Behavioral and Neural Bases of Emotion Regulation in Childhood and Adolescence

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ABSTRACT

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While much research has suggested that emotional experiences change dramatically over the lifespan, less is known about what underlies these changes at a mechanistic level. Specifically, it is unclear whether age predicts differences in bottom-up reactivity to emotional events, or in the ability to exert top-down control over emotional responses. The present studies sought to address these gaps in the literature. Studies 1 and 2 compared the behavioral and neural correlates, respectively, of emotional reactivity to and regulation of emotional responses to social and non-social aversive stimuli in individuals aged 10-22. Study 1 additionally examined the interaction between individual differences in sensitivity to social rejection and age and how this impacts regulation of emotional responses to social stimuli. Across these studies, age predicted differences in neural and behavioral correlates of regulation but not reactivity. Study 3 broadened the sample age range to include children as young as 6 years and obtained results that were generally consistent with those of Studies 1-2. Study 4 examined the generalizability of the findings from Studies 1-3 by examining reactivity and regulation of appetitive, rather than aversive, responses in participants ranging from 6-22 years. Behavioral indices of reactivity and regulation correlated with age in Study 4, but neural effects of age were only found for regulation. Data from Study 4 additionally suggested links between the neural correlates of regulation of craving and body mass index.

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Chapter 1: Introduction

We cannot always avoid life's affective pushes and pulls, but we humans are remarkably skilled at managing our responses to them. Effective emotion regulation is critical for wellbeing – it allows us to keep calm under pressure, resist temptations that can hurt our mental and physical health, and emerge resilient from times of struggle. On the flip side, difficulties with emotion regulation are central to a number of mental and physical health problems including mood and anxiety disorders, disordered eating, and addictive behaviors (Gross & Munoz, 1995; Herman, Polivy, Lank, & Heatherton, 1987; Houben & Wiers, 2009; Safer, Telch, & Agras, 2001). Despite the fact that many of these problems have their origins in adolescence (Costello, Foley, & Angold, 2006; Paus, Keshavan, & Giedd, 2008), research has only recently begun to unpack how emotion regulation develops normatively in childhood and adolescence. Such research seeks to understand not only how regulatory skills develop, but also when regulatory failures are most likely to occur, and why some individuals are more prone to regulatory failures than others. This chapter will synthesize what is presently known about the development of emotion regulation and provide a context for the present four studies. In the first part of this chapter, a working model of the psychological and neural bases of cognitive emotion regulation in healthy adults will be presented. Critical to this model is the notion that emotion regulation involves a dynamic interplay of top-down, regulatory processes and bottom-up, emotional appraisal processes. The second section will describe how top-down, executive processes that support cognitive emotion regulation develop during childhood and adolescence while the third section will outline how emotional processes develop during this same period. The final section will introduce the present studies.

A working model of emotion regulation in healthy adults

Emotions can arise in response to external stimuli, such as an interaction or an event, or in response to internal stimuli, such as a memory, a thought or a feeling. Emotions unfold in a series of steps beginning with perceiving a stimulus, continuing with attending to some or all aspects of a stimulus, followed by appraising a stimulus's emotional significance, and ending with a response that involves some combination of affective experience, autonomic arousal and expressive behavior (Barrett, Mesquita, Ochsner, & Gross, 2007; Scherer, Schorr, & Johnstone, 2001). As such, regulation may occur by modifying an emotion at any point in the generation process (Gross, 1998; Ochsner & Gross, 2005, 2008; Ochsner, Silvers, & Buhle, 2012). Antecedent-focused regulatory strategies alter the inputs that give rise to an emotion while response-focused strategies concern the outward manifestation of an emotion (Gross, 1998). Cognitive reappraisal, an antecedent-focused regulatory strategy that involves changing one's interpretation or appraisal of an emotional stimulus, is among the most commonly studied emotion regulation strategies. This is partially due to the fact that reappraisal effectively modulates affective responses without effecting physiological or cognitive costs the way that some response-focused strategies do (Gross, 1998), and also to the fact that reappraisal's core elements are central to many forms of therapy including cognitive behavioral therapy (Beck, 2005) and dialectical behavioral therapy (Lynch, Trost, Salsman, & Linehan, 2007).

Reappraisal may be used to regulate emotional responses through the use of a variety of "tactics", including reinterpretation and distancing (McRae, Ciesielski, & Gross, 2011; Ochsner et al., 2012; Silvers, Buhle, & Ochsner, 2012). Reinterpretation involves changing one's interpretation of a stimulus or situation by imagining that it is not what it

seems or that it could have an alternative outcome. For example, one might reinterpret a picture of a bloodied person lying on a stretcher by thinking that the blood is actually just ketchup and the person is acting, or that the person actually is injured but will soon be treated at a hospital where they will have a quick recovery. Distancing involves changing the relevance of a stimulus by envisioning it being more or less physically or psychologically distant. In the case of seeing the bloodied person on a stretcher, one might increase the perceived physical distance of the injured person by imagining them on the other side of the world. Alternatively, one could increase the psychological distance between themselves and the injured person by adopting the clinical and detached mindset of a surgeon or a reporter who is focusing purely on the facts of the scene. Since 2009, the proportion of fMRI studies using distancing to study emotion regulation has more than doubled, suggesting an increased interest in this tactic (Buhle et al., Submitted).

Central to most psychological theories of reappraisal is the notion that it relies upon recruitment of cognitive control mechanisms that can not only be used to regulate emotion, but also attention, memory and cognition (Ochsner & Gross, 2005, 2008; Ochsner et al., 2012; Silvers, Buhle, et al., 2012). Support for this idea comes from the fact that brain regions known to support cognitive control, such as the dorsomedial, dorsolateral and ventrolateral prefrontal cortex (dmPFC, dlPFC, vlPFC) and posterior parietal cortex (Duncan & Owen, 2000; Miller, 2000; Miller & Cohen, 2001), are strongly engaged by healthy adults during reappraisal (Diekhof, Geier, Falkai, & Gruber, 2011; Kalisch, 2009; Ochsner et al., 2012). Based on existing models of cognitive control, we may hypothesize that these different prefrontal and parietal control systems support different components of reappraisal (Ochsner & Gross, 2005a, 2008; Ochsner et al., 2012. For example, dlPFC and

parietal cortex, regions thought to play complementary roles in selective attention and working memory (Champod & Petrides, 2010; Corbetta & Shulman, 2002; Ptak, 2012), might assist in maintaining and manipulating reappraisals, while vlPFC, known to support language and response selection (Badre & Wagner, 2007; Hinke et al., 1993; Huang, Carr, & Cao, 2002; Thompson-Schill, Bedny, & Goldberg, 2005), may assist in semantic processing as well as in selecting appropriate reappraisals. Given the role that dmPFC plays in mentalizing and self-monitoring (Amodio & Frith, 2006; Olsson & Ochsner, 2008), it may be recruited during reappraisal to monitor how effectively one is reappraising and to interpret one's changing emotional state.

Although it is useful to consider how reappraisal is implemented, it is equally important to consider the effects of its implementation. At the neural level, this may manifest in altered activity in brain regions that generate emotional responses. Meta-analytic data has revealed that across dozens of neuroimaging studies, the amygdala a bilateral subcortical structure involved in the perceiving, encoding and responding to arousing and salient stimuli, (Cunningham & Brosch, 2012; Phelps & LeDoux, 2005; Wilson-Mendenhall, Barrett, & Barsalou, in press), is more commonly modulated by reappraisal than any other brain region (Buhle et al., Submitted; Diekhof et al., 2011). Yet, meta-analytic data suggests that emotional experiences are often supported by co-activation of a host of brain regions, not just by the amygdala in isolation (Kober et al., 2008; Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012; Vytal & Hamann, 2010). This may include including other subcortical structures such as the ventral striatum which is strongly linked to reward processing (Schultz, Apicella, Scarnati, & Ljungberg, 1992) and coordinating behavioral responses to emotional stimuli more broadly (Reynolds & Berridge, 2001, 2002,

2003). Preliminary evidence suggests that the ventral striatum may be modulated more frequently during reappraisal of positive than negative stimuli (Ochsner et al., 2012), but such assertions remain tentative at present given the relatively small number of studies that have examined reappraisal of appetitive stimuli. A third brain structure that may be modulated by reappraisal is ventromedial PFC (vmPFC), which is believed to integrate memorial, semantic and affective information stored elsewhere in the brain and to evaluate these inputs in the current context of one's goals and situation (Cunningham, Johnsen, & Waggoner, 2011; Davachi, 2006; Fellows, 2011; Murray, O'Doherty, & Schoenbaum, 2007; Ochsner, Bunge, Gross, & Gabrieli, 2002; Ongur, Ferry, & Price, 2003; Price, 1999; Rudebeck & Murray, 2011; Schoenbaum, Takahashi, Liu, & McDannald, 2011). In this role, vmPFC activity may reflect differences in affective value attributed to a given stimulus, with greater activation corresponding to increases in value (Oya et al., 2005; Roy, Shohamy, & Wager, 2012; Schoenbaum, Saddoris, & Stalnaker, 2007; Schoenbaum et al., 2011). Consistent with this notion, a handful of fMRI studies have observed reappraisal-related attenuation of vmPFC responses to positive or appetitive stimuli (Kanske, Heissler, Schonfelder, Bongers, & Wessa, 2011; Kim & Hamann, 2007; Kober et al., 2010; Schardt et al., 2010; Winecoff, Labar, Madden, Cabeza, & Huettel, 2010). Intriguingly, it has also been suggested that vmPFC might support reappraisal, rather than be modulated by it (Diekhof et al., 2011; Schiller & Delgado, 2010). This notion is appealing given that vmPFC plays a critical role in other regulatory processes such as fear extinction (LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998; Phelps, Delgado, Nearing, & LeDoux, 2004; Schiller & Delgado, 2010; Schiller, Levy, Niv, LeDoux, & Phelps, 2008), yet vmPFC recruitment is rarely seen in main effect contrasts in reappraisal studies (Buhle et al., Submitted). That said, vmPFC may

be relevant for reappraisal in a more indirect way, given that individual differences such as psychiatric status predict differential connectivity between vmPFC and the amygdala during reappraisal (Johnstone, van Reekum, Urry, Kalin, & Davidson, 2007).

Age-related changes in cognitive control in childhood and adolescence

Cognitive control processes thought to support reappraisal in adults undergo significant changes during childhood and adolescence. Performance on cognitive control tasks assessing one's ability to withhold inappropriate responses and to hold and manipulate information in working memory improves dramatically during this period (De Luca et al., 2003; Luna, 2009; Zelazo & Carlson, 2012). These improvements in task performance parallel structural maturation of prefrontal regions that support cognitive control processes. Prefrontal development is marked by two age-related changes: an inverted U-shaped trajectory for gray matter and linear increases in white matter (Amso & Casey, 2006; Giedd & Rapoport, 2010; Gogtay et al., 2004; P. Shaw et al., 2008). These structural changes are thought to indicate, respectively, pruning and refinement of synapses and enhancement of neuronal conduction.

With the advent of functional neuroimaging, developmental neuroscientists now not only have the ability to examine how brain structure develops but also brain function. Functional MRI studies of cognitive control have characterized both age-related increases and decreases, as markers of functional neural maturation (Bunge & Wright, 2007; Pfeifer & Allen, 2012). Age-related increases in dorsal and lateral prefrontal recruitment are thought to reflect enhanced recruitment of processes critical to task performance in adults (Rubia, 2012). This pattern of results has been observed across a host of studies examining inhibition (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Christakou et al., 2009;

Rubia, Smith, Taylor, & Brammer, 2007; Rubia et al., 2006) and working memory (Ciesielski, Lesnik, Savoy, Grant, & Ahlfors, 2006; Crone, Wendelken, Donohue, van Leijenhorst, & Bunge, 2006; Klingberg, Forssberg, & Westerberg, 2002; Olesen, Macoveanu, Tegner, & Klingberg, 2007) in development. Age-related decreases in prefrontal recruitment have been most commonly observed in the context of inhibition tasks (Casey et al., 1997; Durston et al., 2002; Somerville, Hare, & Casey, 2011), and such results are generally interpreted as evidence for age-related neural efficiency or selectivity (i.e., activation becomes more specific to a certain area and thus decreases in other areas).

That some studies have found age-related increases and others decreases may be explained by one or more of the following four possibilities. First, given that a wide variety of tasks are used to probe cognitive control in development, it may be that different tasks yield different patterns of results given that different cognitive control functions mature at different rates. Second, differences in results may be attributed to variable age ranges (i.e., comparing children to adults is likely to yield different results than a comparison between children and adolescents) and whether analyses used categorical or continuous measures of age. Third, researchers commonly adopt different tactics when attempting to tease apart age and performance effects. For example, they may: 1) use a task that yields age-related differences in performance and control for these differences by matching participants from different age groups according to performance, examining correct trials only, or controlling for performance statistically; 2) select tasks that afford a high level of accuracy across different ages; or 3) titrate task difficulty for each participant. These different approaches may significantly impact the age-related results. A final, and very likely, possibility is that characterizing maturation as uniform increases or decreases in prefrontal recruitment is

an oversimplification. Many studies see both age-related increases and decreases within the prefrontal cortex (Bunge et al., 2002; Christakou et al., 2009; Klingberg et al., 2002; Olesen et al., 2007), suggesting that perhaps age predicts decreases in recruitment of task-relevant regions and increases in task-relevant regions. Or, put another way, age may predict recruitment of less prefrontal surface area but greater magnitude within specific brain regions critical for a given task (Durston et al., 2006).

Age-related changes in emotion in childhood and adolescence

Since Stanley Hall (1904) first characterized adolescence as a time of "storm and stress" more than a century ago, much debate has ensued about what drives social, emotional and risk-taking behaviors in adolescence. There is substantial evidence suggesting that adolescents tend to experience more extreme, short-lived and variable affective states in their everyday lives than do adults (Larson, Csikszentmihalyi, & Graef, 1980; Larson, Moneta, Richards, & Wilson, 2002; Larson & Richards, 1994). Yet, it is unclear whether this heightened emotionality is unique to adolescents or if it common to children as well. This confusion is at least partially attributable to the facts that 1) different methodologies are typically used to assess emotion at different points in development (i.e., observational studies are more common in early childhood while diary studies are not typically used until late childhood), and 2) it is rare for a single study to examine emotional responses in age ranges that span all the way from early childhood to adulthood (Adrian, Zeman, & Veits, 2011).

With these caveats in mind, drawing from observational, questionnaire, diary and functional and structural MRI studies, at least four broad observations can be made. First, emotional variability and an individual's tendency to express emotional extremes

decreases from early childhood to late childhood (Murphy, Eisenberg, Fabes, Shepard, & Guthrie, 1999; Sallquist et al., 2009), stays stable from childhood to early adolescence (Larson & Lampman-Petraitis, 1989), and declines from early adolescence to adulthood (Larson et al., 1980; Larson et al., 2002). Second, average daily mood declines from childhood to mid-adolescence, before stabilizing just before the transition to young adulthood (Larson & Lampman-Petraitis, 1989; Larson et al., 2002). Third, brain structures that support the formation of affective appraisals, such as the amygdala, undergo dramatic structural change during early childhood and complete maturation around puberty (Giedd et al., 1996; Lenroot & Giedd, 2010; Neufang et al., 2009; Peper, Brouwer, et al., 2009), yet display a more protracted functional trajectory. Specifically, the amygdala fails to respond to negative facial expressions during early childhood (K. M. Thomas et al., 2001; Todd, Evans, Morris, Lewis, & Taylor, 2010), shows age-related increases in activity from early childhood to adolescence (Hare et al., 2008; Todd et al., 2010), and then exhibits decreases in adulthood (Guyer et al., 2008; Hare et al., 2008; Monk et al., 2003). Fourth, age and environmental changes are inextricably linked. For example, adolescents may report more negative affect in their daily lives than children, but adolescents also experience more stressful and negative events in their daily lives than do children (Larson & Ham, 1993). Taken together, these data suggest that maturation of emotional processes does not follow a single trajectory from childhood to adulthood but instead occurs in a series of linear and non-linear trends at the levels of the brain, affective experience and external behavior.

An individual's social world changes dramatically during the transition from childhood to adolescence, making it critical to consider how emotional and social processes interact during this period. In contrast to children, adolescents spend far more time with

their peers and find such interactions to be more rewarding (R. Larson & M. H. Richards, 1991). During adolescence, individuals become increasingly skilled at taking the perspectives of others (Choudhury, Blakemore, & Charman, 2006), and relatedly, become increasingly fearful of social evaluation (Westenberg, Drewes, Goedhart, Siebelink, & Treffers, 2004). This heightened concern with all things social may at least partially underlie adolescents' propensity to make risky decisions in the presence of peers (Chein, Albert, O'Brien, Uckert, & Steinberg, 2011; Gardner & Steinberg, 2005).

Changes in adolescent social behavior are paralleled by functional changes in brain regions known to support social cognition, emotion and reward processing. An example of such a region is the medial prefrontal cortex (MPFC), a brain region implicated in the attribution of mental states and self-referential processing (Amodio & Frith, 2006; Olsson & Ochsner, 2008). In comparison to children or adults, adolescents show heightened MPFC activity in response to viewing facial expressions (Yurgelun-Todd & Killgore, 2006), reflecting on the mental states of themselves or others (Blakemore, den Ouden, Choudhury, & Frith, 2007; Burnett, Bird, Moll, Frith, & Blakemore, 2009; Pfeifer et al., 2009), or being told that they are being evaluated by peers (Somerville et al., in press). Brain regions thought to detect rewarding, valuable or salient stimuli such as the ventral striatum also show age-related changes in recruitment during adolescence. Enhanced ventral striatal responses during adolescence have been linked to failures to exert cognitive control (Somerville et al., 2011) or make optimal decisions (Chein et al., 2011) in the presence of social stimuli or peers. Taken together, this suggests that adolescence marks a time of heightened sensitivity to both positive and negative social cues that is at least partially responsible for age-related changes in emotional behavior.

Interactions between emotion and cognition in childhood and adolescence

While much work has suggested that age-related changes in emotionality and "cold" cognitive control occur in adolescence, less is known about how the ability to use cognitive control to manage emotional responses develops during this period. To date, interactions between cognition and emotion have been primarily studied either by examining performance on "hot" cognitive control tasks, those that include affective stimuli or enhanced motivational salience, or, by using observational or questionnaire methods to examine use of regulatory strategies at different points in development. These two lines of work as well as the small, but growing, body of work examining age-related differences in reappraisal are described below.

Cognitive control has traditionally been studied using tasks that are devoid of emotional or motivational content. More recently, however, cognitive control has been characterized as existing on a continuum of motivational and emotional significance, with abstract tasks that are low on such significance being relatively "cool" and those that are high in motivational and emotional significance being "hot" (Figner, Mackinlay, Wilkening, & Weber, 2009; Hongwanishkul, Happaney, Lee, & Zelazo, 2005; Kerr & Zelazo, 2004; Zelazo & Carlson, 2012). One well-known example of a hot task is the delay of gratification paradigm (DoG) first used by Mischel and colleagues in the 1960s. In these studies, preschool children were given the option to consume one treat immediately or to wait for two treats while the experimenter left the room for an unspecified period of time (in reality, the maximum wait time was 15 minutes). While several significant findings regarding individual differences in executive control emerged from these studies, two are of particular note. First, children who were able to exert attentional control (i.e., those who

distracted themselves or looked away from treats) waited longer than those who did not (Peake, Hebl, & Mischel, 2002). Second, delay ability predicted better life outcomes including enhanced social and academic competence in adolescence and less drug use in adulthood (Ayduk et al., 2000).

Hot tasks contain stimuli (either the task-relevant stimuli or distractor stimuli), decisions or outcomes that are personally relevant, rewarding, or affectively salient (Prencipe et al., 2010). Whether hot and cold tasks rely on overlapping or distinct neurocognitive processes remains a somewhat open question that appears to vary somewhat according to the age group of participants tested as well as the tasks being used. Lesion studies of both human and non-human animals support a hot/cold distinction given that orbitofrontal cortex (OFC) damage is strongly linked with impairments on hot tasks that involve gambling or risky decision making but not on other types of cold tasks (Bechara, 2004; Bechara, Damasio, Damasio, & Anderson, 1994; Paul J. Eslinger, Flaherty-Craig, & Benton, 2004). While such deficits may be dissociable in lesioned populations, other evidence suggests that healthy individuals recruit partially overlapping neural systems during hot and cold tasks.

One way of testing whether hot and cold tasks recruit overlapping neural systems is by examining neural responses within individuals on cognitive control tasks that have hot and cold conditions. An example of such a task is the emotional go-nogo (EGNG). For both the traditional go-nogo task and the EGNG, participants are instructed to respond to a frequently appearing target stimulus and to withhold responses to relatively rare non-target stimuli. In the EGNG, the targets and nontargets are emotional or neutral facial expressions that are thought to elicit automatic approach (happy faces) or avoidance

(fearful faces) tendencies. Congruent with this notion, participants tend to commit more errors of commission on trials when happy faces are nontargets, and are slower to respond on "go" trials when fearful faces are the target (Hare, Tottenham, Davidson, Glover, & Casey, 2005; Hare et al., 2008; Tottenham, Hare, & Casey, 2011). Regardless of a nontarget's valence, right vlPFC is recruited when participants attempt to withhold a response on "nogo" trials (Hare et al., 2005; Hare et al., 2008; Somerville et al., 2011; Swick, Ashley, & Turken, 2011). Yet, the valence of targets or nontargets strongly influence recruitment of subcortical structures involved in forming affective appraisals (Hare et al., 2005; Hare et al., 2008; Somerville et al., 2011). Importantly, age inversely predicts recruitment of vlPFC on the EGNG and is associated with quadratic differences in recruitment of subcortical structures such as the amygdala and ventral striatum (Hare et al., 2008; Somerville et al., 2011). Taken together, this suggests that a common control mechanism is recruited for both hot and cold variants of this task but that subcortical inputs interfere with the effectiveness of this control on hot trials, particularly during adolescence.

In recent years, there has been a growing interest in mapping the development of hot and cold cognitive control abilities. Direct comparisons of hot and cold tasks suggests that performance on both types of tasks improves during childhood and adolescence but that it takes longer to achieve adult-levels of performance on hot tasks (Figner et al., 2009; Hooper, Luciana, Conklin, & Yarger, 2004; Prencipe et al., 2010). Performance on hot and cold tasks is related in children and adolescence, strengthening the argument that these different types of control processes rely on common mechanisms (Hooper et al., 2004; Prencipe et al., 2010). Although hot tasks are generally thought to be more challenging for

adolescents than adults, there are instances when a task's "hotness" can actually improve adolescent performance. For example, monetary rewards can enhance accuracy and reaction times on inhibitory tasks in adolescents (Geier, Terwilliger, Teslovich, Velanova, & Luna, 2010; Peper, Schnack, et al., 2009), although they can also increase error rates more significantly in adolescents than in adults (Geier & Luna, 2012). This suggests that adolescents are more sensitive to affectively or motivationally salient material than are adults and this sensitivity can either enhance or hinder cognitive control, depending on the task and context.

Most of the hot cognitive control tasks described above are designed to examine how emotional content interrupts or alters cognitive control. Reappraisal, however, seeks to do the opposite. In reappraisal tasks, participants use control processes to alter the meaning and thereby modulate the emotional import of a stimulus. Relative to the hot cognitive control tasks described, far less experimental work has examined how the ability to reappraise develops across the lifespan. Although several studies have examined reappraisal in limited age ranges during childhood or adolescence (Carthy, Horesh, Apter, Edge, & Gross, 2010; Levesque et al., 2004; Moore, Mischel, & Zeiss, 1976; Pitskel, Bolling, Kaiser, Crowley, & Pelphrey, 2011), few studies have examined how reappraisal ability differs across broad age ranges. Mischel and colleagues have demonstrated that preschoolers who are taught to reappraise treats have significantly longer delay times than children who are not taught to reappraise on the DoG task (1975). Cross-sectional laboratory studies, including Study 1 presented here, have also shown that performance on reappraisal tasks improves significantly in individuals aged 10-22 years with reappraisal ability plateauing around age 17 (McRae et al., 2012; Silvers, McRae, et al., 2012). Outside of

the laboratory, questionnaire data suggests that older teenagers use cognitive strategies like reappraisal more frequently in their everyday lives than do younger teens (Williams & McGillicuddy-De Lisi, 1999), and that teens who use such strategies endorse higher levels of subjective wellbeing (Fields & Prinz, 1997; Garnefski & Kraaij, 2006). This suggests that the ability to reappraise originates in early childhood but that reappraisal frequency and effectiveness continues to increase throughout adolescence.

