, $t(43)=-2.1$, $p=.04$). However, addition of the interaction term did not account for a significant proportion of the variance in FEEST negative bias scores ($\Delta R^2=.01$, $\Delta F(1,42)=.3$, $p=.57$, $\beta=-.14$, $t(42)=2.9$, $p=.57$).

Age of depression onset followed a similar pattern of results. In step three, age of onset (before age 15 vs. after age 15) did not account for a significant amount of the variance ($\Delta R^2 = .03$, $\Delta F(1,43)=1.8$, $p=.19$, $\beta=-.17$, $t(43)=-1.3$, $p=.19$) nor did the addition of the interaction term ($\Delta R^2=.01$, $\Delta F(1,42)=.4$, $p=.52$, $\beta=-.13$, $t(42)=-.6$, $p=.52$). Finally, chronicity of depression (presence of single episode vs. multiple episodes) also followed a similar pattern. In step three, chronicity accounted for a significant amount of the variance ($\Delta R^2 = .12$, $\Delta F(1,43)=8.6$, $p=.01$, $\beta=-.34$, $t(43)=-2.9$, $p=.01$). However, addition of the interaction term did not account for a significant proportion of the variance in FEEST negative bias scores ($\Delta R^2=.01$, $\Delta F(1,42)=.84$, $p=.37$, $\beta=.22$, $t(42)=.9$, $p=.37$).

In order to address Aim 3 the association between cognitive characteristics and self-reported use of CR was examined within the sample of survey participants. The association between cognitive variables and CR was examined with a series of Pearson's r correlations. Results indicated that self-reported cognitive reappraisal was significantly and positively associated with self-reported working memory ($r=.20$, $p<.01$), attentional shift ($r=.24$, $p<.001$), emotional control ($r=.21$, $p<.001$), and cognitive flexibility ($r=.39$, $p<.01$). Results of all correlations are shown in Appendix A: Table 3.

Given that several significant predictors emerged, a regression analysis was also computed to determine the unique contribution of each variable. Cognitive Reappraisal

was entered as the dependent variable and working memory, attentional shift, emotional control, and cognitive flexibility were entered as the predictors. Results of this simultaneous regression analysis demonstrated that cognitive flexibility ($\beta=.34, p<.001$) was the only variable that remained a significant predictor of CR. Other variables were not significant predictors: working memory ($\beta=.03, p=.61$), attentional shift ($\beta=.02, p=.76$), and emotional control ($\beta=.08, p=.25$), involuntary action ($\beta=.03, p=.67$). Variance inflation factor (VIF) scores were computed for each predictor variable but did not detect multicollinearity.

Because current depressive symptoms were correlated with cognitive flexibility, an additional regression was computed to determine if cognitive flexibility contributed to CR when depressive symptoms were controlled. Cognitive flexibility and current depression scores were entered simultaneously as predictors of self-reported CR. Results showed that cognitive flexibility remains a significant predictor of CR ($\beta=.35, p<.001$).

Additional independent sample t-tests explored differences in CR across history of depression and demographic variables. Results indicated that individuals who had experienced multiple episodes of depression prior to the current episode reported less CR [$t(286)=2.9, p=.004$]. However, there was not a significant difference in CR between individuals who reported longer duration of depression versus shorter duration or between individuals who reported an earlier versus later onset of depression. Further analyses examined self-reported CR use across demographic variables. Results of independent samples t-tests did not suggest significant differences in CR on the basis of

gender [$t(285)=-.4, p=.71$] or ethnicity [$t(286)=-1.1, p=.30$]. Results for all independent-sample t-tests are shown in Appendix A: Table 4.

Exploratory Analyses.

Because the primary analyses failed to yield significant effects consistent with the original hypotheses, additional analyses were conducted to attempt to understand the lack of predicted treatment (experimental) effects.

PFC “warm up” vs. cognitive depletion.

Additional analyses examined the hypothesis that participants in the experimental condition experienced cognitive depletion or fatigue (diminished cognitive capacity) rather than an enhancement through “warm up” and thus failed to benefit from the intervention on the ER task. To examine this hypothesis, Rpsan accuracy scores were graphed to examine the overall pattern of Rspan performance for the experimental condition over time. Accuracy scores were plotted along the y-axis and trial number was plotted on the x-axis (see Appendix B: Figure 7). Cognitive depletion could be indicated by a curvilinear slope—lower accuracy scores at the beginning of the task, followed by improvement in accuracy with practice, an overall peak in performance, and decline in accuracy towards the end of the task. Examination of the graph indicates that, on average, accuracy peaked (66% accuracy) at trial 16, which occurred at approximately 6.3 minutes ($SD=1.6$ minutes). By the end of the task at approximately 10 minutes ($SD=1.5$), participants, on average, obtained accuracy rates of 55 percent. However, a paired samples t-test did not indicate that accuracy significantly declined from peak performance to the end of the task [$t(21)=1.0, p=.32$]. Additionally, a decline in accuracy

across the course of the task did not predict worse performance on the subsequent CR task ($\beta=.09, p=.69$).

To further investigate the cognitive depletion hypothesis, overall FEEST accuracy scores were examined. If it were the case that participants in the working memory task condition were cognitively depleted, they could potentially show poorer overall accuracy scores (incorrectly identifying the affective valence of the facial expressions for both positive and negative faces) on the second FEEST administration, than their counterparts in the control condition. Yet, a 2x 2 repeated measures ANOVA (within subjects variable=time, between subjects variable=condition) failed to detect a main effect of time [$F(1,45)=1.3, p=.26$], or an interaction between time and condition [$F(1,46)=1.0, p=.34$].

Working memory task as a negative mood induction.

Given the challenging nature of the Rspan task (overall accuracy=49%), it was also possible that the task inadvertently induced a heightened negative mood, thus creating a more challenging emotional state to overcome when engaging in CR. Though the sample of participants that were administered mood measures following the Rspan or control task is small ($n=15$), results indicate participants in the experimental condition experienced significantly higher irritation following the Rspan task [$t(13)=-2.6, p=.02$]. Participants in the experimental condition had an average irritation rating of 4.8 ($SD=2.4$) while controls had an average rating of 2.1 ($SD=1.3$). Interestingly however, irritation scores were not predicted by overall Rspan accuracy ($\beta=-.03, p=.95$) nor did irritation scores significantly predict higher time 2 negative bias ($\beta=.15, p=.53$) or higher time 4

sadness ($\beta=.19, p=.51$). Additionally, current depressive symptoms did not predict higher irritation following the Rspan task ($\beta=-.01, p=.98$).

Chapter Four: Discussion

Previous research indicates that CR is an effective strategy for regulating negative affect (Gross & John, 2003), however this strategy is likely to be less effective for adolescents due to immaturity of the PFC, a brain region implicated in successful CR (Bunge & Wright, 2007; Koenigs & Grafman, 2009; Spear, 2000). Difficulties with CR utilization are likely to be amplified in adolescents with depression due to chronic underutilization of the networks underlying CR (Hilari et al., 2009). The primary aim of this study was to test whether CR could be improved by “warming up” the PFC through a working memory task. It was hypothesized that activating a critical brain region implicated in CR would enhance CR performance and reduce negative emotional responses to a sad mood induction and limit affectively associated cognitive biases relative to a non-active control condition. Results from the study did not support this hypothesis.

Contrary to prediction, results failed to show augmentation of CR following “warm up” of the PFC through a working memory task. Although not statistically significant, the interaction of time and condition suggested a slightly steeper decline in

negative bias scores for individuals in the control group but no differences between condition at time 2.

The absence of clear effects for CR on cognitive bias or self-reported mood is consistent with the theory that older adolescents may not use CR effectively. A number of investigators have highlighted developmental constraints on the acquisition of cognitive related coping strategies typically taught in CBT models (e.g. Kingery, Roblek, Suveg, Sherrill, & Bergman, 2006; Shirk, 2010). Additionally, results of imaging studies indicate a pattern of increasing CR use and ability with age (McRae et al., 2012).

Nevertheless, instructing older adolescents to reappraise with or without PFC “warm up” was not sufficient to change mood regulation in the current study. These findings must be viewed with caution, however, as prior research has often relied on self-reported mood as a primary index of CR effects and the loss of data on self-reported mood severely limited power. Further, the use of cognitive bias as an indirect measure of mood *regulation* has not been previously evaluated in this context.

Unexpectedly however, reductions in cognitive bias and sadness following CR instructions were particular to youth with higher levels of depression. Specifically, current level of depressive symptoms predicted smaller increases in sadness ratings following CR instructions and greater reduction in negative bias among *more* depressed youth—essentially better regulation success. Although it is tempting to conclude that more depressed youth benefit from CR prompting, possibly because less depressed youth were spontaneously engaging in CR to a greater degree, the pattern of results shows that more depressed youth also started at a somewhat higher level of sadness prior to the

second film clip. The smaller increase in sadness ratings among more depressed participants could also be indicative of the fact that depressed individuals can, at times, show less reactivity to negative stimuli since these negative stimuli tend to be congruent with their preexisting mood state (Bylsma, Morris, & Rottenberg, 2008), thereby leaving less negative affect to reappraise.