At present, only three studies have examined the neural bases of reappraisal in childhood or adolescence. This work has revealed that, like adults, children and adolescents can use reappraisal to reduce negative affect and that doing so relies upon the recruitment of dorsal and lateral prefrontal control regions (Levesque et al., 2004; McRae et al., 2012; Pitskel et al., 2011). Two of these three studies examined age effects, and while both determined that age predicts differential recruitment of the left inferior frontal gyrus, they found opposite trends. While Pitskel and colleagues observed age-related decreases in left IFG recruitment, McRae and colleagues observed age-related increases in left IFG recruitment. Additionally, while Pitskel and colleagues reported that age predicted enhanced amygdala modulation, McRae and colleagues found no evidence of amygdala modulation across the entire sample. Although these contradictory results are hard to reconcile, it is worthy noting that these two studies differed on a number of dimensions that could have influenced age-related effects, including sample size (Pitskel: 15, McRae: 38), age range (Pitskel: 7-17 years, McRae: 10-22 years), and stimulus type (Pitskel: disgusting images, McRae: a combination of different types of aversive images). Additional work is needed to systematically investigate how the neural bases of reappraisal changes from childhood through adulthood and whether this varies as a function of stimulus type.

Overview of the present research

The four studies presented in the subsequent chapters seek to characterize how emotion regulation develops during childhood and adolescence. A central theme that runs throughout these studies is the question of whether emotional reactivity, bottom-up emotional responses, or regulation success, the ability to regulate emotions using top-down control, changes over the course of child and adolescent development. To assess this question, each of the following studies utilized reappraisal paradigms that assessed both emotional reactivity and regulation success within each participant by examining how participants responded to emotional stimuli in a more naturalistic, reactive state and how they responded to emotional stimuli while reappraising. Study 1 sought to examine whether age predicts differences in bottom-up emotional reactivity or top-down emotion regulation, and how negative emotion interacts with social factors to predict regulatory ability across adolescence. Study 2 used the same paradigm as Study 1 to explore how age and stimulus social content impact the neural bases of reappraisal. Study 3 built on the results of Study 2 by examining how age predicts the neural bases of emotional reactivity and regulation for negative social stimuli across childhood, adolescence and young adulthood. Finally, Study 4 used body mass index, self-reported craving and neuroimaging data to examine how the ability to regulate craving for food develops during childhood and adolescence.

Chapter 2: Age-related differences in emotional reactivity, regulation and rejection sensitivity in adolescence

Introduction

For over a century, scientists have debated whether adolescence is by definition a time of emotional "storm and stress" (Arnett, 1999; Casey et al., 2010; Hall, 1904). While there is considerable evidence that on average adolescents experience more extreme affect (both positive and negative) and more variable mood states in their everyday lives than do their adult counterparts (Larson et al., 1980; Larson et al., 2002; Larson & Richards, 1994), two issues regarding adolescent emotional development remain unresolved. First, the research to date has been contradictory with regards to whether age-related differences in emotional responsivity are linear, with emotionality being highest in children and tapering in adolescents (Carthy et al., 2010; Murphy et al., 1999), quadratic, with emotionality being highest in adolescents (Casey, Getz, & Galvan, 2008; Casey et al., 2010), or both linear and quadratic in nature (Larson et al., 2002; L. A. Thomas, De Bellis, Graham, & LaBar, 2007). Second, while efforts have been made to characterize age-related changes in emotional reactivity (how strong one's emotional response is to affective versus neutral stimuli) and regulation (how effectively one regulates emotional responses) during childhood (Murphy, Eisenberg, Fabes, Shepard, & Guthrie, 1999), little research has examined such changes during adolescence (for a notable exception, see Silk, Steinberg & Morris, 2003). Hence, it is unknown whether differences in emotional responsivity observed between adolescents and adults are due to differences in emotional reactivity or emotion regulation ability. For example, if older adolescents report less negative daily affect than younger adolescents, it would be unclear whether this is due to emotional responses becoming less intense,

increased emotion regulatory ability, or both. Disentangling whether adolescents' natural, bottom-up emotional responses are stronger than adults' or whether their controlled, top-down regulatory processes are weaker than adults' may have important implications for basic and applied models of emotional development.

The present study addressed these issues by examining emotional reactivity and regulation, specifically via cognitive reappraisal, in adolescence. Reappraisal is a powerful and flexible regulation strategy that involves changing how one thinks about an emotional stimulus so as to alter one's emotional response to it. Although prior work has examined reappraisal in limited age groups (Carthy et al., 2010; Levesque et al., 2004; Moore et al., 1976; Pitskel et al., 2011), only one other study has examined reappraisal ability in a broad adolescent age range (McRae et al., 2012). While children as young as 3 years can use reappraisal to modulate emotions when instructed to do so (W. Mischel & Baker, 1975), two types of evidence suggest that over the course of child and adolescent development, individuals become more frequent and effective reappraisers. First, laboratory and survey measures indicate that spontaneous use of cognitive regulatory strategies increases during childhood and adolescence (Fields & Prinz, 1997; Garnefski & Kraaij, 2006; H. N. Mischel & Mischel, 1983; Rodriguez, Mischel, & Shoda, 1989; Williams & McGillicuddy-De Lisi, 1999). Second, behavioral and neural markers of cognitive control processes used in reappraisal improve over the course of adolescence (Casey, Tottenham, Liston, & Durston, 2005; Durston et al., 2006; Pfeifer & Allen, 2012; Steinberg & Morris, 2001).

To directly examine what underlies emotional changes in adolescence, the present study assessed emotional reactivity (baseline responsiveness to affective stimuli) and regulation success (decreases in negative affect achieved via reappraisal) in individuals at

the beginning, middle and end of adolescence. The present study also examined how situational and dispositional social factors interacted with age to predict emotion regulation success. While no prior work has directly examined this issue, two types of evidence suggest that age-related differences in regulation success may be influenced by social factors. Situationally, adolescents find peer interactions more rewarding than do children (Choudhury et al., 2006), but are more sensitive to peer influence and peer rejection than are adults (Brown, 2004; Choudhury et al., 2006; Gardner & Steinberg, 2005; R. W. Larson & M. H. Richards, 1991; Steinberg, 2005; Steinberg & Morris, 2001). Dispositionally, how an adolescent reacts to a given social situation may be influenced by factors like rejection sensitivity (RS), the tendency to anxiously anticipate and perceive (Downey & Feldman, 1996). High RS adolescents may be particularly vulnerable to feelings of rejection and ostracism, which may result in part from self-regulatory failures (Downey, Lebolt, Rincon, & Freitas, 1998; London, Downey, Bonica, & Paltin, 2007).

Given that regulation success involves using control processes to modulate emotional responses, we expected that age would exert both linear and quadratic effects on regulation success. For reactivity, however, we made no predictions because the varying methods (e.g., questionnaire vs. observational measures) and age ranges used in prior work have produced mixed findings about how reactivity differs between children and adolescents (Larson & Lampman-Petraitis, 1989; Murphy et al., 1999) and between children, adolescents and adults (Diener, Sandvik, & Larsen, 1985; Larson et al., 1980; McManis, Bradley, Berg, Cuthbert, & Lang, 2001). It was further hypothesized that age-related improvements in emotion regulation would be seen earlier for non-social than social stimuli and that high RS individuals would be worse at regulating emotional

responses to social stimuli than low RS individuals. Assuming that the effects of RS, social content, and age would be additive, it was hypothesized that reappraisal success would be lowest for younger participants who were high in RS and attempting to regulate emotional responses to aversive social stimuli.

Methods

Participants. The final sample used for all analyses consisted of 77 healthy volunteers aged 10-23 years (36 female; mean age = 17.4 years, S.D.= 3.63). The initial sample consisted of 82 healthy volunteers (41 female; mean age = 17.2 years, S.D.= 3.65). Prior to participating in the study, parents of minor participants completed a brief prescreening telephone interview to confirm that their child could read and write in English, had normal or corrected vision, had never been diagnosed with a developmental or psychiatric disorder and had never been prescribed psychotropic medication. Only children who met these inclusionary criteria were tested. Among these children, four (all female) were excluded from data analysis. One was excluded because the child opted to terminate the experiment after just a few experimental trials. Three others were excluded because their total problem scores on the Child Behavior Checklist (Achenbach, 1991), which was used as an additional screening tool for our child participants, were within the clinical range, suggesting that they exhibited atypically poor emotional and behavioral functioning. These four children did not differ from other children included in analyses in terms of age ($t(40)=.92$, $p=.36$) or rejection sensitivity measures ($t(40)=.72$, $p=.47$). Participants over the age of 18 completed a brief telephone prescreening interview to confirm that they could read and write in English, had normal or corrected vision, had never been diagnosed with a developmental or psychiatric disorder and had never been

prescribed psychotropic medication. Only adult participants who met these inclusionary criteria were tested. One adult female (age=18.33 years) was excluded from analyses due to a computer failure that occurred during her testing session.

Measures of intellectual ability. Participants completed the vocabulary, similarities, matrix reasoning, and block design subtests from the WISC-IV (participants aged 10-16) or WAIS-IV (participants aged 17-22). Scaled scores were prorated so that General Ability Index (GAI) scores could be calculated for each participant. Age was positively associated with GAI scores (r=.24, p=.04) but when added as a covariate, GAI was not a significant predictor in any of the analyses reported below (p<.31 or greater).

Measures of social desirability. To ensure that a participant's need to portray oneself positively did not bias task performance, participants 18-22 completed the Marlowe-Crowne Social Desirability Scale (MCSDS; Crowne & Marlowe, 1960) and participants 10-17 (one participant did not complete the questionnaire correctly) completed the Children's Social Desirability Scale (CSDS; Crandall, Crandall & Katkovsky, 1965). Scores on 19 content-matched items from each questionnaire did not vary in accordance with age (r=-.17, p=.14). See below for results regarding social desirability and regulation success.

Measures of rejection sensitivity. To assess individual differences in RS, participants 18 and older completed the Rejection Sensitivity Questionnaire-Personal (RSQ-Personal) (Downey & Feldman, 1996) and participants 17 and younger completed the Children's Rejection Sensitivity Questionnaire (CRSQ) (Downey et al., 1998). While the CRSQ evaluates both anxious and angry expectations of rejection, for the present study we solely examined responses relating to anxious expectations so as to more easily compare

the RS-Personal and CRSQ scales. These measures ask participants to assess how anxious they would feel and what they would expect to happen in various hypothetical social situations. The range of possible scores on the RS-Personal is 1-36 (published norms: mean=9.69, SD=3.07) and the range for the present sample was 4.39-17.39 (sample: mean=9.85, SD=3.02). The range of possible scores for anxious expectations on the CRSQ is 1-36 (published norms: mean=8.16, SD=3.91) and the range for the present sample was 1.42-17.75 (sample: mean=8.49, SD=3.79). For statistical purposes, standardized scores were calculated for each participant using published norms for each of these measures (Downey & Feldman, 1996; Downey et al., 1998). RS scores did not correlate with age (r=.04, *p*=.73).

Experimental procedure. Prior to performing the task, participants were trained extensively on the immersed ('close') and distanced ('far') strategies in accordance with well-validated procedures (Ochsner et al., 2004). On 'close' trials, participants were told to imagine themselves standing close to the scene depicted in the photograph and to allow themselves to experience any emotions that the photograph evoked. On 'far' trials, participants were told to imagine themselves standing further away from the scene and to focus more on the facts of the photograph than on its emotional details. While participants were not told so, 'close' trials were used to assess baseline emotional responsiveness whereas 'far' trials were used to assess regulation ability.

Nonsocial and social photographs were chosen from the International Affective Picture System (picture #s: 1050, 1930, 2235, 2270, 2514, 2515, 2575, 5395, 5849, 6838, 7000, 7002, 7009, 7025, 7060, 7080, 7090, 7100, 7150, 7170, 7195, 7224, 7235, 7326; (Lang, Greenwald, Bradley, & Hamm, 1993) and public online sources (see

http://scnlab.psych.columbia.edu/stimuli/reactregsoc/index.html) and were normed by an independent sample of 23 participants aged 10-22 (M=18.17, SD=3.01). This pre-testing confirmed that social stimuli reminded participants of social situations (social situations were defined for participants as "situations where people interact with each other") more than non-social stimuli ($t(22)=5.58$, $p<.001$), but did not differ in terms of valence ($t(22)=1.12$, $p=.27$).

All participants completed 120 experimental trials, 60 of which contained aversive stimuli and 60 of which contained neutral stimuli. All adults saw the same set of 120 stimuli. One hundred aversive photographic stimuli, 50 social and 50 nonsocial, were prescreened by a parent for each participant aged 10-17. Parents were permitted to exclude up to 10 aversive social and 10 aversive non-social stimuli so that a pool of 40 stimuli remained for each aversive stimulus type. From this set, 30 aversive social and 30 aversive nonsocial stimuli that were closely matched for valence and arousal were chosen for the experimental task. The remaining stimuli were used for training purposes and if needed, to serve as valence-matched task substitutes for pictures that were excluded by parents. Parents of children 10-17 typically rejected a small number of pictures (M=2.53, SD=3.57) though the rate of rejection was inversely correlated with age (r=-.39, $p=.02$). This procedure allowed all participants to complete the same number of trials.

On each trial, participants first saw a cue word (‘close’ or ‘far’, shown for 2 seconds) and then implemented the strategy indicated by the cue word while viewing a photographic stimulus for 8 seconds. At the conclusion of each trial, participants rated their negative affect on a five-point scale (1=not feeling badly at all, 5=feeling very badly) via button press. A diagram of the trial structure used is shown in Figure 2.1. Conditions

differed in terms of stimulus valence (negative or neutral), stimulus social content (social or nonsocial), and regulation instruction (close or far) for a total of 8 condition types. The assignment of pictures to instruction was counterbalanced between participants. The task was completed on a desktop computer in a windowless testing room.

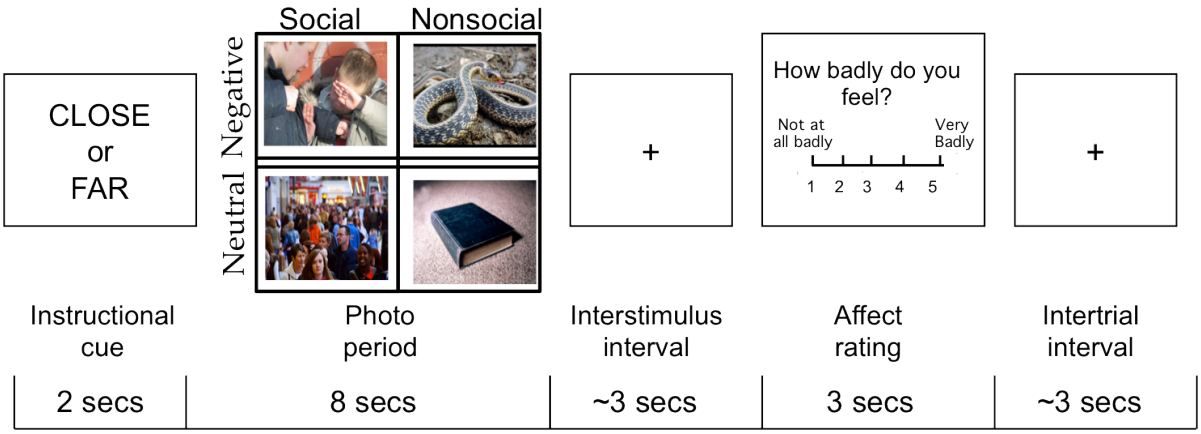

Figure 2.1. Trial structure for Study 1.

Analyses. Analyses took part in three phases. First, a manipulation check was performed to confirm that aversive stimuli elicited more negative affect than neutral stimuli (emotional reactivity) and that the distancing strategy reduced negative affect for aversive stimuli (regulation success). To do this, emotional reactivity ([Close negative – Close neutral]/Close neutral x 100) and regulation success ([Close negative – Far negative]/Close negative x 100) indices were calculated for each participant. Second, we assessed whether age predicted emotional reactivity, regulation success or both. Third, we used a mixed ANOVA to assess how age, social content and RS interacted to predict negative affect during emotion regulation.

Results

Manipulation check. T-tests were used to assess the efficacy of the stimuli and regulation strategy. As expected, emotional reactivity (M=208.17%; $t(76)$=29.96, p<.001) and regulation success scores (M=25.38%; $t(76)$=14.93, p<.001) were significantly greater than zero across all participants. Neither emotional reactivity (r=.17, p=.14) nor regulation success (r=.001, p=.99) correlated with social desirability scores.

Age, emotional reactivity and regulation success. Multiple regression analyses were performed to test for age effects on emotional reactivity and regulation. Age, age^2, and GAI were used as predictors and either emotional reactivity or regulation success were entered as dependent variables for each equation. GAI did not predict emotional reactivity (β=-.13, $t(73)$=.31 p=.76) or regulation success (β=.07, $t(73)$=.69, p=.49). The regression equation for emotional reactivity was non-significant ($F(3,73)$=1.52, p=.22, η^2=.06) and, as shown in Figure 2.2b, neither linear nor quadratic effects of age were observed for emotional reactivity (β_{age}=30.23, $t(73)$=1.55, p=.13; β_{age^2}=-.81, $t(73)$=-1.39, p=.17). However, as shown in Figure 2.2c, the regression equation for regulation success was significant ($F(3,73)$=5.33, p=.002, η^2=.22). Age exerted a significant linear effect and a marginally significant quadratic effect on regulation success (β_{age}=9.01, $t(73)$=2.04, p=.045; β_{age^2}=-.23, $t(73)$=-1.71, p=.09). Visual inspection of the regression line containing both the linear and quadratic terms for age as well as GAI scores (regulation success = -.23*age^2 + 9.01*age + .07*GAI - 69.53) suggested that regulation success improved from age 10 through approximately age 18 before tapering off. This interpretation of the data was tested using change point analyses. To do this, age was centered at each age point and this mean-centered variable along with its resultant mean-centered age^2 were used as

predictors in regression analyses predicting regulation success. This approach allowed for inspection of the "instantaneous" age slope for each age point. These regressions revealed that significant age-related differences in regulation success were observed for each year of age from 10-17 (β's ranged from 1.46-4.57, all *p*'s<.01) and a marginal improvement for age 18 (β=1.02, *p*=.06). No significant effects of age were observed for any ages above 18 (β's ranged from -.75 to .58, *p*'s ranged from .43 to .88).

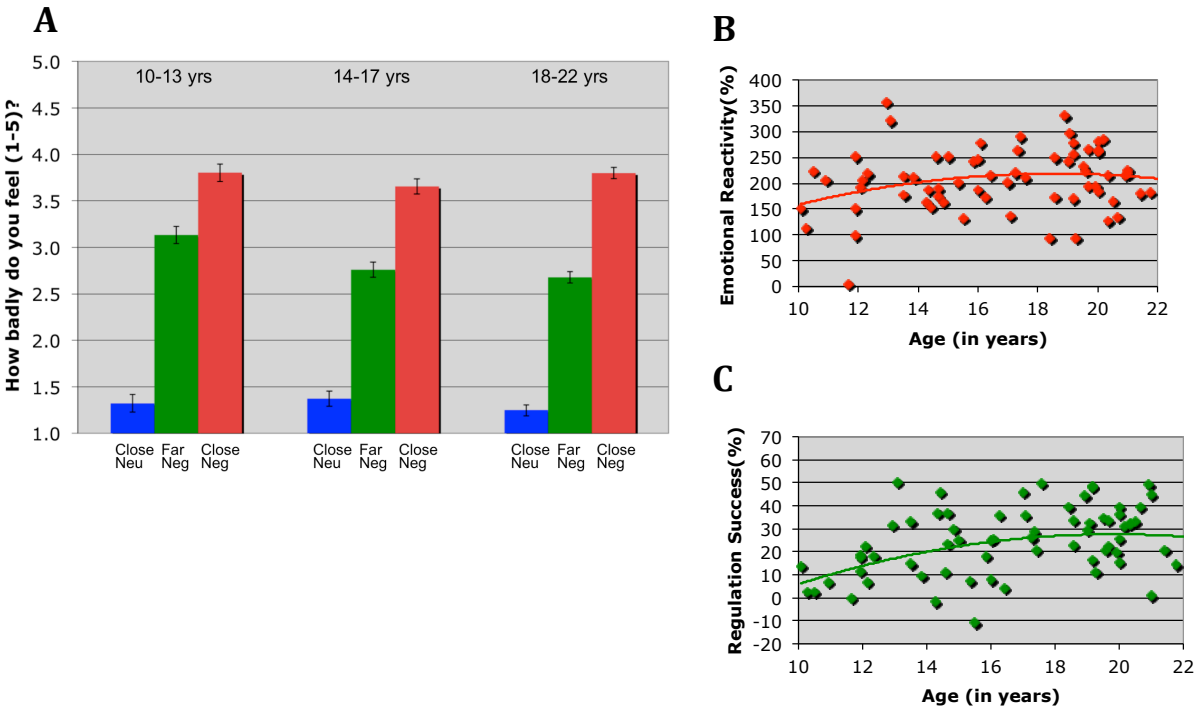

Figure 2.2 Age effects on reactivity and regulation. (a) Negative affect was greater for negative than neutral stimuli and was diminished by distancing. Age is shown categorically for visual purposes. Individual subject datapoints and the regression equations are plotted as a function of age for b) emotional reactivity (emotional reactivity= -0.81*age^2 + 30.23*age -.13*GAI – 47.04) and c) regulation success (regulation success= -0.23*age^2 + 9.01*age +.07*GAI – 69.53). Neither linear (*p*=.13) nor quadratic (*p*=.17) effects of age were observed for emotional reactivity, but significant linear (*p*=.045) and marginally significant quadratic (*p*=.09) effects were observed for regulation success.

Interactions between rejection sensitivity, social content and age. A mixed ANOVA was used to examine how social factors and age predicted affective responses on Far Negative trials, the one trial type for which age effects were found. Stimulus social content (social or non-social), age, trait rejection sensitivity (RS scores) and GAI scores were entered as independent variables while affect ratings were entered as a dependent variable. GAI was not found to predict negative affect ($F(1,72)=.61$, $p=.44$). Aversive social stimuli evoked more negative affect than non-social stimuli ($F(1,74)=6.46$, $p=.01$) and a significant interaction was observed between age and social content ($F(1,74)=6.28$, $p=.01$), such that younger participants were less effective at regulating emotional responses to social stimuli than non-social stimuli but older participants were not (Figure 2.3). RS scores were associated with marginally more negative affect ($F(1,72)=2.59$, $p=.11$) and RS scores interacted with age and stimulus social content ($F(1,74)=7.01$, $p=.01$) such that RS predicted stronger affective responses to social stimuli for younger individuals but not for older individuals.

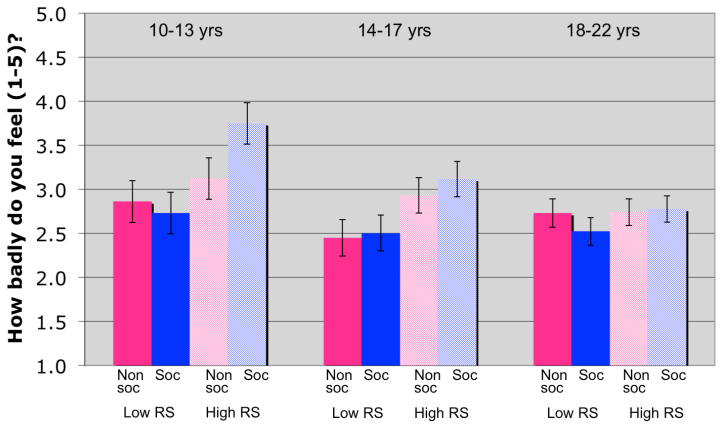

Figure 2.3. Reappraisal of social and non-social negative stimuli. Data is presented as a function of age group, stimulus social content and rejection sensitivity. Analyses were performed using continuous measures of RS and age but for visual purposes, a median split was performed on RS scores so as to create high and low RS groups and three age groups were constructed.

Discussion

Demands for emotion regulation are particularly high in adolescence as individuals experience increased independence, hormonal changes, and a changing social environment (Blakemore, 2008; Casey et al., 2008; Somerville, Jones, & Casey, 2010). While most adolescents successfully navigate these challenges by developing mature regulatory skills that will help them to cope with stressors for the rest of their lives, for some individuals adolescence marks the beginning of a lifelong struggle with emotion regulation and mental health (Kessler et al., 2005). This suggests that understanding the development of emotion regulation processes in adolescence may be important not only for improving the lives of adolescents but also for preventing dysfunctional regulation in adulthood. However, little prior work has attempted to 1) dissociate emotional reactivity and regulation during adolescent development, and 2) characterize how dispositional and situational social factors impact emotion regulation in adolescence.

The present study addressed these issues by experimentally differentiating emotional reactivity and regulation success in individuals aged 10-22 years while also determining whether age-related differences in reappraisal success vary as a function of stimulus content and dispositional tendencies. Two key findings were obtained: 1) that age did not predict emotional reactivity but positively predicted regulation across adolescence, and 2) that situational (social content of an emotional stimulus) and dispositional (RS) social factors impacted regulation success in younger adolescents.

Implications for theories of emotional and cognitive development. The first implication of these results relates to the importance of differentiating emotional reactivity and regulation success in developmental studies of emotion regulation. In a laboratory

context, we found effects of age on regulation success but not on emotional reactivity. Although prior work has suggested that baseline mood and emotional variability in daily affect change over the course of adolescence, such observations have derived primarily from experience sampling measures, self-report questionnaires or from parental/teacher observations (Larson & Lampman-Petraitis, 1989; Larson et al., 2002; Murphy et al., 1999). While such approaches have ecological validity, they lack the ability to fully disentangle emotional reactivity and regulation success. Only one prior study has used a paradigm and participant age range similar to those used in the present design (McRae et al., 2012). Not only does the present study replicate the findings reported by McRae and colleagues in two larger, independent samples, it also furthers this line of work by examining how individual differences and stimulus factors interact with age.

Using the present design, we found that age significantly predicted regulation success, but not emotional reactivity. Age-related differences in reappraisal success were observed up until late adolescence, at which point regulation success stabilized. This is consistent with age effects that have been observed on a host of "cold" cognitive control tasks (De Luca et al., 2003; Huizinga, Dolan, & van der Molen, 2006; Luciana, Conklin, Hooper, & Yarger, 2005; Luna, Garver, Urban, Lazar, & Sweeney, 2004). Interestingly, the age-related differences observed in the present studies dissipated at later ages than is typically observed in "cold" cognitive control tasks. This pattern has also been observed on cognitive control tasks that are highly motivating or emotional in nature (Figner et al., 2009; Hare et al., 2008; Prencipe et al., 2010). While participants across all ages reported significantly less negative affect when reappraising, the fact that reappraisal-related decreases in negative affect were greater for older participants suggests that young

adolescents have the ability to regulate using reappraisal but do not do so as effectively as older adolescents. At least two factors could explain this pattern. First, it may be that older adolescents simply have more experience with reappraisal than do younger adolescents (Garnefski & Kraaij, 2006), perhaps in part because they have encountered more negative life events that have required them to adaptively self-regulate (Larson & Ham, 1993). If this is true, then reappraisal training could neutralize or reduce age-related differences in regulation success. Second, regulation success in adolescence may be constrained by brain maturation, given that prefrontal control regions associated with successful emotion regulation in adults are among the last brain regions to fully develop in adolescence (Barnea-Goraly et al., 2005; Giedd et al., 1999; Ochsner & Gross, 2008; Pfefferbaum et al., 1994). Determining whether one or both of these factors restrict emotion regulation success in younger adolescents will be critical for constructing accurate models of emotion regulation development and for creating effective interventions.

While our finding that regulation success was positively predicted by age during early and mid-adolescence may appear to contradict theories suggesting that adolescents are more emotionally reactive and prone to risk-taking than children (Casey et al., 2010; Somerville et al., 2010; Steinberg, 2008), three points ought to be considered when interpreting the present results. First, it is unclear whether even the youngest participants in this sample ought to be considered children so much as young adolescents given that pubertal development on average begins between the ages of 8 and 10 for girls (Herman-Giddens et al., 1997) and 11 and 12 for boys in the United States (Herman-Giddens, Wang, & Koch, 2001). While the present study utilized one of the widest age ranges tested on a reappraisal paradigm to date, future studies may seek to include younger ages in their

samples so as to more clearly examine differences between children, adolescents and young adults. Additionally, given the growing body of literature suggesting that some affective processes, particularly emotional reactivity, are more strongly impacted by puberty-related effects than age effects (Dahl & Gunnar, 2009; Forbes, Phillips, Silk, Ryan, & Dahl, 2011; Forbes, Ryan, et al., 2011), it may be fruitful for future work to focus on the pre- and early-adolescent age range to examine whether age and pubertal status exert differential effects on affective reactivity and regulation success on cognitive reappraisal tasks. Second, although we observed age-related differences in reappraisal success in the present study, this experiment asked participants to reappraise in a relatively controlled environment while using a very specific type of stimuli. Prior work has shown that adolescents perform disproportionately worse on decision making and executive function tasks when tested in the presence of peers or when responding to affectively arousing stimuli (Cauffman et al., 2010; Figner et al., 2009; Gardner & Steinberg, 2005). Thus, future work should examine how developmental improvements in reappraisal success are impacted by social context and stimulus type. Third, while the present study suggests that age-related changes in regulation success occur from early to late adolescence, these improvements may not occur similarly for all individuals. For example, prior work has shown that individual differences in sensation seeking (Crone, Bullens, van der Plas, Kijkuit, & Zelazo, 2008) and anxiety (Hare et al., 2008) can interact with age to predict variability in decision making and regulation. Therefore, future work may benefit from examining how these or other variables may predict age-related improvements in emotion regulation success both within and across individuals.

While developmental differences in the self-report of emotion have been observed in younger children (Chambers & Johnston, 2002), there are at least three reasons why it is highly unlikely that this would explain the results in the present study. First, prior work has shown that by age 10, children are sufficiently aware of their emotional states so as to provide valid self-reports for psychiatric assessments (Edelbrock, Costello, Dulcan, Kalas, & Conover, 1985; Lonigan, Phillips, & Hooe, 2003). Second, as in previous studies of adults (Ochsner et al 2002), self-reported affect in this study did not correlate with individual differences in the tendency to give socially desirable responses. Third, it seems unlikely that self-report biases could be the driving force behind the age effects observed in the present study given that age effects were *only* observed on trials in which participants were asked to reappraise negative stimuli. If, for example, younger participants lacked the ability to accurately report on or understand their emotions, or either older or younger participants provide biased reports of emotion attributable to experimental expectancy or other effects, it is not clear why such biases would reveal themselves only on trials that required regulation, and not on trials in which participants were asked to respond naturally or to take an immersed perspective. Further, it is not clear how such biases could explain the age-related trends in responses to social stimuli or effects of RS observed.

Implications for understanding individual differences in development. The present findings have implications for understanding both the development of individual differences and potentially, psychopathology. These implications stem from our findings that (1) age-related differences in regulation success were greater for social than for non-social stimuli, (2) individuals who were high in RS were less successful at regulating emotional responses to aversive social stimuli but, (3) this effect was stronger at younger

ages than older ages. Taken together, these data suggest that learning to regulate emotional responses in the social domain is a critical developmental hurdle that, for most individuals, is cleared during adolescence. At the same time, the present data also suggest that being high in RS may make overcoming this obstacle more difficult.

Across the lifespan, individuals who are high in RS are more likely to defensively expect and perceive rejection in social interactions (Downey & Feldman, 1996), yet the degree to which one is high in RS may be particularly important during adolescence. For example, young adolescents who are high in RS are more likely to encounter relationship violence, have low perceptions of self-worth, and experience reduced interpersonal functioning during middle to late adolescence (Ayduk et al., 2000; Purdie & Downey, 2000). Importantly, not all individuals who are high in RS during early adolescence suffer negative outcomes. Research to date has offered two explanations for why this might be the case. The first is that being high in RS may not be detrimental if one possesses other protective factors, such as being highly capable of exerting self-control to delay gratification (Ayduk et al., 2000). Thus, it is possible that the older, high-RS adolescents in the present study have acquired strong self-control skills over the course of adolescence, enabling them to be as effective as their low RS counterparts at regulating affective responses to social stimuli. The second explanation is that positive social experiences, such as being well-liked by one's peers during early adolescence, may actually reduce one's tendency to anxiously expect and perceive rejection in the future (London et al., 2007). Older, high-RS participants in this group may have undergone such experiences and thus reduced their RS tendencies. While the present results suggest an exciting possibility for how age and RS interact over the course of adolescence, we must also consider the possibility that the younger and older

high-RS individuals in this sample differed on a dimension other than age and age-related experiences. In light of this possibility, future studies may seek to employ longitudinal, rather than cross-sectional designs.

Conclusions and Future Directions

Our findings that emotion regulation processes are impacted by age, situational factors, and dispositional differences suggest several directions for future basic and applied research. While the present study used negative photographic stimuli because it allowed us to control the content and intensity of the stimuli, future studies might seek to include a diversity of affective stimuli to further examine how contextual and stimulus-driven factors beyond social content (e.g., appetitive vs. aversive stimuli, low-intensity vs. high-intensity stimuli) impact both emotional reactivity and regulation ability at different points in development. It may be, for example, that adult levels of reappraisal success are reached later for highly arousing emotional stimuli than for moderately arousing emotional stimuli.

Second, the present study differed methodologically from prior field studies by using an experimental laboratory paradigm to assess the development of emotion regulation. Future work might seek to integrate experimental assessments of emotion regulation similar to what we have used in this study with experience sampling, observational, and questionnaire measures used in prior work. Such work could link information about how well adolescents *can* regulate when instructed to do so to information about *whether* they regulate in their everyday lives.

Third, the present study used a cross-sectional design in order to determine which developmental windows were associated with the steepest changes in emotion regulation. While this approach did not allow us to examine within-individual developmental changes,

future work may build on the present findings by examining the same individuals longitudinally. This may be particularly fruitful in early adolescence when situational and individual differences appear to be particularly important for emotion regulation success.

Lastly, the present work gives credence to the notion that early adolescence is a critical developmental window for the acquisition of mature self-regulatory processes. That developmental differences were found in regulation success, but not emotional reactivity, indicates that regulation training may be useful for adolescents in general and may be particularly critical for those who are most at risk for self-regulation failures (e.g., individuals high in RS). This suggests that teaching regulatory skills in a social context and focusing such training on individuals with tendencies to negatively perceive social information may offer a targeted approach for improving wellbeing in adolescence.

Chapter 3: Effects of age and social content on the neural bases of emotion regulation

Introduction

Effective emotion regulation is a critical component of mental and physical health throughout the lifespan. Regulatory failures can be devastating, contributing to impulsivity, poor social functioning and psychiatric symptomology (Denny, Silvers, & Ochsner, 2009; Linehan, 1993; Silvers, Buhle, et al., 2012). Characterizing the neural and developmental bases of emotion regulation may be critical to understanding why regulation sometimes go awry.

In the last ten years, there has been a surge of neuroimaging experiments investigating the neural bases of emotion regulation in healthy adults. Over 50 fMRI studies have been published on a form of emotion regulation called cognitive reappraisal, which involves thinking differently about the meaning of a stimulus so as to alter one's emotional response to it. Reappraisal's popularity in the scientific literature may be attributed to the fact that it is effective, does not negatively impact health like some other strategies, and that it, shares common core principles with several types of therapy (Beck, 2005; Gross, 1998; Linehan, 1993). Across the many reappraisal studies that have been conducted in healthy adults, three consistent findings have been observed: 1) reappraisal effectively modulates affective experience, 2) reappraisal is supported by recruitment of dorsal and lateral prefrontal (PFC) and parietal cortices known to support domain-general cognitive processes such as working memory, attentional control and response inhibition, and 3) reappraisal modulates activity in subcortical structures associated with emotional

responding such as the amygdala (Buhle et al., Submitted; Diekhof et al., 2011; Kalisch, 2009; Ochsner et al., 2012; Silvers, Buhle, et al., 2012).

Cognitive control processes thought to support reappraisal in adults undergo dramatic changes during development. Performance on cognitive control tasks improves throughout childhood and adolescence and these improvements are paralleled by non-linear reductions in gray matter and linear increases in white matter in prefrontal and parietal cortex (Amso & Casey, 2006; Giedd & Rapoport, 2010; Gogtay et al., 2004; Luna, 2009; P. Shaw et al., 2008; Zelazo & Carlson, 2012). Functional neuroimaging data has also demonstrated age-related differences in recruitment of prefrontal and parietal control regions on cognitive control tasks – with some studies reported age-related increases and others reporting decreases (Bunge & Wright, 2007; Pfeifer & Allen, 2012).

In line with the developmental cognitive control literature, older adolescents and young adults use reappraisal more frequently and effectively than do younger adolescents or older children (Fields & Prinz, 1997; Garnefski, Legerstee, Kraaij, Van Den Kommer, & Teerds, 2002; McRae et al., 2012; Silvers, McRae, et al., 2012). Thus far, however, only three studies have examined the neural bases of cognitive reappraisal in children or adolescents. At the group level, these studies have collectively found that children and adolescents can use reappraisal to regulate affective experience and that this relies upon recruitment of dorsal and lateral prefrontal regions commonly observed in adult samples (Levesque et al., 2004; McRae et al., 2012; Pitskel et al., 2011). Within the two studies that examined age effects, one found that age was associated with reduced recruitment of left inferior frontal gyrus (IFG) activity (Pitskel et al., 2011) while the other found that age predicted enhanced recruitment of left IFG (McRae et al., 2012). Though these discrepant findings are on their

face puzzling, they could be at least partially due to the two studies examining different age ranges and sample sizes – Pitskel and colleagues' sample consisted of 15 participants between the ages of 7-17 years while McRae and colleagues' sample consisted of 38 participants between the ages of 10-22 years. These different age effects might also be attributable to the two studies using different types of stimuli – Pitskel and colleagues used disgusting, non-social stimuli while McRae and colleagues used a combination of social and non-social stimuli that evoked a wider range of negative emotions. Additionally, given prior work suggesting that age predicts enhanced recruitment of brain regions that support task performance in adulthood and less recruitment of regions that do not (Durston et al., 2006), it could be that these two studies isolated different portions of left IFG (the cluster reported by McRae was dorsal relative to the cluster reported by Pitskel) that fell under these distinctive categories.

Although the vast majority of emotional experiences in everyday life are caused by social interactions (Scherer & Tannenbaum, 1986), little work has examined the neural bases of regulating emotional responses to social stimuli. The existing literature suggests that regulation of emotional responses to social stimuli is supported by recruitment of left lateral and dorsomedial PFC, yet such inferences are limited because prior work has primarily focused on clinical populations (Goldin, Manber, Hakimi, Canli, & Gross, 2009; Koenigsberg et al., 2009; Koenigsberg, Fan, Ochsner, Liu, Guise, Pizzarello, Dorantes, Guerreri, et al., 2010), individual differences (Vrticka, Bondolfi, Sander, & Vuilleumier, 2012), or has failed to include a non-social control condition (Koenigsberg, Fan, Ochsner, Liu, Guise, Pizzarello, Dorantes, Tecuta, et al., 2010). While no prior work has directly compared the neural bases of reappraisal for social and non-social stimuli in adults and

adolescents, there are at least three reasons to hypothesize that age and social content should differentially impact the neural bases of reappraisal. First, in comparison to adults, adolescents are more sensitive to the influence and presence of peers and show heightened sensitivity to social rejection (R. Larson & M. H. Richards, 1991; Somerville et al., 2010; Steinberg & Morris, 2001). Second, prior behavioral work has suggested that while age predicts improvements in reappraisal ability for both social and non-social stimuli, this occurs more slowly for social emotional stimuli than non-social emotional stimuli (Silvers, McRae, et al., 2012). Third, relative to adults, adolescents show heightened responses to appetitive and aversive social stimuli in subcortical and cortical regions implicated in social cognition and affective processing (Blakemore, 2008; Blakemore & Robbins, 2012).

The present study sought to examine how developing social, emotional and control processes interact at the neural level to support reappraisal during adolescence. To achieve this goal, functional neuroimaging data was collected on individuals aged 10-22 years as they completed a reappraisal task involving both social and non-social stimuli. This paradigm allowed for assessment of the relative impact of valence and social content on brain activity associated with emotional reactivity as well as reappraisal.

Methods

Participants. Participants consisted of 58 healthy volunteers between the ages of 10-22 years (31 female; mean age = 16.3 years, S.D.= 3.9). Three of these participants were excluded from analyses due to excessive head motion resulting in a final sample of 55 individuals (30 female; mean age = 16.5 years, S.D.= 3.85). Participants were prescreened prior to participation to ensure that they could read and write in English, had normal or corrected vision, had never been diagnosed with a developmental or psychiatric disorder,

had never been prescribed psychotropic medication and did not have any conditions contraindicated for MRI scanning. Participants completed the Wechsler Abbreviated Scale of Intelligence (M=112, SD=14.4). The relationship between age and estimated full-scale IQ scores was not significant (r=.21, *p*=.12).

Experimental procedure. The task was identical to that used in Study 1 (Figure 2.1). Prior to performing the task, participants were trained extensively on the immersed ('close') and distanced ('far') strategies in accordance with well-validated procedures for this age range (Silvers, McRae, et al., 2012). On 'close' trials, participants were told to imagine standing close to the scene depicted in the photograph and to allow themselves to experience any emotions that the photograph evoked. On 'far' trials, participants were told to imagine standing further away from the scene and to focus more on the facts of the photograph than on its emotional details. While participants were not told so, 'close' trials were used to assess baseline emotional reactivity whereas 'far' trials were used to assess regulation ability.

Stimuli were drawn from the International Affective Picture System (Lang, Bradley, & Cuthbert, 2001) and from a set of similar pictures that had been previously used with participants in this age range (Silvers, McRae, et al., 2012). Participants between the ages of 18-22 all saw the same set of 120 stimuli. Parents of participants under the age of 18 prescreened one hundred negative photographic stimuli (50 social, 50 non-social) prior to participation. Parents were permitted to exclude up to 10 social and 10 non-social stimuli. From this pool of approved pictures, 60 aversive stimuli (30 social and 30 non-social) that were closely were used for the experimental task. If parents rejected images that were part

of the stimulus set used for adults, those images were replaced with approved images that were closely matched for valence. All participants saw the same set of 60 neutral stimuli.

Each trial began with participants seeing a cue word ('close' or 'far') for 2 seconds. After this, participants used the strategy indicated by the cue word while viewing a photographic stimulus for 8 seconds. A jittered interstimulus interval (averaging 3 seconds) appeared next, followed by a rating screen. On the rating screen, participants rated their current negative affect on a five-point scale (1=not feeling badly at all, 5=feeling very badly) via button press and this was followed by another jittered interstimulus interval (averaging 3 seconds).

All participants completed 120 experimental trials. Conditions differed in terms of stimulus valence (negative or neutral), social content (social or non-social), and regulation instruction (close or far) for a total of 8 condition types. The assignment of pictures to instruction was counterbalanced between participants.

Scanning acquisition. Whole-brain fMRI data were acquired on a 1.5T GE Signa Twin Speed Excite HD scanner (GE Medical Systems). Functional images were acquired with a T2*-sensitive EPI BOLD sequence. Twenty-eight axial slices were collected with a TR of 2000 ms (TE of 34 ms, flip angle of 84°, field of view of 22.4 cm and 3.5 x 3.5 x 4 mm voxels). High-resolution SPGR structural images were collected with a TR of 19 ms (TE of 5 ms, flip angle of 20°, field of view of 25.6 cm). Stimuli were presented using E-Prime. Stimuli were displayed using an LCD projector and a back-projection screen mounted in the scanner suite. Participants made their responses using a five-finger-button-response unit with a molded hand brace (Avotec Inc. and Resonance Technologies).

Behavioral data analysis. Behavioral data were analyzed in SPSS 19.0 (t-tests, repeated-measures ANOVA) and Matlab (robust regression). Robust regression assigns weights to datapoints such that outliers are weighed less strongly than data that fits the group-level pattern. This was used in regressions that contained age as a predictor.

fMRI analysis. Preprocessing was performed using SPM5 preprocessing tools (Wellcome Department of Cognitive Neurology, UCL) implemented in NeuroElf (http://neuroelf.net). Functional images were slice-time and motion corrected and structural images were coregistered to the first functional image for each subject using an iterative procedure of automated registration using mutual information coregistration. Structural images were normalized (spatially warped) to a standard template brain (the MNI avg15T1.img) using SPM5's default options (7 x 8 x 7 nonlinear basis functions) and warping parameters were applied to functional images for each subject. Normalized functional images were interpolated to 3 x 3 x 3 mm voxels and spatially smoothed with a 6-mm Gaussian filter. Runs were excluded from further analyses if participants exhibited more than 2 millimeters of head motion in any direction. This resulted in the removal of three participants.

First and second-level GLM analyses were implemented in NeuroElf (http://neuroelf.net). Cue, stimulus-viewing and response portions of each trial were modeled as boxcar regressors convolved with a canonical hemodynamic response function. Separate regressors were made for the eight different trial types so that neural responses associated with strategy (close vs. far), valence (negative vs. neutral), and social content (social vs. non-social) could be differentiated. For each subject, a robust regression analysis was performed on the conditions of interest. Motion parameters, high-pass filter

parameters and an estimate of the subject's global signal in white matter were included as regressors of no interest. Next, a second-level random effects analysis was performed to identify regions of activation at the group level. Significant voxels were identified using joint voxel and extent thresholds (corresponding to a corrected $p<.05$) as determined by AlphaSim, implemented in NeuroElf. Neuroimaging analyses focused on the portion of the trials when the picture was on the screen and participants were implementing the "close" or "far" strategy.

Two group-level analyses were performed. First, to identify brain regions involved in emotional reactivity, a whole-brain contrast was performed comparing the close negative and close neutral conditions. Amygdala clusters identified in this contrast were then further interrogated offline to determine whether social content differentially impacted amygdala responses to negative and neutral stimuli. Robust regression was used offline to examine whether age predicted amygdala beta values for this contrast. A whole-brain robust correlation was also performed to test whether age predicted activity in any brain regions not identified in the reactivity contrast.

The second main analysis identified brain regions involved in emotion regulation by comparing the far negative and close negative conditions (collapsed across the social and non-social conditions). Clusters in the right superior frontal gyrus and left inferior frontal gyrus were identified in this contrast and were submitted to a repeated measures ANOVA offline to determine whether social content, strategy and location (i.e., the two regions of interest) differentially predicted neural recruitment. Next, robust regression analyses were performed using the betas extracted from these two clusters of interest as dependent variables. Because age and regulation success were highly correlated, both were used as

predictors in these regression analyses, along with their interaction term. To test whether age or regulation success predicted activity in any brain regions not identified in the regulation contrast, whole-brain regressions for social and non-social stimuli using the same predictors were also performed.