Additional moderator tests showed that condition and depression also interacted to predict negative bias scores, such that youth with higher depressive symptoms in the control condition showed lower cognitive bias following the second mood induction than those with lower depressive symptoms. Surprisingly, no differences between depression groups emerged in the working memory condition. This pattern of results is inconsistent with previous work that indicates individuals with depression have particular difficulties utilizing CR effectively (Joormann & Gotlib, 2009). In fact, data from the survey sample indicated that self-reported CR use was negatively associated with current level of depressive symptoms and a previous history of depressive episodes. It may have been the case that youth with lower depression scores were using CR to a greater degree during the initial uninstructed film clip than youth with higher depression. It is also possible that the working memory task washed out similar effects in the experimental condition. Importantly, the lack of a control group that did not receive any CR instruction following the experimental manipulation means that change in bias, even in this subgroup, might be due to other factors such as practice effects. This seems unlikely though given that the low depression symptom group did not show the same pattern. This finding also raises the question of whether there are any active components of the control condition. While

the task was designed to be relatively inactive, semantic processing is involved in cognitive reappraisal (Buhle et al., 2014). Thus, the control condition may have activated another critical underlying component of CR.

These results demonstrating relatively limited improvements in affect regulation following basic CR instructions indicates the need for augmenting this skill. However, the working memory task did not accomplish this goal. In the absence of imaging data we cannot be certain that the experimental condition had its intended effect on the PFC (the dlPFC in particular), though prior studies (e.g. Barbey et al., 2013) certainly suggest that the dlPFC is activated during verbal working memory tasks such as the Rspan used in the current study.

The possibility that the memory task had unintended consequences was also examined. Although the Rspan task was challenging, results did not support cognitive depletion or fatigue that could account for its failed effect. First, while overall Rspan accuracy declined over the course of the task, there was not a significant drop from peak performance to the end of the task. Secondly, an overall decline in Rspan accuracy did not predict subsequent performance on the CR task (i.e. changes in negative bias). Further, the working memory group did not show significant declines in overall accuracy from the first to second cognitive bias administration, when identifying the emotional valance of facial expressions, another task that requires cognitive effort.

There was some evidence to suggest that the memory task was frustrating as youth in this condition showed elevated irritation scores following the experimental manipulation. However, actual Rspan performance was not related to irritation scores

following the task nor did irritation predict subsequent cognitive performance. Additionally, current depressive symptoms were not associated with higher irritation following the Rspan task as might be expected given the fact that individuals with depressive symptoms tend to be more negatively biased in their self-evaluations and more highly attuned to negative stimuli in general (Rottenberg et al., 2005).

There are also multiple methodological considerations that could explain the null findings. For instance, there may have been more proximal outcome measures to consider in addition to mood ratings including physiological data (e.g. Joormann et al., 2015). Participants may also have benefitted from CR instructions that encourage distancing oneself from the current situation rather than reinterpreting the situation, as this can be a more effective reappraisal strategy (Denny & Ochsner, 2014).

Further, several sessions of training may be necessary to strengthen the essential neural pathways underlying successful emotion regulation. This may be especially the case for individuals with depressive symptoms whose regulatory functions tend to be especially poor (Hilari et al., 2009). Lastly, participants were only given a single opportunity to reappraise. A different research paradigm, whereby participants are exposed to several negative stimuli (e.g. using still images from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1999), allows multiple opportunities to practice CR in a relatively short amount of time across the course of the study session. However, still images have less ecological validity than live film clips that portray emotional experiences.

It is also plausible that working memory was the wrong mechanism to target during the “warm up” exercise. While previous research identifies working memory as an essential underlying mechanism of CR (Schmeichel et al., 2010), additional cognitive processes have been implicated as well (Barbey et al., 2013). Indeed, results from the larger survey sample showed that CR was positively associated with executive function variables (e.g. working memory, shifting, emotional control) and cognitive flexibility, at least as assessed by self-report. These findings are consistent with the literature that indicates CR is supported by multiple cognitive processes (Buhle et al., 2014; Ochsner & Gross, 2008). It is crucial to remember, however, that children and adolescents tend to lack highly advanced executive functions like cognitive flexibility until much later in development (Bunge & Wright, 2007). Thus, these findings may highlight the potential challenge of teaching cognitive coping strategies, like CR, in therapy for younger individuals.