Results

Behavioral results. Behavioral data was first examined at the group level and was subsequently analyzed for age-related effects.

Group results. A full factorial repeated-measures ANOVA was performed using social content (social, non-social), strategy (close, far), and valence (neutral, negative) as factors and negative affect as the dependent variable. All main effects and interactions were found to be significant (p<.005). In line with hypotheses, negative stimuli elicited more negative affect than neutral stimuli (F(1,54)=712.85, p<.001), and social stimuli elicited more negative affect than non-social stimuli (F(1,54)=40.38, p<.001). The far strategy was effective at reducing negative affect relative to the close strategy (F(1,54)=78.74, p<.001), particularly for negative stimuli (F(1,54)=75.00, p<.001). Participants showed greater decreases in negative affect when reappraising non-social stimuli than social stimuli (F(1,54)=16.95, p<.001).

Interactions between age and social content. To assess for age effects, age was added to the above repeated-measures ANOVA as a covariate. A significant interaction was observed between age and strategy (F(1,53)=4.30, p=.04), and a marginal interaction was observed between age, strategy and valence (F(1,53)=2.94, p=.09). Means for each age in the close and far conditions for negative and neutral stimuli is shown in Figure 3.1.

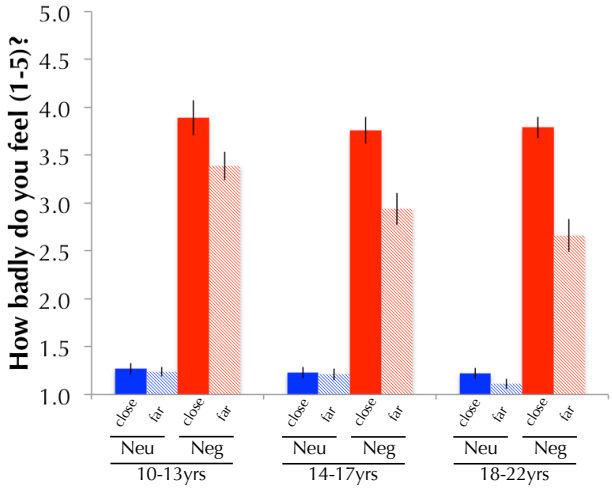

Figure 3.1. Mean negative affect as a function of strategy and valence. All statistical analyses were performed using continuous measures of age. For visual purposes, task effects are shown as a function of three discrete age categories.

To unpack these effects, emotional reactivity and regulation success scores were calculated for each participant and follow-up robust correlations with age were performed. Emotional reactivity ([close negative – close neutral]/close neutral x 100) was defined as the percent increase in negative affect observed on close negative trials in comparison to close neutral trials and regulation success was defined as the percent decrease in negative affect observed on far negative trials in comparison to close negative trials ([close negative – far negative]/close negative x 100). Age did not correlate with emotional reactivity for social (r=.09, p=.50) or non-social stimuli (r=.03, p=.83) but correlated positively with regulation success for social stimuli (r=.31, p<.05) and showed a marginal effect with non-social stimuli (r=.25, p=.07; Figure 3.2). The relationship between age and regulation success was driven by the far negative condition for both social (r=-.27, p<.05) and non-social stimuli (r=-.27, p<.05) and not the close negative condition (p's>.41). Given the possibility of non-linear age effects in this developmental sample, linear and quadratic

models were fit to estimate the relationship between age and regulation success and were compared using the extra-sum-of-squares F test to assess model fit (Motulsky & Christopoulos, 2004). This revealed that the relationship between age and regulation success was best fit using a linear model for both social and non-social stimuli.

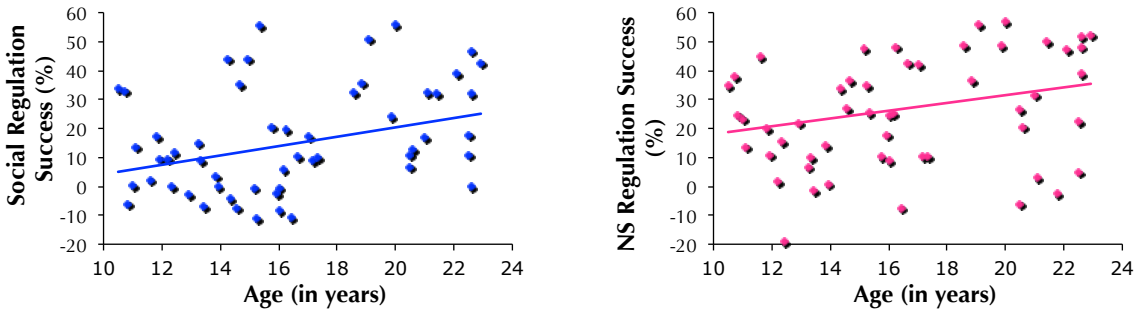

Figure 3.2. Regulation success as a function of age for social and non-social stimuli.

Imaging results. Imaging data was first examined to identify brain regions associated with emotional reactivity and second, to identify brain regions associated with regulation. Within each phase of analyses, main effects are presented first followed by those associated with age.

Reactivity analyses. Examination of the emotional reactivity contrast (close negative > close neutral) suggested that negative stimuli recruited emotional processing regions such as the amygdala, periaqueductal gray, and anterior insula to a great extent than neutral stimuli (Table 3.1). Additional clusters were identified in bilateral lateral prefrontal, occipital and parietal cortex.

				MNI Coordinates		
Region	Side	Extent	t-value	x	y	z
Inferior frontal gyrus	Left	350	5.09	-48	3	30
Inferior frontal gyrus	Left	LM	3.43	-54	30	24
Middle frontal gyrus	Left	LM	5.05	-33	-3	45
Inferior frontal gyrus	Right	4193	7.24	42	6	24

Orbitofrontal cortex	Left	LM	4.32	-24	12	-27
Orbitofrontal cortex	Right	LM	3.55	6	12	-21
Cingulate gyrus	Left	LM	4.21	-9	30	30
Cingulate gyrus	Left	LM	4.7	-3	9	24
Cingulate gyrus	Right	LM	4.89	3	24	33
Cingulate gyrus	Right	LM	5.33	3	18	21
Medial frontal gyrus	Left	LM	4.82	-9	51	18
Medial frontal gyrus	Right	LM	5.58	3	51	27
Medial frontal gyrus	Right	LM	6.63	6	15	54
Superior frontal gyrus	Right	LM	5.25	6	51	36
Inferior frontal gyrus	Right	LM	6.17	33	24	-15
Middle frontal gyrus	Right	LM	6.55	39	3	42
Inferior frontal gyrus	Right	LM	6.97	42	21	15
Inferior frontal gyrus	Right	LM	6.12	48	18	0
Anterior insula	Left	LM	3.43	-51	15	-3
Anterior insula	Left	LM	4.15	-30	24	3
Anterior insula	Left	LM	5.58	-30	18	-15
Anterior insula	Right	LM	4.84	30	24	3
Temporal pole	Left	LM	4.81	-48	18	-18
Caudate	Left	LM	4.75	-9	12	9
Caudate	Right	LM	5.3	9	9	9
Putamen	Right	LM	4.24	30	9	-6
Extended amygdala	Left	LM	4.24	-30	3	-15
Amygdala	Left	LM	4.79	-27	-6	-21
Amygdala	Left	LM	5.61	-18	0	-18
Amygdala	Right	LM	5.44	21	-6	-18
Amygdala	Right	LM	4.98	30	-3	-18
Midbrain	Left	LM	4.73	-18	-18	-9
Midbrain	Left	LM	4.31	-6	-30	-18
Midbrain	Medial	LM	4.2	0	-12	-18
Midbrain	Right	LM	3.8	3	0	-15
Midbrain	Right	LM	5.36	3	-33	-3
Midbrain	Right	LM	4.66	6	-15	-9
Hippocampus	Left	LM	5.28	-24	-30	-3
Hippocampus	Right	LM	4.81	24	-33	6
Hippocampus	Right	LM	6.04	30	-24	-6
Parahippocampal gyrus	Left	LM	5.97	-33	-18	-15
Thalamus	Left	LM	5.13	-6	-6	0
Thalamus	Right	LM	5.14	6	-18	12
Thalamus	Right	LM	5.38	15	-30	0
Superior parietal lobule	Left	655	8.77	-30	-48	45
Superior parietal lobule	Left	LM	4.70	-51	-36	54
Inferior parietal lobule	Left	LM	4.73	-66	-39	33
Inferior parietal lobule	Left	LM	4.84	-54	-33	39
Inferior parietal lobule	Left	LM	6.37	-45	-36	33
Superior parietal lobule	Right	431	9.26	33	-51	51

Middle occipital gyrus	Left	1487	10.15	-45	-81	-3
Middle occipital gyrus	Left	LM	9.02	-48	-69	3
Fusiform gyrus	Left	LM	8.06	-42	-45	-21
Inferior occipital gyrus	Left	LM	6.66	-42	-75	-15
Inferior occipital gyrus	Left	LM	6.96	-30	-87	-6
Cerebellum	Left	LM	7.15	-45	-60	-24
Cerebellum	Left	LM	4.23	-9	-81	-30
Middle occipital gyrus	Right	2018	10.72	45	-63	0
Parieto-occipital sulcus	Right	LM	3.75	30	-69	27
Superior occipital gyrus	Right	LM	7.83	33	-87	0
Superior temporal gyrus	Right	LM	4.69	51	-45	21
Fusiform gyrus	Right	LM	9.24	42	-54	-15
Fusiform gyrus	Right	LM	8.20	45	-39	-18
Medial frontal gyrus	Right	132	-5.06	6	51	-12
Medial frontal gyrus	Left	LM	-4.37	-9	48	-12
Medial frontal gyrus	Right	LM	-3.83	12	39	-12
Cingulate gyrus	Right	943	-7.35	12	0	39
Cingulate gyrus	Left	LM	-5.60	-12	3	42
Cingulate gyrus	Right	LM	-6.78	12	-9	45
Posterior cingulate gyrus	Medial	LM	-5.60	0	-36	36
Posterior cingulate gyrus	Right	LM	-5.23	9	-27	48
Posterior cingulate gyrus	Right	LM	-4.09	18	-33	45
Precentral gyrus	Left	LM	-4.17	-48	-15	45
Precentral gyrus	Right	LM	-4.34	24	-15	63
Central sulcus	Left	LM	-4.66	-33	-18	42
Central sulcus	Left	LM	-5.30	-3	-18	54
Postcentral gyrus	Left	LM	-4.99	-24	-30	57
Postcentral gyrus	Right	LM	-4.20	24	-30	57
Cuneus	Right	3932	-10.79	12	-57	9
Cuneus	Left	LM	-7.94	-21	-63	15
Cuneus	Left	LM	-7.83	-12	-66	15
Cuneus	Left	LM	-7.82	-6	-75	18
Cuneus	Right	LM	-5.61	15	-84	21
Anterior insula	Right	LM	-3.86	33	12	9
Lateral fissure	Right	LM	-4.72	57	0	9
Parahippocampal gyrus	Right	LM	-4.35	15	-21	-24
Middle temporal gyrus	Left	LM	-5.14	-69	-42	-9
Superior temporal gyrus	Left	LM	-5.21	-63	-27	3
Superior temporal gyrus	Left	LM	-6.13	-57	-15	6
Superior temporal sulcus	Left	LM	-4.82	-48	-36	6
Superior temporal gyrus	Right	LM	-4.13	57	-27	12
Superior temporal gyrus	Right	LM	-5.68	63	-15	3
Posterior insula	Left	LM	-5.71	-33	-18	21
Posterior insula	Left	LM	-4.63	-30	-33	18
Posterior insula	Right	LM	-5.87	42	-30	15
Fusiform gyrus	Left	LM	-8.25	-27	-48	-9

Fusiform gyrus	Right	LM	-7.9	27	-54	-12
Lingual gyrus	Left	LM	-7.96	-12	-63	6
Lingual gyrus	Left	LM	-7.56	-9	-54	0
Lingual gyrus	Right	LM	-7.75	9	-72	-6
Parieto-occipital sulcus	Left	135	-5.23	-36	-75	33
Parieto-occipital sulcus	Right	68	-4.79	42	-72	39

Table 3.1. Brain regions associated with emotional reactivity (close negative > close neutral contrast). Clusters responding more strongly on close negative trials than close neutral trials are presented first (positive t values). Local maxima with 10 or more voxels are indicated by "LM" under the Extent column.

Amygdala responses were examined using a repeated-measures ANOVA to assess whether responses varied as a function of social content and valence. Responses in the left (-18, 0, -18) and right amygdala (21, -6, -18) were highly correlated (r=.67, p<.001) and were thus collapsed in all subsequent analyses. Significant main effects of social content (F(1,54)=6.39, p=.014) and valence (F(1,54)=48.9, p<.001) were identified such that social stimuli and negative stimuli elicited more activation than non-social stimuli or neutral stimuli. An interaction between social content and valence (F(1,54)=14.58, p<.001) revealed that amygdala recruitment was significantly greater for neutral social, but not neutral non-social stimuli (Figure 3.3).

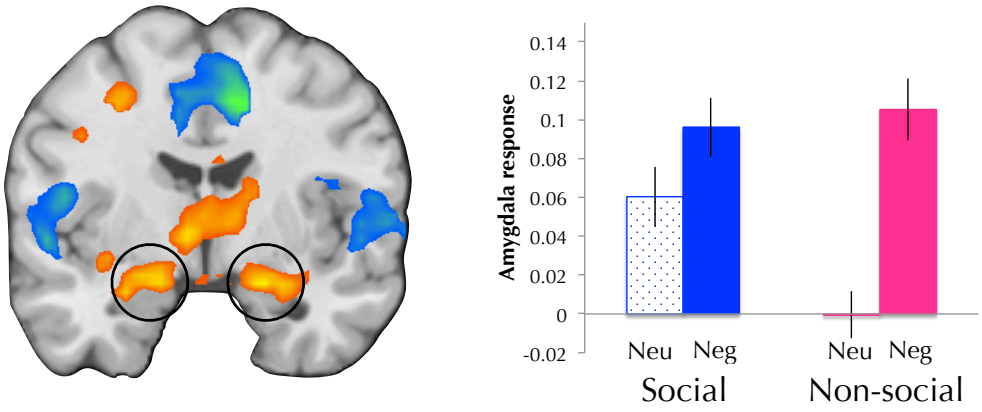

Figure 3.3. Amygdala response as a function of social content and valence.

In the next phase of analyses, amygdala beta values correlated robustly with age. Age did not predict amygdala responses for social (r=-.04, *p*=.77) or non-social stimuli (r=.07, *p*=.61). Age did not predict activity in any other brain regions identified in the reactivity contrast. A whole-brain robust correlation between the reactivity contrast and age revealed that age predicted increased recruitment of dorsal ACC for social stimuli (r=.47, *p*<.001) but not for non-social stimuli (r=.11, *p*=.36).

Regulation analyses. The emotion regulation contrast (far negative > close negative) revealed recruitment of right superior frontal gyrus (SFG), the left inferior frontal gyrus (IFG), and bilateral posterior parietal cortex (Table 3.2). Additional clusters were observed in posterior temporal cortex and the posterior cingulate gyrus.

				MNI Coordinates		
Region	Side	Extent	t-value	x	y	z
Inferior frontal gyrus	Left	70	4.10	-60	21	6
Inferior frontal gyrus	Left	LM	3.93	-45	24	18
Superior frontal gyrus	Right	112	5.46	21	30	42
Middle temporal gyrus	Left	136	5.02	-51	-42	0
Superior temporal sulcus	Left	LM	4.72	-54	-33	0
Middle temporal gyrus	Left	LM	4.12	-54	-45	-12
Middle temporal gyrus	Right	70	4.30	69	-45	-6
Posterior cingulate gyrus	Right	151	4.79	9	-57	15
Precuneus	Right	LM	3.47	6	-51	39
Parieto-occipital sulcus	Left	522	5.41	-33	-75	42
Angular gyrus	Left	LM	5.10	-42	-63	30
Superior parietal lobule	Left	LM	4.98	-42	-81	30
Superior parietal lobule	Right	345	5.39	45	-75	39
Superior parietal lobule	Right	LM	4.63	57	-63	30

Table 3.2. Brain regions associated with emotion regulation. Activity in all clusters listed above was greater for far negative trials than close negative trials.

ROIs in the right SFG and the left IFG were interrogated using a repeated-measures ANOVA to determine whether social content (social vs. non-social), strategy (close vs. far), and location (right SFG vs. left IFG) differentially predicted recruitment. Results revealed significant main effects of social content ($F(1,54)=43.36$, $p<.001$), strategy ($F(1,54)=113.38$, $p<.001$), and location ($F(1,54)=12.22$, $p=.001$). Social stimuli, the far condition and left IFG were associated with greater activation than non-social stimuli, the close condition and right SFG, respectively. Additionally, a 2-way interaction was observed between strategy and location ($F(1,54)=4.82$, $p=.03$), and a 3-way interaction was observed between strategy, location and social content ($F(1,54)=5.21$, $p=.03$). Follow-up t-tests revealed that reappraisal of social stimuli more strongly recruited left IFG than reappraisal of non-social stimuli, while reappraisal of non-social stimuli more strongly recruited right SFG than reappraisal of social stimuli (Figure 3.4).

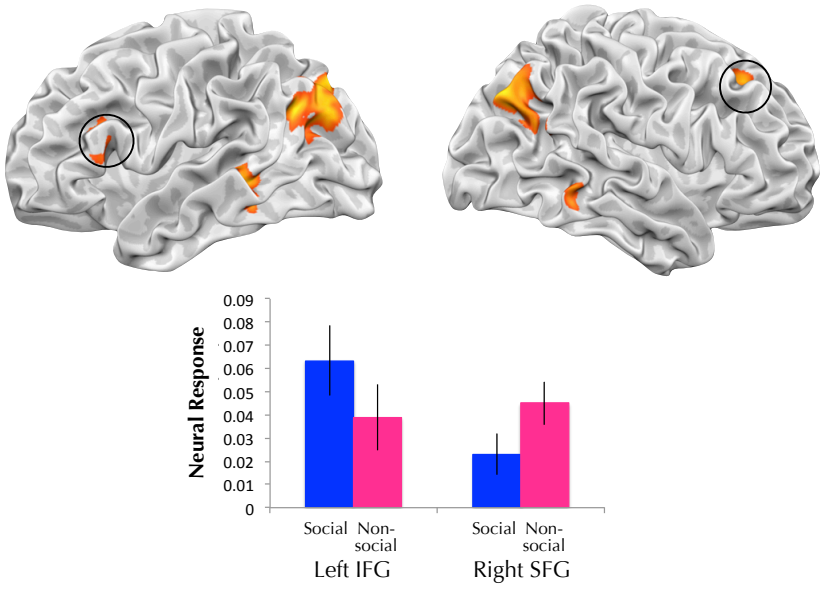

Fig 3.4. Contrast values for the regulation contrast are plotted as a function of cluster and social content.

Whole-brain contrasts examining regulation (far negative > close negative) did not reveal differential modulation of the amygdala. To test whether reappraisal modulated activity in amygdala voxels that support the experience of negative emotion, beta values were extracted from the amgydala ROI identified in the reactivity contrast. These values were then subjected to a repeated-measures ANOVA to examine the effects of strategy (close vs. far) and social content (social vs. non-social). This revealed a main effect of strategy ($F(1,54)=4.15$, $p<.05$), whereby reappraisal significantly reduced amgydala responses, but no effect of social content ($F(1,54)=.007$, $p=.93$) and no interaction between strategy and social content ($F(1,54)=.09$, $p=.77$).

Given that age and regulation success were highly correlated, both were used as predictors in multiple regression analyses in order to determine the relative effects of both variables. To investigate the possibility that regulation success may be supported by different brain regions at different ages, the interaction between age and regulation success was added as a third predictor in these regression analyses. Because the results of the analysis above suggested that the left IFG was particularly critical for reappraisal of social stimuli and right SFG for reappraisal of non-social stimuli, analyses for each region focused on the respective class of stimuli relevant to it. Regulation success ($\beta=.009$, $t(51)=.2.20$, $p=.03$), but not age ($\beta=.0008$, $t(51)=.16$, $p=.88$), predicted left IFG recruitment during reappraisal of social stimuli. An interaction was observed between age and regulation success ($\beta=-.0004$, $t(51)=-1.99$, $p=.05$) such that regulation success was more strongly associated with left IFG recruitment at younger ages than at older ages (Figure 3.5). Age predicted less activity in right SFG ($\beta=-.01$, $t(51)=-2.25$, $p=.03$) for reappraisal of non-social stimuli (Figure 3.6). No relationship was found between regulation success and right SFG

recruitment, nor was there an interaction between age and regulation success (*p's*>.15). Neither age nor regulation success predicted amygdala modulation for social or non-social stimuli (*p*'s>.12).

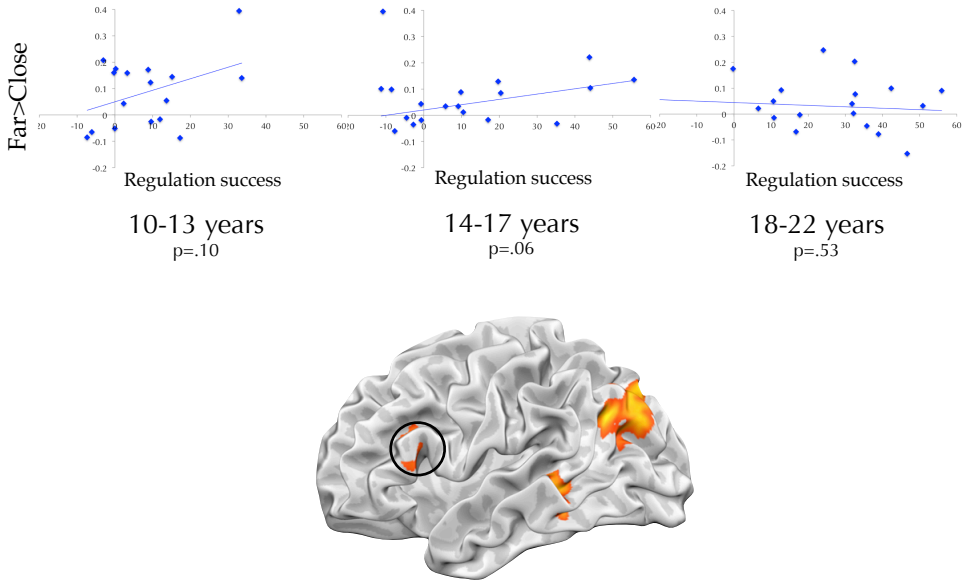

Figure 3.5. Recruitment of left IFG differs as a function of regulation success and age for regulation of social stimuli. All analyses were conducted using continuous measures of age but age is shown categorically for visual purposes.

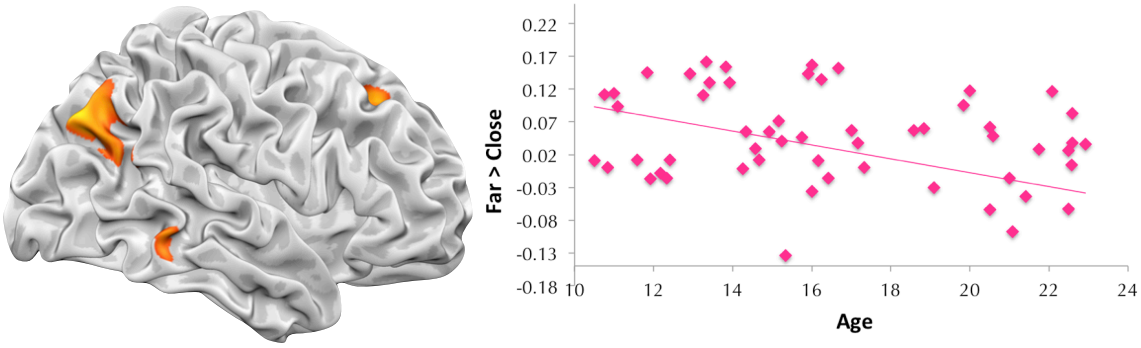

Figure 3.6 Age predicts less recruitment of right SFG during reappraisal of aversive non-social stimuli.

In the final analysis, whole-brain robust regression analyses using age, regulation success and their interaction term were performed on the regulation contrasts for the social and non-social negative stimuli. Both reappraisal success and age predicted enhanced recruitment of distinct portions of right dorsolateral PFC (dlPFC) for social stimuli. An interaction was also observed in the cluster that was correlated with regulation success, such that recruitment of this region at younger ages predicted greater regulation success than at older ages. No additional clusters were revealed for the whole-brain regression for non-social stimuli.

Discussion

Adolescence is a time when individuals acquire social and self-regulatory skills that will serve them throughout the rest of their adult lives. Yet, little work has examined how social processing and emotion regulation interact over the course of adolescent development. Additionally, while prior work has suggested that age predicts reappraisal success in adolescence, no prior studies have examined how age and reappraisal success independently contribute to the neural bases of reappraisal. With these points in mind, three key findings were observed for the present study. First, in line with prior work, age predicted differences in top-down regulation, but not bottom-up emotional reactivity. Second, at the group level, social content interacted with task to predict differential recruitment of subcortical and cortical regions involved in emotion generation and regulation. Third, age-related changes in prefrontal recruitment differed as a function of reappraisal success and stimulus social content.

Age predicts differences in regulation, not emotional reactivity. The present study found that age predicted enhanced regulation success and differential patterns of

prefrontal recruitment, but not differences in self-reported emotional reactivity or amygdala recruitment. Taken together, this suggests that baseline emotional reactivity does not change over the course of adolescence but that the ability to exert top-down control over one's emotional experiences does. At first glance, it is somewhat surprising that age did not predict amygdala responses in the reactivity contrast given prior work showing that adolescents hyperengage the amygdala in comparison to adults when viewing emotional stimuli (Guyer et al., 2008; Monk et al., 2003). However, unlike these prior studies, the present study did not use a "passive viewing" or "respond naturally" condition, and instead sought to examine emotional reactivity by asking participants to immerse themselves in the affective stimuli on 'close' trials. Thus, it may be that when adolescents and adults respond without instruction to affective stimuli, they adopt different approaches but when attention is constrained, such as it was on 'close' trials, age-related differences are no longer apparent. Study 3 in the present manuscript examined this possibility. Another possibility, however, is that the type of stimuli used in an emotional task can significantly impact age-related effects in the amygdala. Most prior work examining age-related differences in passive viewing of emotional stimuli has used emotional facial expressions while the present study used emotionally evocative scenes (i.e., pictures from the IAPS and related types of stimuli). Indeed, prior work examining naturalistic emotional responses to IAPS stimuli failed to observe age-related differences in amygdala responding, further supporting this possibility (McRae et al., 2012; Pitskel et al., 2011). In line with prior work, the results of the present study indicate that regulation success tracks positively with age (McRae et al., 2012; Silvers, McRae, et al., 2012). This developmental pattern is comparable to what has observed in prior work examining the development of

"cold", or unemotional, cognitive control (Luna et al., 2004). At the group level, reappraisal recruited left IFG and right SFG and attenuated activity in the amygdala. Like prior work examining reappraisal in this age range, amygdala attenuation did not vary as a function of age, while recruitment of prefrontal regions did (McRae et al., 2012). Yet, the exact pattern of age-related effects differed in accordance with prefrontal region and the social content of emotional stimuli. While age predicted decreased recruitment in right SFG, a more complex interaction between age and regulation success predicted recruitment of left IFG.

Social content influences emotion generation and regulation

The present findings suggest that emotional responses to social and non-social stimuli differ at both behavioral and neural levels during adolescence. Social stimuli elicited more negative affect at the group level, and as a group participants were less effective at reappraising these stimuli in comparison to non-social stimuli. This sensitivity to social content extended even to neutral social stimuli, as evidenced by the fact that amygdala responses were elevated for neutral social stimuli but not neutral non-social stimuli. While such effects have been observed in healthy adults (Norris, Chen, Zhu, Small, & Cacioppo, 2004), the present study is the first to examine such social-emotional interactions in a developmental sample. While one prior study has examined the neural bases of reappraisal for social and non-social stimuli in healthy adults, that study focused primarily on brain regions that were modulated by reappraisal rather than examining brain regions that support reappraisal (Vrticka, Sander, & Vuilleumier, 2011).

The present results suggest that reappraisal of social stimuli relies more heavily on recruitment of left IFG while reappraisal of non-social stimuli relies more heavily on recruitment of right SFG. Left IFG is known to support semantic processing, working

memory and response selection in language and executive function tasks (Badre & Wagner, 2007; Hinke et al., 1993; Thompson-Schill et al., 2005). It is among the most commonly recruited brain regions observed in reappraisal paradigms where it is thought assist in holding and manipulating reappraisals in working memory and in selecting goal-congruent appraisals (Buhle et al., Submitted; Diekhof et al., 2011; Silvers, Buhle, et al., 2012). Right SFG, on the other hand, is only rarely observed in studies of reappraisal in adults (Buhle et al., Submitted; Diekhof et al., 2011; Kalisch, 2009), suggesting that its recruitment in the present study may be related to the participants' age.

Age, social content and task performance interact to predict prefrontal recruitment. While social content impacted emotional reactivity at the group level, interactions between age and social content were only observed when participants attempted to regulate their emotional responses. At the group level, left IFG was found to be more critical for regulation of social emotional responses than non-social responses while the reverse was observed in right SFG. Interestingly, the age effects observed in these regions were quite different.

No direct relationship was observed between age and left IFG activation, yet an intriguing interaction between reappraisal success and age was observed such left IFG recruitment was associated with better reappraisal success for individuals at the beginning and middle, but not the end, of adolescence. While other reappraisal studies have found age-related decreases and increases in left IFG recruitment (McRae et al., 2012; Pitskel et al., 2011), no prior work has examined controlled for differences in task performance while doing so. Prior work has shown that for children, but not adults, task performance predicts increased recruitment of left IFG on cognitive control tasks such as the Flanker (Bunge et

al., 2002). Given left IFG's role in language and semantic processing (Dronkers, 1996; Hinke et al., 1993; Huang et al., 2002), this may suggest that younger individuals rely more heavily upon internal speech to successfully guide reappraisal of social stimuli than do older individuals.

At the group level, right SFG was recruited more strongly during reappraisal of non-social stimuli than social stimuli but age predicted decreased recruitment of this region, even when controlling for differences in task performance. Prior work has suggested that prefrontal recruitment becomes less diffuse and more focal with age, such that structures that support task performance in adulthood show increased activity while others show less activity (Durston et al., 2006). Other tasks examining cognitive processes such as inhibitory control, working memory and visuospatial processing have found age-related decreases in the right SFG, similarly to what was observed in the present study (P. J. Eslinger et al., 2009; Libertus, Brannon, & Pelphrey, 2009; Velanova, Wheeler, & Luna, 2008, 2009). This taken together with the fact that this region has not been strongly implicated in reappraisal studies of adults (Buhle et al., Submitted; Diekhof et al., 2011; Kalisch, 2009), suggests that younger adolescents may recruit this region to compensate for immature prefrontally-mediated cognitive control processes.

Limitations and future directions. The results of the present study suggest that regulation success, but not emotional reactivity, increases with age during adolescence and that developing prefrontal systems support these improvements. As prior behavioral work has suggested (Silvers, McRae, et al., 2012), the present results indicate that social content and age interact to predict differences in emotion regulation. While these findings are exciting, there are at least three limitations that ought to be noted with regards to the

present methods and results. First, the present study focused exclusively on individuals at the beginning, middle and end of adolescence. Although primarily linear age effects were identified in this age range, it is unknown whether additional non-linear effects may be observed if the age range was extended to include younger children. Second, although most reappraisal studies conducted in adult samples use a "respond naturally" instruction as an emotional baseline, participants in the present study were instructed to immerse themselves in the stimuli on the baseline 'close' trials. This was done to constrain attention, to encourage participants to approach the two conditions as similarly as possible, and to ensure that any fMRI activations observed were not due simply to comparing a task condition to an absence of task condition. However, this leaves open the possibility that the 'close' condition actually increased negative affect in reference to participants' "true" affective baseline. In order to investigate this, future studies ought to directly compare 'close' and 'far' trials to a naturalistic response condition. Lastly, the present study induced affective experience using photographic stimuli. While self-report confirms that these stimuli were effective at eliciting emotional responses, additional research is needed to determine whether these same results generalize to other, more emotionally potent stimuli such as memories or personalized vignettes.

Chapter 4: Regulation of social emotional responses in childhood and adolescence

Introduction

We humans are social creatures. Given this, it is perhaps unsurprising that our relationships with other humans are the most common causes of emotional experiences in our everyday lives (Scherer & Tannenbaum, 1986). Although social interactions are important throughout the lifespan, the way in which we respond to social emotional situations changes dramatically with age. Prior work has suggested that young adults are better than adolescents at regulating their emotional responses to social stimuli (Silvers, McRae, et al., 2012), but it is presently unknown how this ability develops across a wider age span and what neural mechanisms support this change.

Although only a handful of neuroimaging studies have investigated the neural bases of emotion regulation in developmental populations, dozens have examined emotion regulation in adults. The most commonly studied emotion regulation strategy is reappraisal, which involves changing one's interpretation or appraisal of a stimulus so as to alter its emotional impact. Reappraisal has been widely studied in neuroimaging contexts for three key reasons: (1) understanding the mechanisms that underlie reappraisal has clinical value given that reappraisal is frequently taught in therapies such as cognitive behavioral therapy (Beck, 2005), (2) reappraisal is highly effective and, unlike other strategies such as suppression, it does not lead to negative physiological consequences (Gross, 1998), and (3) it can be easily taught and implemented in a neuroimaging environment. In adults, reappraisal robustly recruits prefrontal and parietal regions known to support domain-general cognitive control processes (Duncan & Owen, 2000; Miller,

2000; Miller & Cohen, 2001). Such findings have fueled models of reappraisal that suggest that (1) dorsolateral (dlPFC) and parietal cortex, regions known to support selective attention and working memory, may be critical for holding reappraisals in working memory, (2) ventrolateral prefrontal cortex (vlPFC), a region involved in language and response selection, may facilitate semantic processing and choosing appropriate reappraisals, and, (3) dorsomedial prefrontal cortex (dmPFC), a region relevant to reflecting on mental states, may be recruited to assist in reinterpreting the meaning of changing emotional states (Ochsner & Gross, 2005, 2008; Ochsner et al., 2012). Reappraisal has also been shown to modulate activity in the amygdala (Diekhof et al., 2011; Kalisch, 2009; Ochsner et al., 2012), a subcortical structure located in the medial temporal lobes that is relevant for detecting, learning about, and coordinating appropriate responses to affectively salient stimuli (Cunningham & Brosch, 2012; Garnefski, Rieffe, Jellesma, Terwogt, & Kraaij, 2007; Ochsner & Gross, 2005; Whalen, 1998). When individuals reappraise to increase negative affect, amygdala responses tend to increase, whereas when individuals reappraise to decrease negative affect, amygdala responses tend to decrease (Eippert et al., 2007; Leiberg, Eippert, Veit, & Anders, 2012; Ochsner et al., 2004).

The ability to perceive, interpret and respond to social emotional information is a critical skill for humans and relies on a complex and interconnected set of brain regions. Interpreting social information requires brain regions such as the medial prefrontal cortex (MPFC) and posterior temporal and parietal regions known to support social cognition, while generating emotional responses to such information may rely upon recruitment of brain regions involved in forming affective appraisals such as the amygdala (Adolphs, 1999; Frith & Frith, 2007; Olsson & Ochsner, 2008). While much work has examined

socioemotional processes and emotion regulation in isolation, little work has examined them in concert. Preliminary findings from two studies suggest that, like other variants of reappraisal, reappraising socioemotional stimuli recruits dlPFC and modulates amygdala responses (Koenigsberg, Fan, Ochsner, Liu, Guise, Pizzarello, Dorantes, Tecuta, et al., 2010; Vrticka et al., 2012). Intriguingly, one of these studies additionally found that reappraisal modulated brain regions commonly implicated in social cognition and mentalizing such as medial PFC and posterior cingulate cortex (Vrticka et al., 2011). Taken together, this suggests that reappraisal of socioemotional stimuli relies upon interactions between brain structures implicated in cognitive control, social cognition and emotion.

The social landscape changes dramatically during adolescence and with these changes comes a growing need for self-regulation in social contexts. Yet, learning to effectively self-regulate in social situations does not occur overnight. Adolescents are more sensitive to peer influence, and show heightened sensitivity to social rejection and social evaluation than are adults (R. Larson & M. H. Richards, 1991; Somerville et al., 2010; Steinberg & Morris, 2001). These age differences may be observed not only in behavior but also in the brain. In comparison to adults, adolescents show heightened responses to social stimuli in subcortical and cortical regions implicated in social cognition and affective processing (Blakemore, 2008; Blakemore & Robbins, 2012). Taken together, it is perhaps unsurprising that prior work has shown it takes longer for adolescents to reach adult levels of reappraisal success for social stimuli than non-social stimuli (Silvers, McRae, et al., 2012). Yet, it is unclear what brain mechanisms underlie age-related differences in reappraisal success for social stimuli.

The ability to control cognition and emotion develops dramatically over the course of adolescence. Performance on "cold" cognitive control tasks as well as reappraisal improves from childhood through to early adulthood, and is paralleled by structural maturation of prefrontal control regions (Amso & Casey, 2006; Giedd & Rapoport, 2010; Gogtay et al., 2004; Luna, 2009; McRae et al., 2012; P. Shaw et al., 2008; Silvers, McRae, et al., 2012; Zelazo & Carlson, 2012). The handful of fMRI studies that have examined reappraisal in developmental samples have generally found that, like adults, children and adolescents recruit dorsal and lateral prefrontal control regions when reappraising and that can reappraisal can be an effective strategy for regulating affect (Levesque et al., 2004; McRae et al., 2012; Pitskel et al., 2011). Yet, age-related differences have also been observed with regards to the recruitment of prefrontal control regions during reappraisal. For example, while Pitskel and colleagues (2011) found that age predicted reduced recruitment of the left inferior frontal gyrus (IFG), McRae and colleagues (2012) found exactly the opposite. These discrepant findings could be attributed to a number of factors including the fact that the participants in Pitskel and colleagues' sample ranged in age from 7-17 years while those in McRae and colleagues' sample ranged in age from 10-22 years.

At present, it is unclear whether age-related differences in reappraisal of social stimuli are due to differential recruitment of lateral and dorsal prefrontal control regions, medial prefrontal brain regions that support social cognition, or subcortical structures such as the amygdala that support affective processing. The present study sought to address this issue by examining reappraisal of social emotional stimuli in children, adolescents and young adults. The present design improved upon prior developmental emotion regulation work in two key ways. First, the present study's sample size is the

largest (n=59) and the participant age range is the widest (6-22 years) to be used in any reappraisal study to date. Second, prior developmental studies have compared reappraisal to different "baseline" conditions, making cross-study comparisons difficult. To better evaluate the effects of different types of regulatory strategies on emotional responses in development, the present study utilized two different baseline conditions: one that constrained the way participants responded to affective stimuli by encouraging them to immerse themselves in the emotional scenes they viewed, and one that allowed them to respond without any instruction.

Methods

Participants. Seventy-one healthy individuals between the ages of 6-22 years participated in the experiment (42 female; mean age = 13.50 years, S.D. = 4.01). However, twelve participants (8 female; mean age = 9.77 years, S.D. = 3.20 years), had to be excluded from analyses due to excessive head motion, resulting in a final sample of 59 participants as is described in the Methods section below (34 female; mean age = 14.26 years, S.D. = 3.74). Participants were prescreened prior to participation to ensure that they could read and write in English, had normal or corrected vision, had never been diagnosed with a developmental or psychiatric disorder, and had never been prescribed psychotropic medication. Those who were scanned were screened to ensure they did not have any conditions contraindicated for MRI scanning. All participants completed the Wechsler Abbreviated Scale of Intelligence (mean score = 111.58, S.D. = 16) and no relationship was observed between age and IQ scores (r=-.16, p=.23).

Experimental procedure. The modal approach to identifying rain regions involved in reappraisal in adults is to compare a regulation condition (i.e., downregulation of negative affect) to a baseline condition wherein participants "respond naturally" to affective stimuli. Implicit in this contrast is the notion that participants interpret the instruction to respond naturally in a similar manner, yet this assumption may be unwarranted given all of the emotional changes known to occur during child and adolescent development (Church, Petersen, & Schlaggar, 2010) . To assess this possibility, the present study included examined emotional responding using three different instructions. These conditions consisted of: 1) a condition where participants responded naturally ('look'), 2) a reappraisal condition wherein participants distanced themselves so as to reduce negative affect ('far'), and 3) an immersed condition wherein participants drew themselves closer to the emotional aspects of the stimulus ('close'). Including three conditions allowed not only for an examination of within-subject strategy effects across the entire group, but also whether age-related changes were greater for some strategies than others. For example, it may be that responses observed during the 'look' condition are more similar to those observed in the 'close' condition earlier in development, but more similar to those observed in the 'far' condition later in life.

Prior to performing the task, participants were trained extensively on the immersed ('close') and distanced ('far') strategies in accordance with well-validated procedures (Silvers, McRae, et al., 2012). On 'close' trials, participants were told to imagine standing close to the scene depicted in the photographic stimulus they were looking at and to allow themselves to experience any emotions that it evoked. On 'far' trials, participants were told to imagine themselves standing further away from the scene and to focus more on the facts

of the photograph than on its emotional details. Instructions for the 'close' and 'far' trials as well as the trial structure were modeled closely after prior work examining reappraisal in a developmental sample (Silvers, McRae, et al., 2012). Participants were told to respond how they "normally would" on 'look' trials. While participants were not told so, 'close' trials were used to assess emotional reactivity, 'far' trials were used to assess regulation ability, and 'look' trials were used to assess participants' baseline emotional responsiveness. It was hypothesized that 'close' trials would elicit the greatest amount of negative affect, followed by 'look' trials, and that 'far' trials would elicit the least amount of negative affect.

All participants completed 90 experimental trials, 45 of which contained aversive stimuli and 45 of which contained neutral stimuli. Conditions differed in terms of stimulus valence (negative or neutral) and regulation instruction (close, far or look) for a total of 6 condition types. Stimuli were drawn from the International Affective Picture System (Lang et al., 2001) and from a set of similar pictures that had been previously used with participants in this age range (Silvers, McRae, et al., 2012). Because the focus of this study was on examining age-related differences in the ability to regulate emotional responses to social stimuli, all of the photographic stimuli used contained pictures of people. Parents of participants under the age of 18 prescreened sixty aversive photographic stimuli prior to participation. Parents were permitted to exclude up to 10 stimuli so that 50 stimuli remained. Among the stimuli that parents approved, 45 were used for the task and the remaining stimuli were used for training purposes. If a parent rejected a stimulus that was typically included in the version of the task that adults completed, a valence-matched task substitute was used in its place from within the pool that the parent had approved. This approach closely mirrors practices used in prior work in a similar age range (Silvers,

McRae, et al., 2012), and allowed all participants to see the same number of pictures that were as similar as possible. The assignment of pictures to instruction was counterbalanced between participants.

For each of the 90 trials completed, participants were first shown a cue word for 2 seconds that indicated what strategy they were to use on that trial ('close', 'far', or 'look'). Next, a photographic stimulus appeared for 8 seconds. It was during this time that participants employed the strategy they had been cued to use. Next, a jittered fixation cross appeared (for an average of 3 seconds), followed by a rating scale that appeared for 3 seconds. Participants were asked to respond to the rating scale by assessing how badly they felt at that moment in time on a five-point scale (1=not feeling badly at all, 5=feeling very badly) via button press. Each trial concluded with an additional jittered fixation cross (for an average of 3 seconds). A diagram of the trial structure used is shown in Figure 4.1.

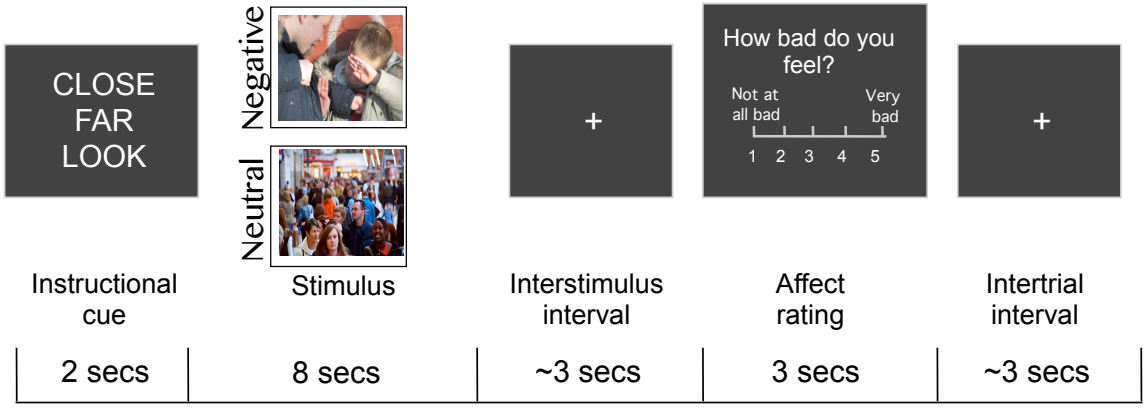

Figure 4.1. Trial structure for Study 3.

fMRI acquisition. Whole-brain fMRI data were acquired on a 3T Siemens Magnetom Trio scanner. Structural images were acquired using a high-resolution, T1-weighted MPRAGE sequence (TR=2170 ms, TE=4.33 ms, 120 1.5 mm slices). Functional

images were acquired with a T2*-sensitive EPI BOLD sequence. Thirty-four axial slices were collected with a TR of 2000 ms (TE of 34 ms, flip angle of 90°, field of view of 22.4 cm and 3.5 x 3.5 x 4 mm voxels). Stimuli were presented using E-Prime and were projected onto a flat screen mounted in the scanner bore. Subjects viewed the screen using a mirror mounted on a 16-channel head coil. Participants made their responses using a five-finger-button response pad.

Behavioral data analysis. Effects of valence, strategy and age were analyzed using repeated measures GLM models, as implemented in SPSS 19.0. Follow-up t-tests were performed, when necessary, to disambiguate significant *F* statistics. Robust correlations were performed in Matlab to disambiguate effects relating to age.

fMRI analysis. Preprocessing was performed using SPM8 preprocessing tools (Wellcome Department of Cognitive Neurology, UCL) as implemented in NeuroElf (http://neuroelf.net). Functional images were corrected for motion, slice-time corrected and coregistered to the first functional image for each subject. Head motion was estimated for each run and all runs with more than 2.5 mm of head motion were excluded from further analyses. Structural images were normalized (spatially warped) to a standard template brain (the MNI avg15T1.img) using SPM8's default options and warping parameters were applied to functional images for each subject. Normalized functional images were interpolated to 3 x 3 x 3 mm voxels and spatially smoothed with a 6-mm Gaussian filter.

First and second-level GLM analyses were implemented in NeuroElf (http://neuroelf.net). Cue, stimulus-viewing and response portions of each trial were modeled as boxcar regressors convolved with a canonical hemodynamic response function.

Separate regressors were made for the six different trial types so that neural responses associated with strategy (close, look and far) and valence (negative vs. neutral) could be differentiated. For each subject, a robust regression analysis was performed on the conditions of interest and motion parameters and high-pass filters were included as additional regressors of no interest. We next performed a second-level random effects analysis to identify regions of activation at the group level. Significant voxels were identified using joint voxel and extent thresholds (corresponding to a corrected $p<.05$) as determined by AlphaSim, implemented in NeuroElf.