Overall, results suggested that current level of depressive symptoms had some impact on changes in mood regulation. Current level of depression predicted cognitive bias after CR instructions, and this effect was qualified by an interaction with condition. Contrary to hypotheses, additional depression variables including age of depression onset and duration of depressive episode did not moderate treatment response. This is inconsistent with Siegle and colleagues’ theory (2007) that depression can result in chronic under-utilization of PFC networks in the face of negative stimuli thus causing these regions to atrophy. However, it is also important to note that history of depression was measured using self-report and thus may not be an entirely accurate assessment.

The final aim of the study was to examine cognitive correlates of self-reported CR use. As expected, CR was associated with a variety of self-reported cognitive variables including working memory, attention shifting, emotional control, and cognitive flexibility. However, when these processes were considered together, only cognitive flexibility accounted for unique variance in CR. Cognitive flexibility continued to predict CR even when controlling for depression symptoms. Prior work supports the link between CR and cognitive flexibility. In a study by Troy and colleagues (2013), individuals that participated in mindfulness training increased their cognitive flexibility which was then associated with improved overall CR ability. It is possible then that CR might be enhanced by targeting cognitive flexibility either as a “warm-up” or as a component skill, particularly when treating depression. For example, practice with generating multiple options or solutions to problems, engaging in re-classification of stimuli, and examining situations from different perspectives could help not only boost CR ability but also problem solving, another strategy with which individuals with depression tend to struggle (Aldao, et al, 2010).

Limitations and Future Directions

The current study has a number of methodological limitations. First and foremost, the lack of self-reported mood data prior to the second film clip for many participants precludes a full understanding of individuals’ affective experience during their study participation. Analyses included a maximum of 48 participants and dropped as low as 15 due to missing data. This sample size is less than optimal for detecting even moderate effects.

Additionally, study procedures did not include comprehensive diagnostic interviews of depression or other disorders. Potential participants were instructed to refrain from participation if they had a previous diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) for which they did not take medications. However, the lack of comprehensive diagnostic interviewing prevents consideration of other comorbid conditions (e.g. anxiety) that could disrupt the process of CR.

The current study also did not utilize brain imaging methodology. While previous research certainly supports the notion that working memory tasks (like the Rspan task used in the current study) involve the dlPFC, the lack of imaging data does not allow a definitive conclusion that the dlPFC was, in fact, activated and thus “warmed up.”

Finally, the sample of participants was fairly homogenous in terms of ethnicity and gender (the current sample was predominantly Caucasian and female) reducing the generalizability of these findings. Underlying processes of cognitive reappraisal may be different in a sample of males or a racially and ethnically diverse sample of individuals.

In summary, current results did not support the use of PFC “warm up” using a working memory task to improve CR performance, at least as measured in this study. The absence of broad effects for CR instruction is certainly consistent with the notion that older adolescents may be less effective at cognitive reappraisal, but adding a PFC “warm up” did not enhance their performance. As noted above, several possible explanations were explored. Despite the WM task being challenging, results did not support the notion of cognitive depletion or fatigue. Further, while the task was likely frustrating, thus contributing to the observed elevated irritation in these participants, irritation did not

predict subsequent CR performance. Multiple methodological factors could have contributed to the lack of effects as well including a relatively low dose of PFC “warm up.” It is also possible that working memory may not be the optimal target for intervention especially when only one practice session is delivered. Results support a significant association between cognitive flexibility and CR, even when depression is controlled, and this might represent a better target for intervention.

The literature will benefit from additional studies that further explore the underlying processes of CR, particularly in individuals with depression, so as to create better targets for future neurobehavioral therapies. Relatedly, future work should test these additional targets (e.g. cognitive flexibility) prior to engaging in a CR task. Lastly, future work should aim to recruit a community-based sample so as to better understand CR processes in a more diverse population.

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Appendix A

Table 1.
Means, standard deviations, skew and kurtosis values for online survey variables

Variable	N	Minimum	Maximum	Mean	Std. Dev.	Skew	Kurtosis
Depression	288	0.00	28.00	9.11	6.42	.73	-.08
Cog Reapp	288	2.83	7.00	5.10	0.90	-.22	-.36
Emotion Sup	288	1.00	6.50	3.7	1.23	.06	-.72
Emo Arousal	288	3.00	12.00	8.72	2.25	-.41	-.69
Physio Arousal	288	3.00	12.00	6.82	2.14	.27	-.61
Invol Arousal	288	3.00	12.00	5.33	2.06	.80	-.09
Working Memory	288	0.00	16.00	5.07	3.38	-.65	.07
Shift	288	0.00	12.00	3.57	2.39	-.47	.05
Emo Control	288	0.00	20.00	6.00	4.26	-.58	-.13
Cognitive Flexibility	288	36	66	52.04	5.83	-.34	-.05

Depression=Beck Depression Inventory; Cog Reapp=Emotion Regulation Questionnaire: Cognitive Reappraisal; Emotion Sup=Emotion Regulation Questionnaire: Suppression; Emo Arousal=Response to Stress Questionnaire: Emotional Arousal; Physio Arousal=Response to Stress Questionnaire: Physiological Arousal; Invol Arousal=Response to Stress Questionnaire: Involuntary Arousal; Working Memory=BREIF Working Memory; Shift=BRIEF Attention Shift; Emo Control=BRIEF Emotion Control; Cognitive Flexibility=Cognitive Flexibility Scale

Table 2.

Participant Characteristics by Treatment condition

Variable	Experimental (N=22) Mean (SD)	Control (N=26) Mean (SD)	Statistic (df)	<i>P</i>
Age	19.4 (1.3)	18.8 (1.0)	t(46)=-1.56	.13
Depression	16.5 (9.8)	10.7 (6.4)	t(46)=-2.45	.02
Cognitive Reappraisal	4.2 (1.1)	4.8 (1.0)	t(46)=2.03	.05
Emotion Suppression	4.1 (1.3)	3.7 (1.6)	t(46)=-1.05	.30
Emo Arousal	9.9 (2.4)	9.8 (1.7)	t(46)=-.11	.92
Physio Arousal	8.3 (1.9)	7.2 (2.3)	t(46)=-1.76	.09
Involuntary Arousal	7.2 (2.9)	6.3 (2.5)	t(46)=-1.19	.24
Working Memory	7.6 (3.4)	5.6 (2.5)	t(19)=-1.50	.15
Attention Shift	5.4 (2.9)	5.3 (1.9)	t(19)=-.08	.94
Emotion Control	10.3 (4.4)	8.9 (5.2)	t(19)=-.66	.52
Cognitive Flexibility	47.5 (6.2)	50.7 (5.8)	t(46)=1.87	.07
Variable	Number (% of group)	Number (% of group)	Statistic (df)	<i>P</i>
Female	18 (82)	23 (88)	$\chi^2(1)=.50$.48
Caucasian	14 (63)	20 (77)	$\chi^2(1)=2.0$.16
Dep History 1	21 (95)	23 (88)	$\chi^2(1)=.76$.38
Dep History 2	16 (73)	18 (69)	$\chi^2(1)=.07$.79
Dep History 3	2 (1)	0 (0)	$\chi^2(1)=2.45$.12
Dep History 4	16 (73)	18 (69)	$\chi^2(1)=.07$.79

Dep History 1=Depressive Episode Longer Than Past Two Weeks, Dep Hist 2= Presence of Previous Depressive Episodes, Dep History 3= Age of Depression Onset Before Age 10, Dep History 4= Presence of Multiple Previous Depressive Episodes

Table 3.
Survey Data: Pearson's r correlations

Variable	1	2	3	4	5	6	7	8	9	10
1.CR	1									
2.BDI	-.23**	1								
3.EA	-.01	.39**	1							
4.PA	-.10	.38**	.55**	1						
5.IA	-.18**	.37**	.27**	.41**	1					
6.WM	.20**	-.33**	-.19**	-.27**	-.38**	1				
7.SFT	.24**	-.45**	-.37**	-.35**	-.46**	.54**	1			
8.EC	.21**	-.41**	-.36**	-.37**	-.49**	.32**	.57**	1		
9.CF	.39**	-.39**	-.13*	-.25**	-.38**	.39**	.46**	.31**	1	
10.Sup	-.07	.23**	.08	.10^	.07	-.12*	-.13*	.00	-.18**	1

* $p < .05$, ** $p < .01$, ^p-value trending

CR=Emotion Regulation Questionnaire: Cognitive Reappraisal; BDI=Beck Depression Inventory; EA=Response to Stress Questionnaire: Emotional Arousal; PA=Response to Stress Questionnaire: Physiological Arousal; IA=Response to Stress Questionnaire: Involuntary Action; WM=BREIF Working Memory; SFT=BRIEF Shift; EC=BRIEF Emotion Control; CF=Cognitive Flexibility Scale; Sup=Emotion Regulation Questionnaire: Suppression.