To identify brain regions responsive to valence, a whole-brain t-test was performance comparing negative stimuli to neutral stimuli, while collapsing across strategy. The amygdala cluster identified in this contrast was then interrogated in Matlab using robust correlation to examine whether age predicted responses in any of the negative stimuli conditions ('close', 'far', or 'look'). Next, a two-way ANOVA was performed examining strategy ('close', 'far', or 'look') and age for trials containing negative stimuli. Follow-up contrasts were then performed to determine the direction of strategy effects and robust correlations were performed with age to determine the nature of age effects.

Results

Behavioral results. Behavioral data were first analyzed to perform a manipulation check and subsequently examine age effects.

Manipulation check. To assess whether strategy and stimulus valence elicited expected emotional responses, a repeated measures GLM was conducted with strategy and valence as the factors of interest. As shown in Figure 4.2, negative stimuli elicited significantly more negative affect than neutral stimuli ($M=2.34$, $F(1,58)=666.28$, $p<.001$)

and negative affect differed significantly as a function of strategy ($F(2,57)=8.85$, $p<.001$). Post-hoc comparisons revealed that 'close' trials elicited significantly more negative affect than 'look' ($M=.14$; $t(58)=4.18$; $p<.001$) and 'far' trials ($M=.18$; $t(58)=2.81$, $p<.001$), but 'look' trials elicited only marginally more negative affect than 'far' trials ($M=.05$; $t(58)=1.48$, $p=.14$). An interaction between strategy and valence was also observed ($F(2,57)=7.51$, $p<.001$), such that the effect of strategy was significant for negative, but not neutral stimuli.

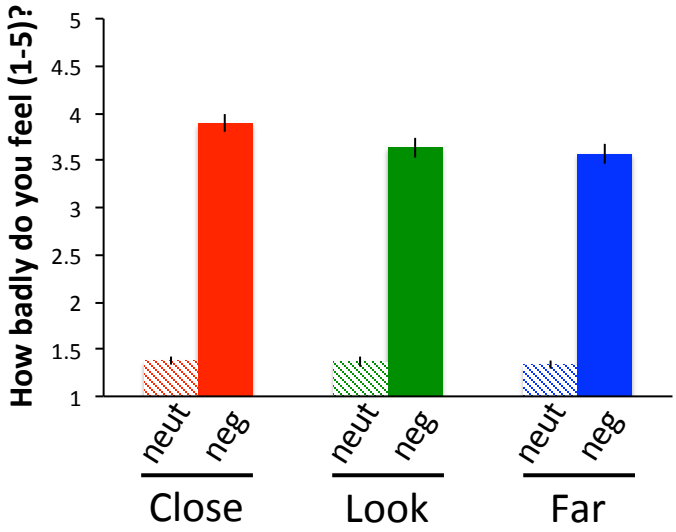

Figure 4.2. Reported negative affect as a function of strategy and valence.

Effects of age. When age was added to the repeated measures GLM, only the effect of valence remained significant ($F(1,57)=45.74$, $p<.001$). Exploratory analyses were conducted to examine whether age correlated with any of the three negative conditions (Figure 4.3). While none of these robust correlations achieved significance when was α was set to .05, a trend was observed between age and self-reported negative affect for 'far' negative trials ($r=-.20$, $p=.06$, 1-tailed). To examine whether age may predict increasing differences between the conditions, percent difference scores were calculated between

each of the three conditions and correlated robustly with age. The percent difference in negative affect reported for close trials relative to far trials increased marginally with age (r=.25, *p*=.06) as did the percent differences in negative affect reported for close trials relative to look trials (r=.22, *p*=.09). The percent difference in negative affect for look compared to far trials did not differ as a function of age (r=.10, *p*=.22). The extra sum-of-squares F test was used to determine whether a linear or quadratic model of age was more appropriate and for each of the negative conditions, a linear test was identified as providing a better fit and was thus used for all behavioral and imaging data.

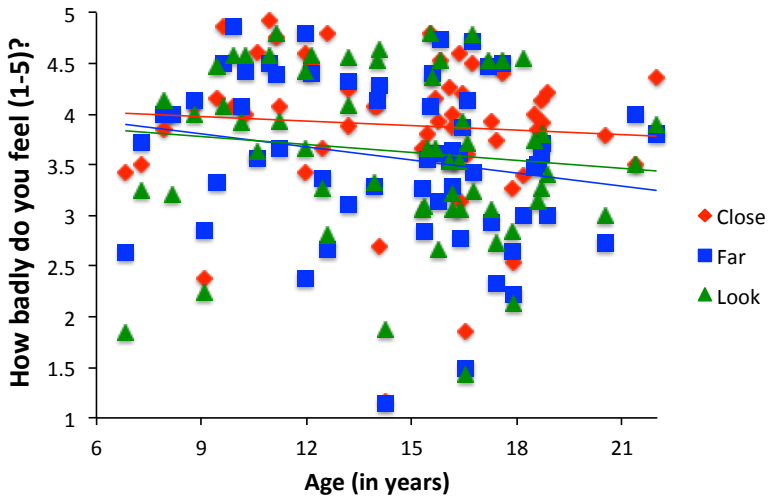

Figure 4.3. Affective responses to aversive stimuli, shown as a function of strategy and age.

Imaging results. Imaging data was analyzed in two phases. First, brain regions were identified that responded differentially to negative and neutral stimuli. Second, a two-way ANOVA was performed to assess the effects of strategy and age on neural responses to negative stimuli.

Effects of valence. To identify brain regions involved in emotional responding, a contrast was performed between negative and neutral stimuli, collapsing across strategy

type. This contrast revealed a host of brain regions involved in emotional and social processing including bilateral anterior insula, amygdala, and dmPFC (Table 4.1).

				MNI Coordinates		
Region	Side	Extent	t-value	x	y	z
Middle frontal gyrus	L	5147	9.99	-39	0	45
Middle frontal gyrus	L	LM	9.19	-45	3	33
Middle frontal gyrus	L	LM	4.57	-39	0	63
Middle frontal gyrus	L	LM	5.60	-27	-3	48
Inferior frontal gyrus	L	LM	6.67	-54	21	6
Inferior frontal gyrus	L	LM	8.23	-51	18	18
Inferior frontal gyrus	L	LM	7.52	-51	33	0
Inferior frontal gyrus	L	LM	6.60	-51	24	-9
Inferior frontal gyrus	L	LM	3.48	-51	36	21
Inferior frontal gyrus	L	LM	6.95	-48	27	15
Inferior frontal gyrus	L	LM	8.41	-45	12	24
Inferior frontal gyrus	L	LM	6.67	-39	21	-18
Inferior frontal gyrus	L	LM	3.99	-24	15	-24
Middle frontal gyrus	R	LM	6.37	33	0	48
Middle frontal gyrus	R	LM	4.48	39	12	24
Inferior frontal gyrus	R	LM	5.87	36	18	-21
Inferior frontal gyrus	R	LM	4.81	48	6	21
Inferior frontal gyrus	R	LM	4.80	48	24	6
Inferior frontal gyrus	R	LM	4.28	48	30	12
Inferior frontal gyrus	R	LM	4.31	51	42	-6
Inferior frontal gyrus	R	LM	4.91	54	12	12
Inferior frontal gyrus	R	LM	4.89	54	33	21
Inferior frontal gyrus	R	LM	4.67	57	18	24
Precentral gyrus	R	LM	4.59	27	-9	54
Precentral gyrus	R	LM	5.39	30	-3	63
Precentral gyrus	R	LM	5.05	36	0	39
Precentral gyrus	R	LM	5.54	51	3	36
Anterior insula	L	LM	6.40	-36	24	-9
Anterior insula	L	LM	5.57	-30	27	0
Anterior insula	R	LM	6.68	33	24	0
Anterior insula	R	LM	5.86	42	21	-9
Anterior insula	R	LM	3.59	48	12	3
Amygdala	R	LM	7.91	27	-6	-18
Caudate	L	LM	7.29	-12	3	12
Caudate	L	LM	7.15	-12	-6	15
Caudate	L	LM	6.58	-12	9	3
Caudate	R	LM	7.64	12	0	12

Putamen	L	LM	3.88	-30	0	-3
Putamen	R	LM	4.82	30	3	-9
Hippocampus	L	LM	8.15	-30	-33	-3
Hippocampus	L	LM	8.01	-30	-15	-12
Hippocampus	R	LM	5.41	21	-27	-6
Hippocampus	R	LM	5.43	30	-30	-6
Hippocampus	R	LM	6.57	33	-21	-9
Parahippocampal gyrus	L	LM	3.96	-24	-3	-36
Inferior temporal gyrus	L	LM	4.98	-39	6	-33
Inferior temporal gyrus	L	LM	5.40	-36	9	-42
Inferior temporal gyrus	R	LM	5.15	36	-9	-36
Middle temporal gyrus	L	LM	5.70	-48	-21	-12
Middle temporal gyrus	L	LM	4.13	-48	3	-27
Middle temporal gyrus	L	LM	3.86	-45	-9	-24
Midbrain	L	LM	6.48	-9	-15	-12
Midbrain	L	LM	7.25	-6	-30	-6
Midbrain	R	LM	7.38	3	-33	-6
Temporal pole	L	LM	5.49	-45	15	-27
Thalamus	L	LM	7.37	-15	-33	3
Thalamus	L	LM	7.39	-6	-12	9
Thalamus	R	LM	7.11	9	-6	3
Thalamus	R	LM	5.86	9	-15	-3
Thalamus	R	LM	5.63	9	-18	12
Thalamus	R	LM	4.86	18	-15	18
Thalamus	R	LM	5.77	21	-30	9
Superior frontal gyrus	L	812	7.59	-3	54	27
Superior frontal gyrus	L	LM	5.79	-6	33	51
Superior frontal gyrus	L	LM	5.69	-6	69	18
Superior frontal gyrus	L	LM	6.86	-3	48	39
Superior frontal gyrus	L	LM	3.97	-3	18	66
Superior frontal gyrus	R	LM	3.71	18	60	33
Medial frontal gyrus	L	LM	4.88	-6	15	51
Medial frontal gyrus	L	LM	4.32	-6	18	42
Medial frontal gyrus	R	LM	3.96	6	21	42
Cingulate gyrus	L	LM	3.55	-9	24	30
Cingulate gyrus	R	LM	4.41	12	27	27
Middle temporal gyrus	L	6285	15.59	-51	-63	3
Middle temporal gyrus	R	LM	12.95	51	-57	9
Superior temporal gyrus	L	LM	8.82	-57	-54	9
Superior temporal gyrus	L	LM	9.36	-51	-48	18
Fusiform gyrus	L	LM	12.83	-42	-54	-15
Fusiform gyrus	R	LM	10.23	45	-45	-21
Inferior parietal lobule	L	LM	4.12	-63	-30	36
Inferior parietal lobule	L	LM	8.43	-60	-45	24
Superior parietal lobule	L	LM	5.46	-39	-39	39
Superior parietal lobule	L	LM	9.48	-30	-51	45

Superior parietal lobule	L	LM	7.72	-27	-60	54
Superior parietal lobule	L	LM	4.07	-27	-54	66
Precuneus	L	LM	5.43	-27	-72	24
Precuneus	L	LM	4.28	-6	-57	51
Precuneus	L	LM	4.22	-3	-60	36
Inferior occipital gyrus	L	LM	13.51	-42	-78	-6
Inferior occipital gyrus	L	LM	13.31	-42	-69	-12
Inferior occipital gyrus	L	LM	10.97	-36	-87	-3
Inferior occipital gyrus	L	LM	8.86	-27	-87	-6
Inferior occipital gyrus	R	LM	6.10	30	-87	-15
Inferior occipital gyrus	R	LM	10.09	45	-87	-6
Inferior occipital gyrus	R	LM	11.83	51	-69	-3
Middle occipital gyrus	L	LM	9.44	-27	-93	9
Middle occipital gyrus	R	LM	6.96	30	-81	-6
Middle occipital gyrus	R	LM	8.03	39	-78	6
Middle occipital gyrus	R	LM	12.51	51	-69	9
Cerebellum	L	LM	5.41	-24	-75	-24
Cerebellum	L	LM	5.37	-18	-75	-39
Cerebellum	L	LM	5.30	-18	-51	-24
Cerebellum	L	LM	5.69	-15	-72	-27
Cerebellum	L	LM	4.45	-12	-57	-45
Cerebellum	L	LM	4.57	-9	-75	-36
Cerebellum	L	LM	4.18	-9	-60	-36
Cerebellum	L	LM	3.58	-9	-39	-33
Cerebellum	L	LM	4.72	-3	-78	-21
Cerebellum	M	LM	6.79	0	-54	-33
Cerebellum	M	LM	3.46	0	-42	-9
Cerebellum	R	LM	5.25	6	-60	-48
Cerebellum	R	LM	5.08	12	-54	-39
Cerebellum	R	LM	8.38	15	-72	-30
Cerebellum	R	LM	8.38	24	-78	-33
Cerebellum	R	LM	4.41	30	-57	-33
Cerebellum	R	LM	3.95	36	-63	-51
Cerebellum	R	LM	7.79	42	-69	-21
Cerebellum	R	LM	5.66	51	-51	-30
Precuneus	R	761	8.35	30	-45	51
Postcentral sulcus	R	LM	5.42	42	-30	39
Postcentral sulcus	R	LM	4.58	48	-24	63
Postcentral sulcus	R	LM	4.81	57	-30	51
Inferior parietal lobule	R	LM	5.21	60	-30	30
Inferior parietal lobule	R	LM	6.16	66	-33	39
Inferior parietal lobule	R	LM	5.00	69	-27	30
Superior parietal lobule	R	LM	4.70	21	-63	54
Superior parietal lobule	R	LM	5.92	42	-33	51
Precentral gyrus	R	93	-5.87	51	-9	45
Precentral gyrus	R	LM	-4.61	39	-15	42

Postcentral gyrus	L	256	-4.92	-24	-30	66
Precentral gyrus	L	LM	-3.53	-60	-3	39
Postcentral gyrus	L	LM	-4.61	-45	-15	48
Precentral gyrus	L	LM	-4.09	-45	-18	63
Precentral gyrus	L	LM	-4.10	-33	-21	48
Precentral gyrus	L	LM	-3.41	-30	-30	57
Superior parietal lobule	L	LM	-3.53	-15	-42	63
Superior temporal gyrus	L	593	-6.49	-51	-15	9
Posterior insula	L	LM	-3.59	-42	-30	9
Posterior insula	L	LM	-3.93	-42	-33	21
Posterior insula	L	LM	-5.15	-36	-18	15
Posterior insula	L	LM	-4.27	-39	-24	0
Posterior insula	L	LM	-4.18	-36	-9	3
Superior temporal gyrus	R	177	-5.19	57	-6	6
Superior temporal gyrus	R	LM	-3.78	69	-21	0
Cingulate gyrus	L	330	-7.64	-6	-36	39
Cingulate gyrus	R	LM	-6.46	6	-36	33
Cingulate gyrus	L	955	-6.29	-9	-54	9
Precuneus	L	LM	-5.04	-15	-57	24
Precuneus	L	LM	-4.50	-9	-75	33
Precuneus	R	LM	-6.16	9	-57	15
Cuneus	L	LM	-4.61	-6	-66	-3
Cuneus	L	LM	-5.84	-6	-84	24
Cuneus	R	LM	-5.40	3	-84	30
Cuneus	R	LM	-5.62	12	-69	-6
Cuneus	R	LM	-5.25	12	-78	3
Cuneus	R	LM	-4.34	12	-96	27
Parahippocampal gyrus	L	72	-5.67	-30	-42	-9
Superior parietal lobule	R	152	-5.27	48	-66	45
Superior parietal lobule	R	LM	-3.68	33	-81	45
Superior parietal lobule	R	LM	-4.29	45	-78	36
Lateral fissure	R	LM	-3.37	63	-12	15
Inferior parietal lobule	L	91	-4.34	-39	-72	42
Inferior parietal lobule	L	LM	-4.24	-48	-72	36

Table 4.1. Brain regions associated with emotional responding across strategy type (close negative + look negative + far negative > close neutral + look neutral + far neutral). Brain regions responding more strongly to negative stimuli than neutral stimuli are presented first. Laterality is indicated in the column labeled "Side" (L=Left, R=Right, M=Medial). Local maxima with 10 or more voxels are listed below and are indicated by "LM" in the Extent column. T-values listed indicate the maximum t-value for each cluster.

Within the amygdala subcluster identified in this contrast (27, -6, -18), age predicted attenuated responses for far negative trials (r=-.25, *p*=.05), but not for close (r=-.15, *p*=.27) or look (r=-.10, *p*=.45) negative trials.

Effects of age and strategy on neural responses to negative stimuli. To identify brain regions that responded differentially to negative stimuli as a function of strategy, a two-way ANOVA was performed using task (close negative, far negative, look negative) and age as predictors. Several brain regions commonly implicated in cognitive control and reappraisal differed as a function of strategy, including left dlPFC, vlPFC and posterior parietal cortex (Table 4.2). Follow-up t-tests revealed that the far strategy recruited all brain regions more strongly than did the close strategy, while the look strategy typically recruited brain regions an intermediate amount.

				MNI Coordinates			
Region	Side	Extent	F-value	x	y	z	Pattern
Middle frontal gyrus	L	191	19.89	-45	51	-3	F>L>C
Superior frontal gyrus	L	LM	7.09	-30	63	9	
Superior frontal gyrus	L	LM	7.85	-27	54	21	
Superior frontal gyrus	L	LM	8.59	-24	63	21	
Middle frontal gyrus	L	192	9.36	-30	21	51	F=L>C
Middle frontal gyrus	L	LM	7.40	-36	39	33	
Middle frontal gyrus	L	LM	8.86	-39	30	33	
Middle frontal gyrus	L	LM	9.24	-36	27	42	
Middle frontal gyrus	L	LM	9.19	-36	36	24	
Insula	R	54	8.03	54	-6	12	F=L>C
Precentral gyrus	R	LM	7.66	48	-9	21	
Cingulate gyrus	M	47	8.87	0	-36	42	F=L>C
Inferior parietal lobule	L	173	11.08	-48	-57	39	F>C=L
Inferior parietal lobule	L	LM	10.46	-45	-57	48	
Inferior parietal lobule	R	98	9.29	42	-51	51	F>C=L
Precuneus	R	292	9.02	15	-66	51	F=L>C
Precuneus	L	LM	8.36	-30	-78	42	
Precuneus	L	LM	8.43	-15	-63	39	
Precuneus	L	LM	8.18	-9	-81	45	

Precuneus	R	LM	7.17	18	-60	30
Inferior parietal lobule	L	LM	6.89	-39	-69	51
Inferior parietal lobule	L	LM	8.81	-30	-87	36

Table 4.2. Brain regions identified in the main effect of strategy analysis. Side indicates whether the cluster was located on the left ("L"), right ("R"), or medially ("M"). Local maxima with 10 or more voxels are indicated by "LM" in the Extent column. F-values refer to the peak F statistic for a given cluster. Pattern indicates the relationship between the three conditions (C=Close, L=Look, F=Far) when assessed at p<.05.

Widespread prefrontal and temporal regions, including the amygdala, showed main effects of age (Table 4.3). To further examine what was driving these effects of age, robust correlations were performed between age and the close, far and look negative conditions for all clusters. Bilateral middle frontal gyri and bilateral posterior parietal cortex were among the only regions to show significant increases in recruitment as a function of age across all strategy types. The right amygdala (33, 3, -27) correlated negatively with the 'far' condition (r =-.33, *p*=.01) but not the other two conditions (*p*>.73), as shown in Figure 4.4. The relationship between age and the amygdala response remained significant when controlling for self-reported negative affect (r=-.31, *p*<.05).

				MNI Coordinates			Correlation with age		
Region	Side	Extent	F	x	y	z	Close	Far	Look
Anterior orbital gyrus	L	45	38.30	-27	48	-18	+	n.s.	+
Middle frontal gyrus	L	28	18.23	-39	12	45	+	+*	+
Superior frontal gyrus	R	50	25.83	6	66	-9	n.s.	-*	n.s.
Superior frontal gyrus	R	LM	17.28	15	69	-9			
Superior frontal gyrus	R	27	15.70	18	69	12	~ +	n.s.	n.s.
Middle frontal gyrus	R	104	37.35	24	60	27	+	n.s.	n.s.
Superior frontal gyrus	R	LM	21.70	12	63	27			
Middle frontal gyrus	R	LM	21.32	24	60	18			
Middle frontal gyrus	R	LM	14.41	36	51	33			
Middle frontal gyrus	R	32	19.01	39	9	54	+	+*	+
Amygdala	R	196	28.04	33	3	-27	n.s.	-	n.s.

Amygdala	R	LM	18.62	15	0	-24			
Amygdala	R	LM	19.57	21	-6	-33			
Amygdala	R	LM	21.02	27	-6	-18			
Hypothalamus	L	LM	16.01	-6	-9	-9			
Globus pallidus	R	LM	19.02	9	3	-12			
Posterior orbital gyrus	R	LM	19.85	24	12	-21			
Hippocampus	L	51	23.97	-27	-42	0	~ -	~ -	~ -
Hippocampus	R	30	17.32	21	-39	6	n.s.	~ -	~ -
Precentral gyrus	R	38	14.97	33	-24	48	n.s.	-	-
Precentral gyrus	R	LM	12.66	42	-21	54			
Temporal pole	L	27	28.91	-51	18	-12	+	+*	+
Temporal pole	R	27	30.98	42	21	-30	n.s.	n.s.	~ -
Middle temporal gyrus	L	123	34.82	-69	-42	9	n.s.	-	-
Inferior parietal lobule	L	LM	14.50	-66	-51	15			
Middle temporal gyrus	L	LM	13.90	-51	-39	6			
Superior temporal gyrus	R	27	14.93	45	3	-18	n.s.	-	n.s.
Superior temporal gyrus	R	46	15.86	48	-18	3	n.s.	-	n.s.
Superior temporal gyrus	R	26	16.82	57	-33	15	n.s.	-	n.s.
Fusiform gyrus	L	27	39.64	-45	-27	-27	n.s.	n.s.	n.s.
Superior parietal lobule	L	33	16.78	-21	-69	57	+	+	+
Superior parietal lobule	R	41	20.21	33	-57	57	+	+	+
Superior parietal lobule	R	LM	16.76	42	-57	57			
Cerebellum	L	52	31.98	-36	-39	-45	+	+*	+
Cerebellum	L	LM	18.92	-48	-42	-39			
Cerebellum	L	27	17.04	-21	-81	-45	+	n.s.	~ +
Cerebellum	L	253	27.75	-21	-54	-24	n.s.	-	n.s.
Cerebellum	L	LM	14.47	-30	-54	-36			
Cerebellum	L	LM	13.86	-12	-45	-33			
Cerebellum	L	LM	20.40	-3	-57	-6			
Cerebellum	R	LM	14.27	3	-45	-9			
Cerebellum	R	LM	13.91	6	-39	-21			
Cerebellum	R	LM	12.87	6	-36	-12			
Cerebellum	R	47	21.12	57	-66	-30	+	+*	+
Cerebellum	R	LM	15.08	42	-69	-27			
Cerebellum	R	135	63.15	21	-45	-51	+	+	+
Cerebellum	R	LM	26.73	21	-33	-39			
Cerebellum	R	LM	49.03	30	-36	-54			
Cerebellum	R	LM	19.99	36	-48	-54			
Cerebellum	R	LM	34.18	45	-42	-42			
Pons	L	26	24.47	-9	-30	-45	+	+*	+
Pons	L	LM	16.99	-9	-39	-51			

Table 4.3. Brain regions identified in the main effect of age analysis. Side indicates whether the cluster was located on the left ("L"), right ("R"), or medially ("M"). Local maxima with 10 or more voxels are marked "LM." F refers to the peak F statistic for a given cluster. Significant ($p<.05$) robust negative correlations are labeled "-" and positive correlations are labeled "+". Trends ($p<.10$) are labeled "~" and non-significant are labeled "n.s." . Correlations in the Far column marked "*" did not survive when affect was controlled for. Affect did not correlate with age for the other conditions and was therefore not examined.