Table 4.
Differences in Cognitive Reappraisal in Categorical Variables

History of Depression Variables	Mean (SD)	Statistic	df	<i>p</i>
Previous Depressive Episodes	5.02 (.91)	t=2.9	286	.004
No Previous Episodes	5.38 (.77)			
Short Duration of Current Episode	5.23 (.86)	t=1.53	286	.13
Long Duration	5.05 (.91)			
Age of Onset Before 10 Years Old	4.83 (.82)	t=.73	286	.47
Onset after 10	5.10 (.90)			
Demographic Variables	Mean (SD)	Statistic	df	<i>p</i>
Caucasian	5.05 (.90)	t=-1.05	286	.30
Non-Caucasian	5.16 (.91)			
Female	5.11 (.91)	t=.38	285	.71
Male	5.07 (.88)			
18 years old	5.11 (.85)	F=.45	4	.77
19 years old	4.99 (.96)			
20 years old	5.09 (.89)			
21 years old	5.26 (.72)			
22 years old	5.05 (1.1)			

Appendix B

Figure 1.
Interaction of Time and Condition on FEEST Bias Scores

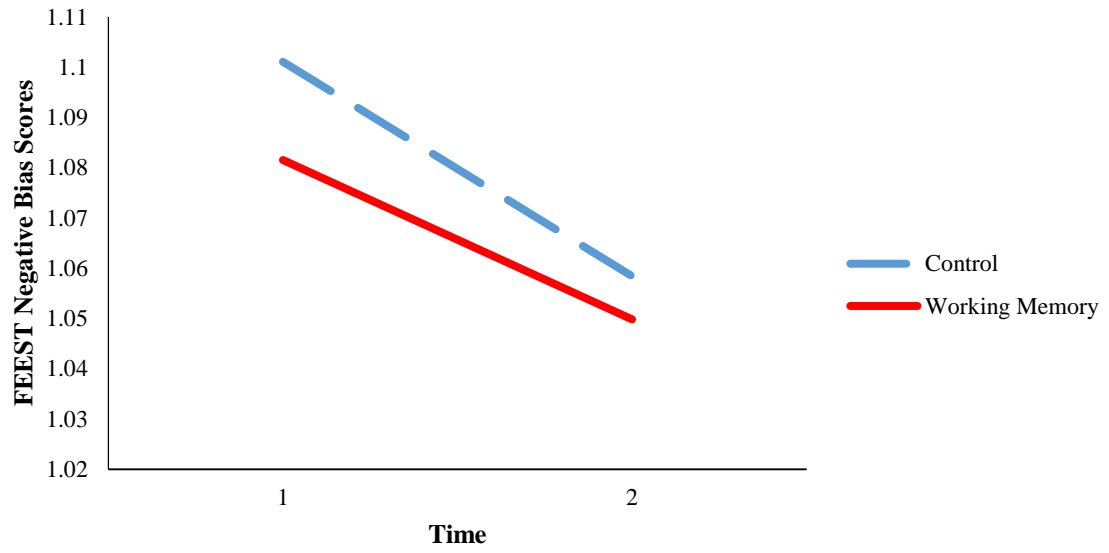


Figure 2.
Interaction of Time and Depression on FEEST Bias Scores

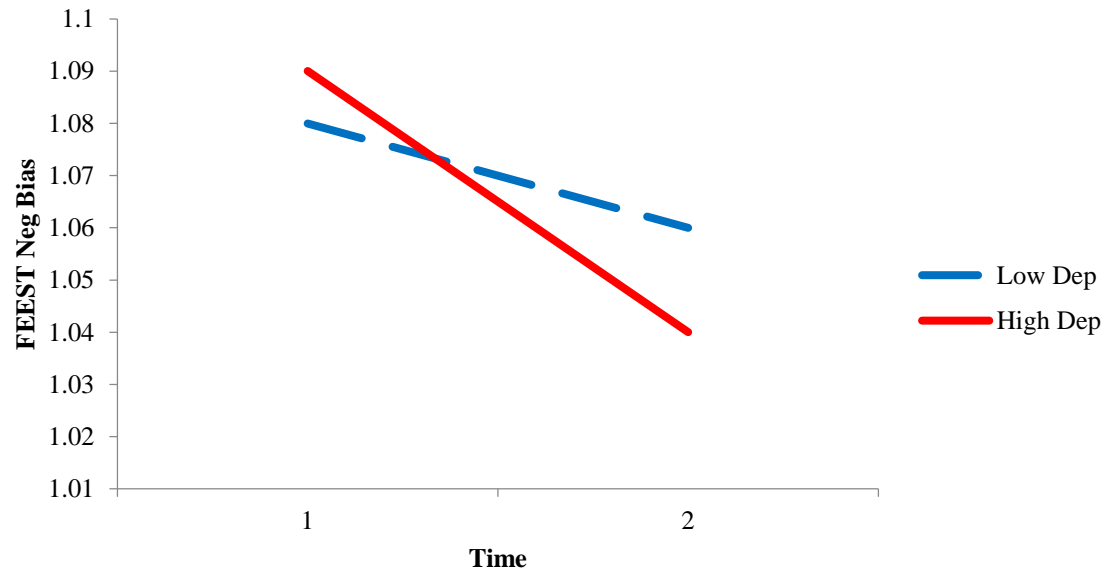


Figure 3.
Interaction of Time and Depression on PANAS Sadness Scores

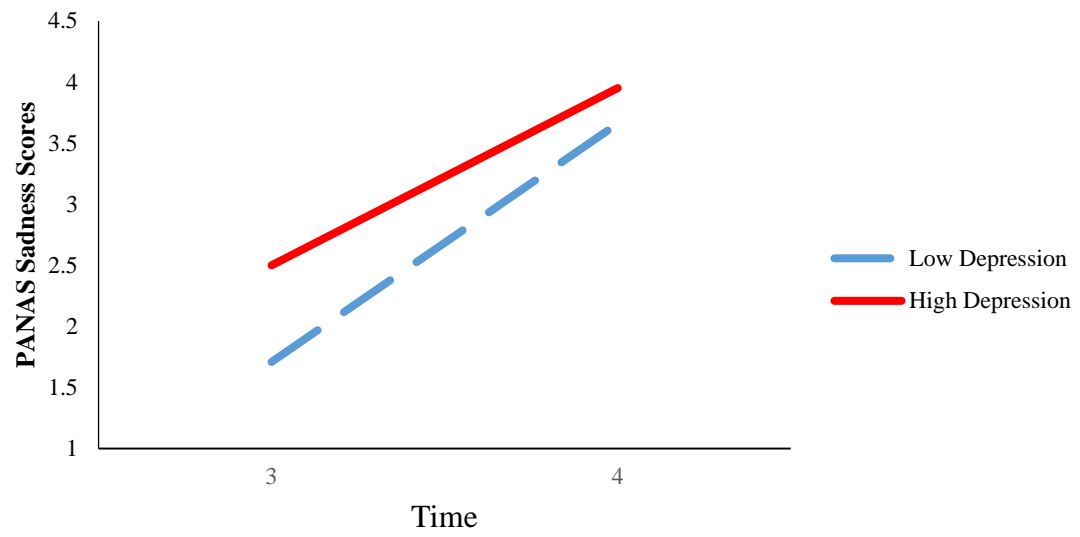
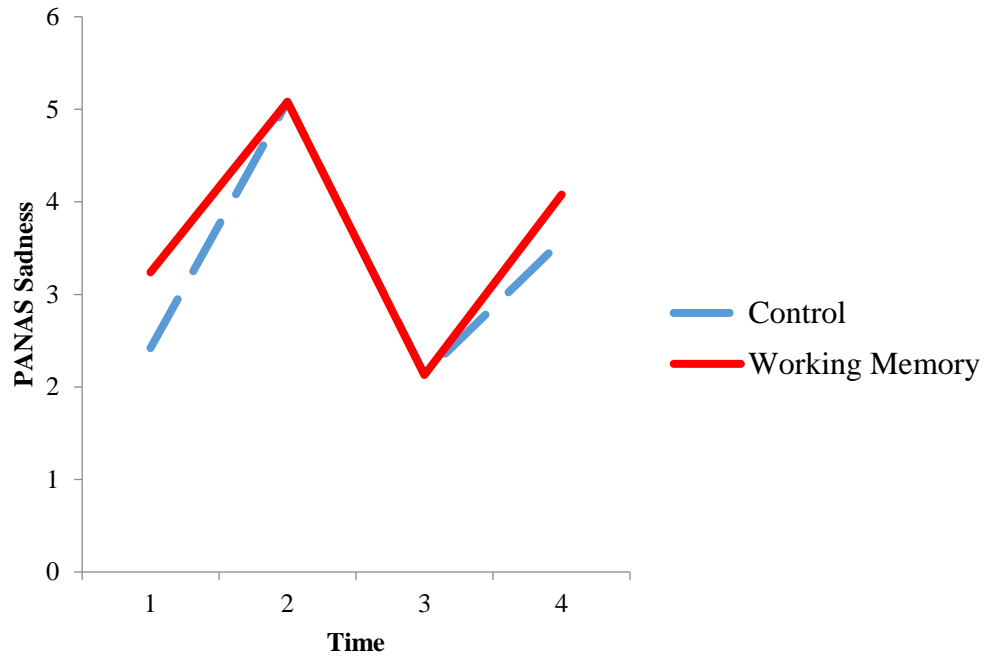
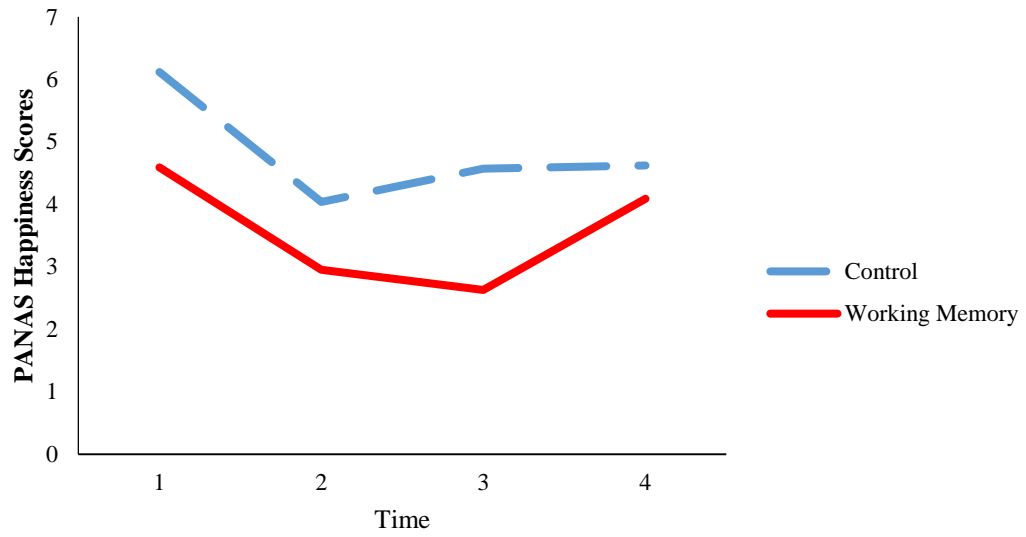