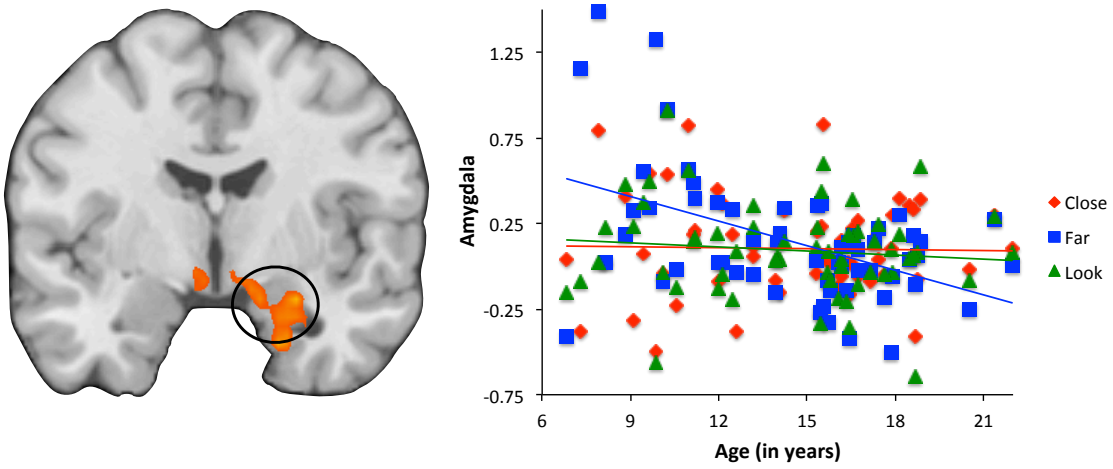

Figure 4.4. Amygdala cluster revealed by main effect of age contrast. Age predicted significant reductions in amygdala response for far trials, but not close or look trials.

Age and strategy interacted to predict recruitment of a rostral portion of the right middle frontal gyrus, posterior temporal cortex, posterior cingulate gyrus, and visual cortex (Table 4.4). Robust correlations revealed that age predicted increased recruitment for the 'close' condition in nearly all clusters, while only a handful of clusters showed age-related differences for the look and far conditions (primarily in occipital cortex and the cerebellum). In most clusters, there was greater differentiation between the three conditions at younger ages than at older ages. An example of this pattern is shown for the right middle frontal gyrus in Figure 4.5.

				MNI Coordinates			Correlation with age		
Region	Side	Extent	F	x	y	z	Close	Far	Look
Middle frontal gyrus	R	451	13.16	39	54	27	+	~+*	n.s.
Middle frontal gyrus	R	LM	12.46	24	60	27			

Middle frontal gyrus	R	LM	8.31	30	39	39			
Middle frontal gyrus	R	LM	11.32	33	60	-9			
Middle frontal gyrus	R	LM	7.90	36	33	39			
Middle frontal gyrus	R	LM	8.20	45	36	39			
Middle frontal gyrus	R	LM	11.16	48	54	9			
Superior frontal gyrus	R	LM	11.56	12	57	27			
Superior frontal gyrus	R	LM	8.31	21	66	9			
Inferior frontal gyrus	R	39	9.18	51	6	12	+	n.s.	n.s.
Superior temporal gyrus	R	LM	7.84	63	9	-6			
Globus pallidus	R	35	9.56	12	0	-12	n.s.	-	n.s.
Middle temporal gyrus	L	54	11.74	-69	-42	9	n.s.	-	n.s.
Middle temporal gyrus	L	LM	9.08	-63	-30	0			
Middle temporal gyrus	L	34	10.56	-66	-39	-15	+	∼+*	∼+
Inferior temporal gyrus	L	LM	9.87	-63	-42	-24			
Middle temporal gyrus	R	182	11.71	66	-30	0	+	∼-*	n.s.
Inferior parietal lobule	R	LM	11.07	57	-27	27			
Superior temporal gyrus	R	LM	7.98	60	-33	12			
Superior temporal gyrus	R	LM	9.70	63	-21	3			
Superior temporal gyrus	R	LM	9.42	69	-39	15			
Inferior temporal gyrus	R	60	11.54	54	-51	-21	+	n.s.	+
Cerebellum	R	LM	7.43	45	-57	-30			
Cingulate gyrus	R	152	10.26	3	-15	42	+	n.s.	n.s.
Cingulate gyrus	M	LM	9.65	0	-9	33			
Postcentral gyrus	L	51	9.44	-6	-39	72	+	n.s.	
Postcentral gyrus	L	LM	8.00	-3	-30	69			
Precentral gyrus	R	LM	7.58	3	-12	72			
Middle occipital gyrus	L	43	11.94	-57	-69	3	+	n.s.	n.s.
Middle occipital gyrus	L	38	7.87	-33	-87	12	+	+*	+
Precuneus	R	126	11.37	9	-51	51	+	n.s.	n.s.
Precuneus	L	LM	8.41	-9	-45	45			
Precuneus	L	LM	7.23	-18	-54	51			
Precuneus	R	38	7.75	18	-54	54	+	∼+*	+
Precuneus	R	LM	7.66	15	-75	51			
Precuneus	R	LM	7.46	18	-66	54			
Cuneus	L	49	12.66	-21	-93	33	+	∼+*	∼+
Cuneus	L	LM	12.26	-21	-87	42			
Cuneus	R	69	8.89	9	-78	6	+	n.s.	+
Cuneus	R	LM	6.85	3	-75	-6			
Cerebellum	M	LM	8.49	0	-75	-15			
Cerebellum	L	269	12.25	-21	-75	-27	n.s.	n.s.	n.s.
Cerebellum	L	LM	8.87	-36	-69	-18			
Cerebellum	L	LM	7.97	-33	-54	-36			
Cerebellum	L	LM	9.63	-27	-66	-21			
Cerebellum	L	LM	9.10	-27	-45	-30			
Cerebellum	L	LM	10.94	-21	-81	-42			
Cerebellum	L	LM	8.81	-6	-81	-48			
Cerebellum	L	121	12.48	-18	-42	-51	+	n.s.	n.s.
Cerebellum	L	LM	10.68	-42	-54	-54			
Cerebellum	L	LM	10.53	-30	-51	-51			
Cerebellum	L	LM	11.05	-24	-60	-54			

Cerebellum	L	LM	9.38	-15	-57	-54			
Cerebellum	R	56	11.22	33	-48	-48	+	+*	+
Cerebellum	R	LM	7.16	27	-36	-51			
Cerebellum	R	LM	8.05	45	-48	-51			

Table 4.4. Brain regions identified by the interaction term between strategy and age. Side indicates whether the cluster maximum was located on the left ("L"), right ("R"), or medially ("M"). Local maxima with 10 or more voxels are labeled "LM". F refers to the peak F statistic for a given cluster. Significant (p<.05) robust negative correlations are indicated by "-" and positive correlations are indicated by "+". Trends (p<.10) are indicated by "~" and non-significant correlations are indicated by "n.s." . Correlations in the Far column marked "*" did not survive when affect was controlled for. Affect did not correlate with age for the other conditions and was therefore not examined.

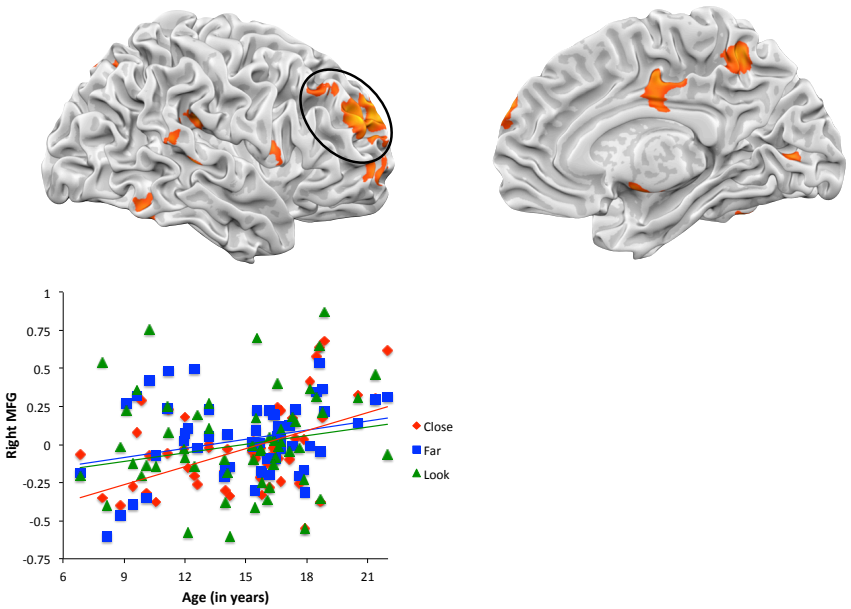

Figure 4.5. Effects of task and age on recruitment of right MFG. Scatter plot depicts MFG response for close, far and look strategy on trials involving negative stimuli.

Discussion

Our social and emotional lives are inextricably linked. From the loving bonds infants form with their parents, to the frustration and exhilaration adolescents feel towards their peers, to the romantic partnerships formed by adults, our interactions with others are what make us human. As such, learning to effectively manage emotional responses to social

emotional situations is a critical developmental milestone. The present study tested how this ability develops by examining reappraisal of aversive social stimuli in children, adolescents and young adults. While a handful of other fMRI studies have examined reappraisal in developmental samples, this is the largest sample size and age range to date. Three key findings were obtained. First, across all ages participants were capable of reappraising to modulate self-reported negative affect. Second, reappraisal recruited prefrontal control regions to a greater degree than responding naturally or immersing across all ages. Third, age predicted enhanced modulation of amygdala responses for the reappraisal condition, but not for the other conditions.

Reappraisal efficacy in childhood and adolescence. As expected, participants reported the most negative affect on close trials, the least on far trials and an intermediate amount on look trials. This suggests that reappraisal is an effective means of regulating negative affect starting at a relatively young age. While reappraisal's effectiveness has been demonstrated in older children (McRae et al., 2012; Silvers, McRae, et al., 2012), no prior work has examined whether children as young as six years can effectively reappraise aversive stimuli. Though no significant interactions between age and strategy were observed, exploratory correlational analyses revealed that age predicted greater differences in self-reported negative affect for the close condition relative to the far condition. This replicates the results of Studies 1 and 2 by showing that reappraisal success, as defined by the decrease in negative affect when distancing versus immersing, increases with age. That age predicted greater differentiation between the close and look conditions as well suggests that older individuals respond in a more regulated fashion even when responding naturally to emotional stimuli than do younger individuals.

Although a trend was observed between age and self-reported negative affect for far trials, it is somewhat surprising that this effect was not stronger given that prior research has suggested that the ability to use distancing strategies to manage negative affect increases from late childhood to adulthood (Silvers, McRae, et al., 2012). This result may be at least partially due to underrepresentation of older adolescents and young adults in the present sample, leading to unreliable age effects at the upper age limit of the sample. Another possibility is that neither linear nor quadratic age effects effectively captured age-related trends in this wide of an age range and more complex models may be needed to explain the present data.

Prefrontal recruitment as a function of strategy and age. Across all strategy types, responding to negative stimuli strongly recruited bilateral dlPFC, vlPFC and dmPFC. Yet, recruitment also varied as a function of strategy. For example, left vlPFC responded in a stepwise pattern to regulatory demands such that recruitment was weakest for close trials, slightly stronger for look trials, and strongest for far trials. Taken together, this suggests that immersing, responding naturally, and reappraising emotional stimuli may rely upon partially overlapping cognitive processes but the degree to which they are recruited varies as a function of regulatory goal. Left vlPFC has been implicated in retrieving information from semantic memory, producing internal and external speech, and forming goal-relevant responses (Badre & Wagner, 2007; Hinke et al., 1993; Huang et al., 2002; Thompson-Schill et al., 2005). Given this, left vlPFC may support appraisal of emotional stimuli by integrating semantic information to construct a narrative about the stimulus, and it may support distancing by forming new appraisals that are congruent with regulatory goals.

Age predicted increased recruitment of prefrontal control regions across strategy types but to different degrees. For all strategy types, age predicted enhanced recruitment of bilateral dlPFC but did not impact vlPFC recruitment. This pattern is similar to prior work showing that age predicts recruitment of dlPFC, on a working memory task with manipulation demands, but not vlPFC, on a working memory task with maintenance demands (Crone et al., 2006). Surprisingly, in the present experiment, age-related increases in dlPFC were strongest for the close condition. This was due to the fact that younger individuals showed relative deactivation in dlPFC on close trials while older individuals showed dlPFC activation for all trial types. This may suggest that when children respond to emotionally evocative material in a more reactive way they do not engage prefrontal control circuitry, while adults recruit PFC across different regulatory contexts.

Regulation of affective appraisal circuitry as a function of age. Age strongly predicted reductions in amgydala response on trials when participants reappraised. This suggests that age is associated with enhanced reappraisal-related modulation of affective appraisal regions known to detect, appraise and encode salient and affectively relevant stimuli (Anderson et al., 2003; Cunningham & Brosch, 2012; Ochsner & Gross, 2005). Intriguingly, age did not predict any differences in amygdala responses during close or look trials. On the one hand, this finding is somewhat surprising given prior work showing age-related differences in amygdala responses during passive viewing of emotional facial expressions (Guyer et al., 2008; Monk et al., 2003). On the other hand, this finding is very much in line with prior work suggesting that age predicts differences in regulation ability but not in bottom-up emotional reactivity (McRae et al., 2012; Silvers, McRae, et al., 2012).

Conclusions and future directions. The present data suggest that reappraisal is an effective regulatory strategy across childhood and adolescence for managing affective responses to negative social stimuli. While age was associated with differences in prefrontal recruitment across strategies, only reappraising showed age-related reductions in amygdala recruitment. Taken together, this suggests that prefrontal-subcortical interactions that underlie amygdala modulation during reappraisal become increasingly robust over the course of childhood and adolescence.

Chapter 5: Effects of age on regulation of craving for food

Introduction

Over the past 30 years, the prevalence of obesity in the United States has grown dramatically (Flegal, Carroll, Ogden, & Curtin, 2010; Flegal, Carroll, Ogden, & Johnson, 2002; Ogden et al., 2006). Perhaps even more concerning is the fact that the rate of obesity among children has tripled during this time, suggesting that a growing percentage of the population will spend much of their lives overweight or obese (Lee et al., 2010; Skelton, Cook, Auinger, Klein, & Barlow, 2009). Prior work has shown that childhood self-regulatory ability is predictive of lower body mass indices (BMI) in both the short and long-term (Francis & Susman, 2009; Schlam, Wilson, Shoda, Mischel, & Ayduk, 2013). Yet, it is unknown how the ability to regulate craving for food develops over the lifespan and how it is supported in the brain.

The bulk of research examining self-regulation in adults has focused on the use of cognitive strategies such as reappraisal, which involves thinking about a stimulus differently so as to alter its affective impact. While most reappraisal studies to date have examined its use in regulating negative affect, a growing body of work suggests that reappraisal can also be used to reduce craving for food (Giuliani, Calcott, & Berkman, 2013; Kober et al., 2010; Wang et al., 2009). In healthy adults, reductions in self-reported craving are accompanied by attenuated responses in the ventromedial prefrontal cortex and the ventral striatum (Kober et al., 2010; Wang et al., 2009). Such findings have been interpreted as evidence for reappraisal modulating craving-related processes at the neural level given the vmPFC's role in evaluating the significance or value of stimuli in a given

context (Hare, Camerer, & Rangel, 2009; Oya et al., 2005; Schoenbaum et al., 2007; Schoenbaum et al., 2011) and the VS's role in reward processing and coordinating behavioral responses to emotional stimuli (Roitman, Wheeler, & Carelli, 2005; Schultz et al., 1992). In healthy adults, reappraisal of food stimuli is supported by recruitment of dorsal and lateral prefrontal regions commonly implicated in cognitive control and reappraisal of aversive stimuli (Hollmann et al., 2012; Kober et al., 2010). Given that such prefrontal regions and the cognitive control skills they support undergo dramatic maturational changes during childhood and adolescence (Amso & Casey, 2006; Bunge & Wright, 2007; Giedd & Rapoport, 2010; Luna, Padmanabhan, & O'Hearn, 2010; P. Shaw et al., 2008), it stands to reason that the ability to regulate craving for food using reappraisal may improve as a function of age. While prior work has shown that age does indeed predict enhanced reappraisal success for negative emotion (McRae et al., 2012; Silvers, McRae, et al., 2012), it is unknown whether age also predicts improved regulation success for craving for food.

While no prior work has examined age-related differences in craving for food or regulation of craving for food in adolescence, there is strong evidence suggesting that age predicts differences in appetitive processing more broadly. Relative to adults, incentives improve cognitive control abilities to a greater degree in adolescents (Geier et al., 2010; Hardin et al., 2009; Smith, Halari, Giampetro, Brammer, & Rubia, 2011), yet adolescents also show relative deficits in their ability to use cognitive control to resist approaching appetitive stimuli (Somerville et al., 2011). This overall sensitivity to rewarding and appetitive stimuli may be related to adolescents' tendency to appraise appetitive stimuli as being more positive than adults (Galvan & McGlennen, 2013) and to show hyperresponsive ventral striatal responses to rewarding or appetitive stimuli (Galvan, 2010). Consistent

with this notion, adolescents show exaggerated ventral striatal responses and blunted prefrontal responses when passively viewing food cues in comparison to adults (Killgore & Yurgelun-Todd, 2005).

Taken together, prior research suggests that over the course of adolescence and during the transition into adulthood appetitive stimuli are perceived to be less positive, responses in reward-related circuitry decline, and recruitment of prefrontal control regions increases. However, no prior work has examined 1) whether age predicts improved ability to use cognitive strategies to regulate craving for food, and 2) how this is implemented in the brain. To address these issues, the present study examined children, adolescents and young adults' (aged 6-22) self-reported craving and neural responses to appetizing but unhealthy foods. While participants were shown appetizing food on every trial, the way they thought about the food varied from trial to trial. On half of all trials, participants focused on the appetitive features of the food they were viewing ('close' trials), while on the other half of trials they reappraised the food by imagining it being farther away ('far' trials). Inclusion of these two trial types allowed for an examination of whether age is associated with differences in bottom-up, reactivity to food stimuli ('close' trials), reappraisal-related regulation of food stimuli ('far' trials), or both.

Methods

Participants. Seventy-three healthy individuals between the ages of 6-22 years participated in the experiment (46 female; mean age = 13.49 years, S.D. = 4.08). However, three participants (2 female; mean age = 7.75 years, S.D. = 1.43) were excluded from analyses due to excessive head motion (see Methods for more details), resulting in a final sample of 70 participants (44 female; mean age = 13.73 years, S.D. = 3.97). Participants

were prescreened prior to participation to ensure that they could read and write in English, had normal or corrected vision, had never been diagnosed with a developmental or psychiatric disorder, and had never been prescribed psychotropic medication. Those who were scanned were screened to ensure they did not have any conditions contraindicated for MRI scanning. All participants completed the Wechsler Abbreviated Scale of Intelligence (mean score = 111.91, S.D. = 15.82) and no relationship was observed between age and IQ scores (r=-.14, *p*=.25).

Experimental procedures. Prior to performing the task, participants were trained extensively on the immersed ('close') and distanced ('far') strategies in accordance with well-validated procedures (Ochsner, et al., 2004)(Goldin et al., 2012). Instructions for the prior developmental studies (Silvers, McRae, et al., 2012), but were modified so that they were appropriate for food stimuli. On 'close' trials, participants were told to imagine the food was right in front of them and were told to focus on the taste and smell of the food. On 'far' trials, paticipants were told to imagine the food was a little further away and to focus more on the visual aspects of the food stimuli (shape, color, etc) than its appetitive features.

All participants completed 40 experimental trials, 20 Far trials and 20 Close Trials. On each trial, participants were first shown a cue word for 2 seconds that indicated what strategy they were to use on that trial ('close' or 'far'). Next, a photograph of appetizing food appeared for 8 seconds. It was during this period that participants were to apply the strategy they had been cued to use. Next, a jittered fixation cross appeared (for an average of 3 seconds), followed by a rating scale that appeared for 3 seconds. Participants were asked to respond to the rating scale by assessing how much they wanted to eat the food they had just seen on a five-point scale (1=not at all, 5=very much so) via button press.

Each trial concluded with an additional jittered fixation cross (for an average of 3 seconds). A diagram of the trial structure used is shown in Figure 5.1. The assignment of pictures to instruction was counterbalanced between participants. All participants were weighed and measured so that BMI could be calculated using standard procedures.

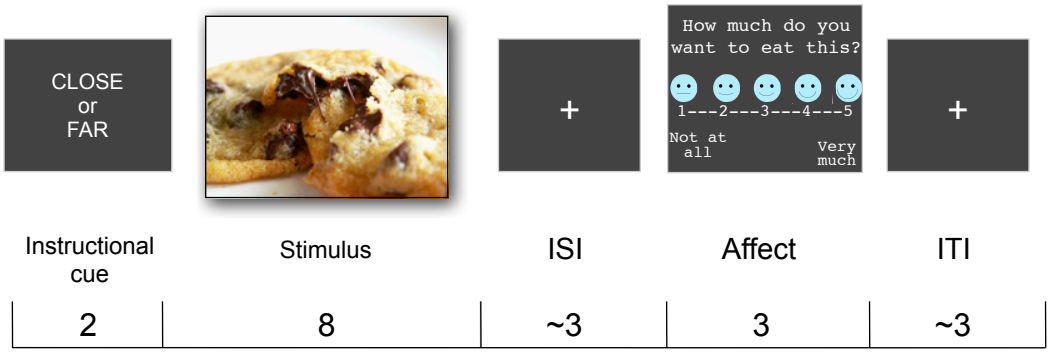

Figure 5.1. Trial structure for Study 4.

fMRI acquisition. Whole-brain fMRI data were acquired on a 3T Siemens Magnetom Trio scanner. Structural images were acquired using a high-resolution, T1-weighted MPRAGE sequence (TR=2170 ms, TE=4.33 ms, 120 1.5 mm slices). Functional images were acquired with a T2*-sensitive EPI BOLD sequence. Thirty-four axial slices were collected with a TR of 2000 ms (TE of 34 ms, flip angle of 90°, field of view of 22.4 cm and 3.5 x 3.5 x 4 mm voxels). Stimuli were presented using E-Prime and were projected onto a flat screen mounted in the scanner bore. Subjects viewed the screen using a mirror mounted on a 16-channel head coil.

Behavioral data analysis. Effects of strategy and age were analyzed using repeated measures GLM models, as implemented in SPSS 19.0. Follow-up t-tests were performed, when necessary, to disambiguate significant *F* statistics. Correlations were used to disambiguate effects relating to age.

fMRI analysis. Preprocessing was performed using SPM8 preprocessing tools (Wellcome Department of Cognitive Neurology, UCL) as implemented in NeuroElf (http://neuroelf.net). Functional images were corrected for motion, slice-time corrected and coregistered to the first functional image for each subject. Head motion was estimated for each run and all runs with more than 2.5 mm of head motion were excluded from further analyses. Structural images were normalized (spatially warped) to a standard template brain (the MNI avg15T1.img) using SPM8's default options and warping parameters were applied to functional images for each subject. Normalized functional images were interpolated to 3 x 3 x 3 mm voxels and spatially smoothed with a 6-mm Gaussian filter.