Figure 4.
PANAS Sadness Scores Across Study Time Points



Time 1=Before Film Clip 1, Time 2=After Film Clip 1, Time3=Before Film Clip 2, Time 4=After Film Clip 2

Figure 5.
PANAS Happiness Scores Across Study Time Points



Time 1=Before Film Clip 1, Time 2=After Film Clip 1, Time3=Before Film Clip 2, Time 4=After Film Clip 2

Figure 6.
Interaction of Depression and Condition on FEEST Bias Scores

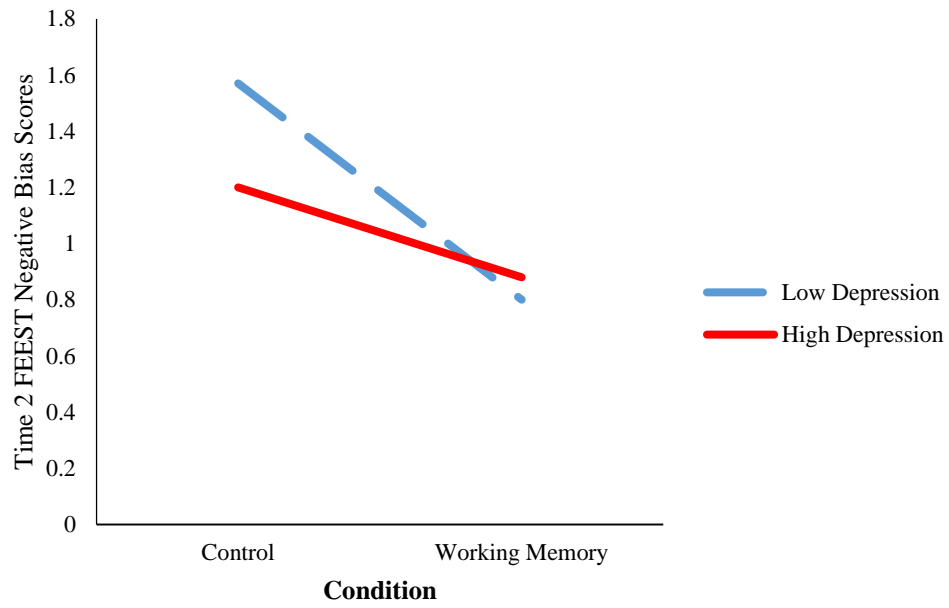


Figure 7.
Mean RSpan Accuracy Scores Across Task Trials