First and second-level GLM analyses were implemented in NeuroElf (http://neuroelf.net). Cue, stimulus-viewing and response portions of each trial were modeled as boxcar regressors convolved with a canonical hemodynamic response function. Separate regressors were made for the two different trial types (as well as for the instructional cue and response period) so that neural responses associated with strategy (close vs. far) could be differentiated. For each subject, a robust regression analysis was performed on the conditions of interest and motion parameters and high-pass filter parameters were included as additional regressors of no interest. Second-level random effects analyses were next performed to identify regions of activation at the group level that included each subject's mean global signal as a covariate of no interest. All maps were first thresholded to an uncorrected $p<.005$ and then significant voxels were identified using joint voxel and extent thresholds (corresponding to a corrected $p<.05$) as determined by AlphaSim, implemented in NeuroElf.

Two group-level analyses were performed. First, a conjunction analysis was performed between the close and far conditions (each compared to fixation baseline) to identify brain regions that responses to appetitive stimuli across strategy. Second, a contrast between the close and far conditions was performed. To examine age effects, whole-brain correlations were performed for both the close and far conditions (relative to fixation). A conjunction analysis was performed to identify brain regions that showed effects of age across conditions. To examine brain regions that changed with age for one condition but not the other, a whole-brain correlation between age and the far>close contrast was also performed. Lastly, the effects of BMI on neural responses were evaluated by conducting a whole-brain correlational analyses between BMI and the close, far and close>far contrast.

Results

Behavioral results. A repeated-measures ANOVA using strategy type (Close, Far) and age as predictors revealed a trend for strategy type such that Far trials were associated with less craving than Close trials (M=.52, F(1,68)=3.37, p=.07). A significant main effect of age (F(1,68)=5.03, p<.05) was also revealed and follow-up correlational analyses revealed that age correlated negatively with craving ratings for both the Close (r=-.26, p<.05) and Far conditions (r=-.21, p=.09; Figure 5.2). No interaction was observed between age and strategy type (F(1,68)=.04, p=.85). The extra sum-of-squares F test was used to determine whether a linear or quadratic model of age was more appropriate and for each of the negative conditions, a linear test was identified as providing a better fit for both Close and Far trials and was thus used for all subsequent imaging analyses.

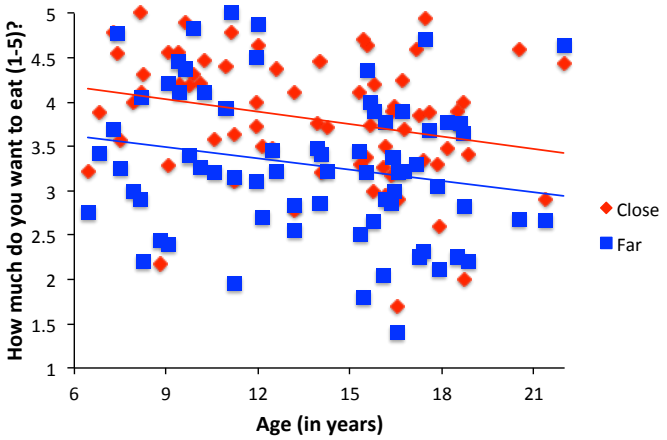

Figure 5.2. Self-reported craving for close and far conditions as a function of age.

A repeated-measures ANOVA was also performed using strategy type (Close, Far) and BMI as predictors, while controlling for age. Age was added as a covariate to control for the fact that BMI and age were correlated (r=.47, p<.001). BMI was not found to be a significant predictor of craving (F(1,64)=1.59, p=.21), nor did it interact significantly with strategy to predict craving (F(1,64)=.031, p=.86).

Imaging results. Imaging data were first analyzed at the group level and were subsequently tested for age and BMI effects.

Group results. The conjunction analysis between the close and far conditions revealed that both strategies strongly recruited the ventral striatum, bilateral dmPFC and dlPFC, as well as large swaths of visual cortex (Table 5.1; Figure 5.3). A direct contrast between the conditions revealed several regions that differed as a function of strategy as well. Several brain regions known to support reappraisal responded more strongly on far trials than close trials, including dmPFC, bilateral dlPFC and vlPFC (Table 5.2; Figure 5.4).

vmPFC was the only brain region to show attenuated activity for the far condition relative to the close condition.

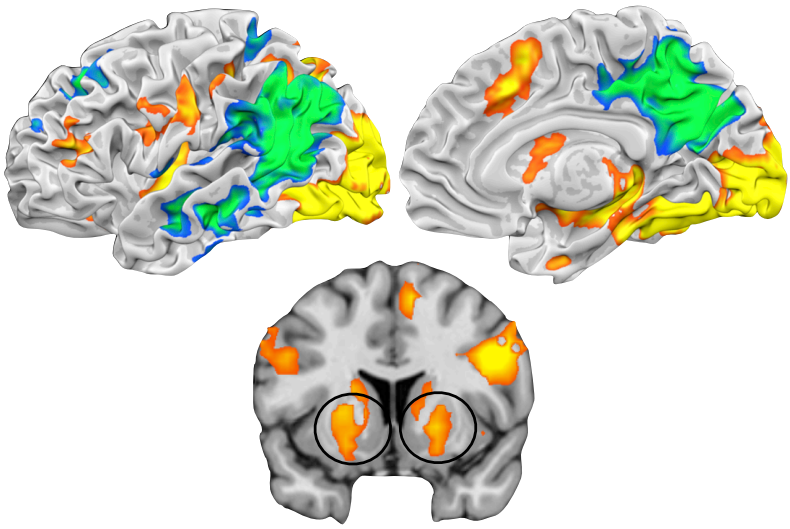

Figure 5.3. Brain regions identified in conjunction between close and far conditions.

				MNI Coordinates		
Region	Side	Extent	t-value	x	y	z
Inferior frontal gyrus	L	148	5.59	-42	36	12
Middle frontal gyrus	L	LM	4.44	-51	30	30
Middle frontal gyrus	L	LM	4.79	-48	39	27
Superior frontal gyrus	R	186	6.30	9	12	54
Superior frontal gyrus	R	LM	6.17	6	18	42
Superior frontal gyrus	R	LM	3.67	6	18	69
Cingulate gyrus	L	LM	3.78	-9	21	39
Cuneus	L	9701	23.57	-12	-96	-6
Cuneus	L	LM	6.02	-24	-66	0
Cuneus	L	LM	19.13	-21	-90	-12
Cuneus	L	LM	6.23	-21	-75	0
Cuneus	R	LM	21.24	18	-90	-9
Cuneus	R	LM	18.72	18	-99	3
Cuneus	R	LM	7.34	21	-75	3
Inferior frontal gyrus	R	LM	3.53	33	18	24
Inferior frontal gyrus	R	LM	4.31	51	15	3
Inferior frontal gyrus	R	LM	3.95	51	45	12
Inferior frontal gyrus	R	LM	3.79	51	30	21
Middle frontal gyrus	L	LM	4.03	-60	9	36
Middle frontal gyrus	R	LM	3.49	30	9	30
Middle frontal gyrus	R	LM	4.84	42	36	15
Posterior orbital gyrus	L	LM	4.89	-24	27	-15

Posterior orbital gyrus	L	LM	3.77	-21	15	-18
Posterior orbital gyrus	R	LM	4.81	27	30	-15
Amygdala	L	LM	5.82	-21	-6	-18
Anterior insula	R	LM	3.87	30	30	3
Anterior insula	R	LM	3.39	36	15	0
Caudate	L	LM	4.69	-18	6	15
Caudate	L	LM	4.14	-18	-6	18
Caudate	L	LM	3.90	-12	9	3
Caudate	R	LM	4.05	12	12	3
Caudate	R	LM	4.65	18	-3	15
Caudate	R	LM	4.25	18	6	12
Caudate	R	LM	5.35	27	-33	9
Globus pallidus	R	LM	4.17	21	3	6
Globus pallidus	R	LM	7.06	24	-12	-6
Putamen	L	LM	5.10	-21	6	3
Putamen	L	LM	4.47	-21	6	-12
Putamen	R	LM	4.79	21	9	-3
Putamen	R	LM	4.16	21	9	-12
Putamen	R	LM	4.12	21	18	-9
Fusiform gyrus	L	LM	5.10	-51	-48	-30
Fusiform gyrus	L	LM	13.19	-33	-57	-12
Fusiform gyrus	R	LM	12.74	30	-63	-9
Fusiform gyrus	R	LM	7.90	30	-36	-24
Hippocampus	L	LM	7.06	-30	-18	-12
Hippocampus	L	LM	11.71	-27	-33	-3
Hippocampus	R	LM	10.19	27	-30	-6
Inferior parietal lobule	L	LM	5.82	-45	-36	42
Midbrain	R	LM	4.14	15	-12	-12
Middle occipital gyrus	L	LM	13.67	-45	-69	-9
Middle occipital gyrus	L	LM	18.12	-24	-96	9
Middle occipital gyrus	R	LM	17.31	30	-90	9
Middle occipital gyrus	R	LM	15.57	36	-78	-3
Middle occipital gyrus	R	LM	13.07	48	-63	-9
Parahipppocampal gyrus	L	LM	5.74	-30	-3	-33
Parahipppocampal gyrus	R	LM	5.90	30	-3	-33
Pons	R	LM	4.47	12	-36	-33
Postcentral gyrus	L	LM	5.03	-66	-15	39
Postcentral gyrus	L	LM	4.67	-60	-24	45
Postcentral gyrus	R	LM	4.09	54	-15	36
Postcentral gyrus	R	LM	4.72	57	-21	54
Posterior insula	L	LM	6.11	-39	-6	3
Posterior insula	L	LM	5.96	-33	-9	18
Posterior insula	R	LM	5.11	36	-6	18
Posterior insula	R	LM	4.71	39	-6	6
Precentral gyrus	L	LM	5.93	-66	-9	30
Precentral gyrus	L	LM	4.37	-60	0	36
Precentral gyrus	L	LM	4.06	-57	3	45
Precentral gyrus	L	LM	3.68	-54	0	21
Precentral gyrus	L	LM	4.05	-48	-9	30
Precentral gyrus	R	LM	4.77	42	-9	66

Precentral gyrus	R	LM	5.73	57	3	45
Precentral gyrus	R	LM	4.07	66	-9	36
Precentral sulcus	L	LM	4.33	-48	6	30
Precentral sulcus	R	LM	6.53	48	9	30
Inferior parietal lobule	R	LM	6.73	42	-36	48
Inferior parietal lobule	R	LM	5.71	42	-27	42
Superior parietal lobule	L	LM	5.99	-30	-51	45
Superior parietal lobule	L	LM	9.08	-27	-69	33
Superior parietal lobule	L	LM	8.12	-24	-66	51
Superior parietal lobule	R	LM	9.47	24	-63	51
Superior parietal lobule	R	LM	7.46	27	-51	45
Superior parietal lobule	R	LM	6.90	30	-66	30
Superior parietal lobule	R	LM	7.20	33	-45	51
Superior parietal lobule	R	LM	7.17	33	-42	42
Inferior occipital gyrus	L	LM	16.20	-30	-81	-12
Inferior occipital gyrus	R	LM	17.41	30	-84	-9
Inferior occipital gyrus	R	LM	15.26	39	-78	-18
Lingual gyrus	R	LM	14.95	39	-69	-12
Thalamus	R	LM	4.59	15	-24	9
Cerebellum	L	LM	5.07	-42	-54	-33
Cerebellum	L	LM	3.27	-36	-69	-36
Cerebellum	L	LM	4.07	-33	-60	-42
Cerebellum	L	LM	4.22	-24	-63	-45
Cerebellum	L	LM	4.00	-24	-60	-36
Cerebellum	M	LM	5.95	0	-57	-33
Cerebellum	R	LM	5.71	18	-42	-42
Cerebellum	R	LM	4.83	48	-48	-30
Cerebellum	R	63	5.08	30	-57	-45
Middle frontal gyrus	L	246	-7.94	-27	30	42
Middle frontal gyrus	L	LM	-7.01	-24	21	45
Superior frontal gyrus	L	LM	-5.46	-24	18	54
Middle frontal gyrus	R	57	-4.54	27	30	45
Medial frontal gyrus	M	433	-8.52	0	54	6
Medial frontal gyrus	L	LM	-6.41	-3	45	-9
Medial frontal gyrus	M	LM	-4.54	0	48	18
Cingulate gyrus	M	LM	-7.57	0	45	3
Superior frontal gyrus	L	LM	-3.39	-3	48	33
Superior frontal gyrus	M	LM	-4.81	0	57	21
Middle temporal gyrus	L	2080	-9.50	-57	-18	-12
Middle temporal gyrus	L	LM	-6.02	-57	-48	0
Middle temporal gyrus	L	LM	-5.68	-54	-30	-6
Middle temporal gyrus	L	LM	-5.85	-51	-36	-15
Inferior temporal gyrus	L	LM	-4.16	-63	-33	-27
Inferior temporal gyrus	L	LM	-4.83	-57	-24	-36
Superior temporal gyrus	L	LM	-8.90	-63	-57	18
Superior temporal gyrus	L	LM	-4.53	-54	-6	3
Superior temporal gyrus	L	LM	-3.87	-54	-24	9
Posterior insula	L	LM	-3.95	-45	-15	0
Posterior insula	L	LM	-3.78	-42	-21	9
Posterior insula	L	LM	-4.65	-39	-24	0

Inferior parietal lobule	L	LM	-5.69	-63	-48	36
Inferior parietal lobule	L	LM	-5.94	-57	-33	18
Inferior parietal lobule	L	LM	-8.44	-54	-69	18
Inferior parietal lobule	L	LM	-7.09	-51	-57	42
Inferior parietal lobule	L	LM	-6.08	-48	-36	21
Inferior parietal lobule	L	LM	-9.31	-48	-54	21
Inferior parietal lobule	L	LM	-9.30	-45	-69	30
Inferior occipital gyrus	L	LM	-6.40	-63	-57	6
Inferior parietal lobule	R	1487	-8.72	45	-72	39
Inferior parietal lobule	R	LM	-8.33	57	-63	21
Inferior parietal lobule	R	LM	-4.68	63	-42	45
Superior parietal lobule	R	LM	-7.22	57	-63	33
Middle temporal gyrus	R	LM	-5.63	51	-27	-15
Middle temporal gyrus	R	LM	-5.67	54	-15	-18
Middle temporal gyrus	R	LM	-6.35	57	-3	-18
Middle temporal gyrus	R	LM	-5.61	60	-30	-9
Middle temporal gyrus	R	LM	-5.19	60	-15	-27
Middle temporal gyrus	R	LM	-7.73	63	-57	12
Superior temporal gyrus	R	LM	-4.47	45	-18	-9
Superior temporal gyrus	R	LM	-6.22	51	-51	21
Superior temporal gyrus	R	LM	-4.60	60	0	3
Superior temporal gyrus	R	LM	-4.58	60	0	-9
Superior temporal gyrus	R	LM	-7.07	63	-27	21
Superior temporal gyrus	R	LM	-4.45	66	-21	-6
Posterior insula	R	LM	-4.87	42	-18	0
Precuneus	L	2185	-11.49	-3	-45	45
Precuneus	L	LM	-10.11	-9	-69	27
Precuneus	L	LM	-9.42	-3	-69	36
Precuneus	M	LM	-11.01	0	-48	54
Precuneus	M	LM	-10.53	0	-54	42
Precuneus	R	LM	-9.46	9	-72	30
Precuneus	R	LM	-6.75	9	-63	18
Precuneus	R	LM	-7.21	12	-60	27
Cingulate gyrus	L	LM	-9.57	-6	-51	33
Cingulate gyrus	L	LM	-10.49	-3	-27	45
Cingulate gyrus	M	LM	-4.33	0	-24	30
Cingulate gyrus	R	LM	-7.57	9	-27	42
Postcentral gyrus	L	LM	-5.30	-24	-45	63
Postcentral gyrus	R	LM	-4.34	27	-39	60
Precentral gyrus	L	LM	-4.29	-6	-9	63
Superior parietal lobule	R	LM	-4.01	18	-45	63
Cerebellum	R	61	-4.53	18	-90	-36
Cerebellum	R	LM	-4.16	3	-90	-36

Table 5.1. Brain regions identified in the conjunction analysis between the close and far conditions. Side indicates whether the cluster was located on the left ("L"), right ("R"), or medially ("M"). Extent indicates the number of voxels in the cluster. Local maxima with 10 or more voxels are indicated by "LM" in the Extent column. t-values refer to the t statistic identified in the peak voxel for a given cluster.

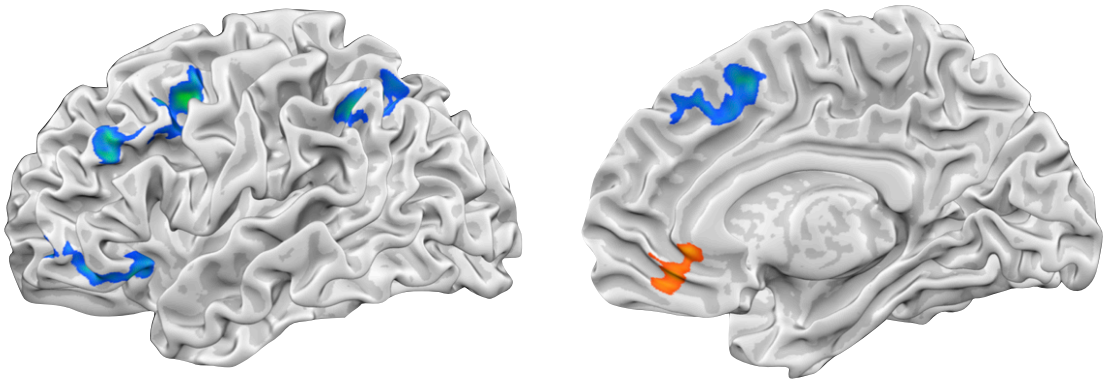

Figure 5.4. Brain regions identified as responding more strongly to close (hot colors) or far trials (cool colors).

				MNI Coordinates		
Name	Side	Extent	t-value	x	y	z
Inferior frontal gyrus	L	162	4.46	-45	18	-3
Inferior frontal gyrus	L	LM	4.34	-48	24	-15
Inferior frontal gyrus	L	LM	4.28	-42	39	-9
Middle frontal gyrus	L	LM	4.45	-39	51	-3
Anterior insula	L	LM	3.84	-33	24	0
Middle frontal gyrus	L	217	5.20	-36	9	45
Middle frontal gyrus	L	LM	4.46	-45	15	48
Middle frontal gyrus	L	LM	3.73	-45	24	36
Middle frontal gyrus	L	LM	4.76	-42	33	33
Middle frontal gyrus	L	LM	4.71	-42	6	54
Middle frontal gyrus	L	LM	3.61	-39	9	36
Inferior frontal gyrus	L	LM	3.51	-48	12	30
Superior frontal gyrus	M	199	5.60	0	24	48
Superior frontal gyrus	R	LM	3.93	3	39	45
Superior frontal gyrus	R	LM	3.48	3	36	36
Superior frontal gyrus	R	LM	4.25	6	15	51
Middle frontal gyrus	R	82	3.89	39	57	12
Middle frontal gyrus	R	LM	3.86	36	45	0
Middle frontal gyrus	R	LM	3.69	36	57	0
Middle frontal gyrus	R	469	5.91	45	6	48
Middle frontal gyrus	R	LM	4.88	33	6	30
Middle frontal gyrus	R	LM	4.39	33	9	57
Middle frontal gyrus	R	LM	5.01	39	9	39
Middle frontal gyrus	R	LM	5.26	42	30	39
Middle frontal gyrus	R	LM	4.77	48	15	45
Superior frontal gyrus	R	LM	4.22	24	27	57
Superior frontal gyrus	R	LM	5.68	24	15	57
Inferior frontal gyrus	R	LM	4.97	45	18	33
Inferior frontal gyrus	R	81	4.42	51	24	-9
Inferior frontal gyrus	R	LM	3.57	54	21	0

Anterior insula	R	LM	3.42	33	21	3
Anterior insula	R	LM	3.41	48	9	3
Inferior parietal lobule	L	209	4.85	-48	-48	42
Inferior parietal lobule	L	LM	4.29	-42	-60	48
Inferior parietal lobule	L	LM	4.79	-36	-54	36
Superior parietal lobule	R	359	5.68	39	-57	48
Inferior parietal lobule	R	LM	4.50	45	-45	39
Inferior parietal lobule	R	LM	3.64	48	-51	27
Inferior parietal lobule	R	LM	3.53	48	-39	30
Inferior parietal lobule	R	LM	4.63	57	-48	48
Inferior parietal lobule	R	LM	4.23	63	-45	39
Medial frontal gyrus	R	71	-4.38	6	39	-12
Cingulate gyrus	R	LM	-4.09	3	33	-3

Table 5.2. Brain regions identified in the far>close contrast. Side indicates whether the cluster was located on the left ("L"), right ("R"), or medially ("M"). Extent indicates the number of voxels in the cluster. Local maxima with 10 or more voxels are indicated by "LM" in the Extent column. t-values refer to the peak t statistic. Brain regions that responded more strongly to the far condition are listed first (positive t values) followed by those that responded more strongly to the close condition (negative t values).

Age effects. To examine age effects, correlations were performed between age and the close and far conditions separately. A conjunction analysis between these two correlations revealed that age predicted enhanced recruitment of posterior parietal cortex for both the close and far conditions (Table 5.3). Age predicted reductions in ventral striatum recruitment for the far condition, but not the look condition (Figure 5.5). When the same correlation was conducted while controlling for self-reported craving, a sizeable cluster (k=114 voxels) in right putamen (27,15,0) remained. A correlation between age and the far>close contrast did not reveal any clusters that survived whole-brain correction.

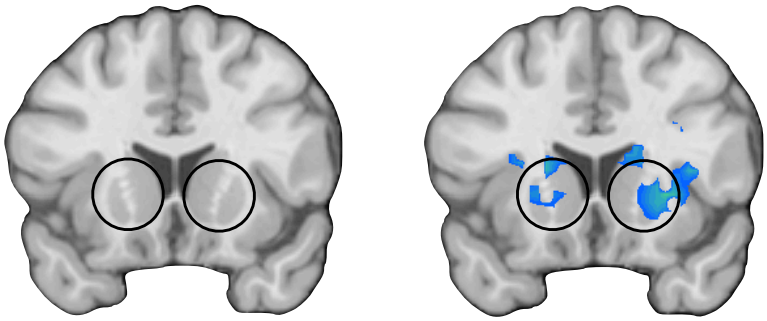

Figure 5.5. Age was associated with an attenuated response to food stimuli in the ventral striatum (y=15) for the far condition (right), but not the close condition (left). The correlation in right putamen remained when controlling for age-related differences in self-reported craving.

					MNI Coordinates		
Condition	Region	Side	Extent	r	x	y	z
Close							
	Superior parietal lobule	R	136	0.48	48	-48	57
	Superior parietal lobule	R	LM	0.42	30	-63	60
	Inferior parietal lobule	R	LM	0.46	42	-72	45
	Inferior parietal lobule	R	LM	0.45	57	-60	42
	Cerebellum	R	76	-0.48*	24	-69	-36
	Cerebellum	R	LM	-0.39*	24	-63	-45
	Cerebellum	R	LM	-0.40*	27	-72	-54
	Cerebellum	R	LM	-0.40*	33	-54	-45
Far	Inferior temporal gyrus	L	74	0.50	-54	-51	-21
	Middle temporal gyrus	L	LM	0.46	-57	-39	-12
	Superior parietal lobule	L	244	0.51	-30	-63	63
	Cuneus	L	LM	0.40*	-15	-93	36
	Cuneus	L	LM	0.41*	-12	-87	45
	Cuneus	L	LM	0.43*	-6	-90	36
	Cuneus	R	LM	0.40*	15	-84	45
	Inferior parietal lobule	R	LM	0.44*	42	-75	39
	Precuneus	L	LM	0.50	-9	-69	60
	Precuneus	M	LM	0.38*	0	-78	39
	Superior parietal lobule	R	170	0.50	12	-69	63
	Superior parietal lobule	R	LM	0.40	15	-60	66
	Superior parietal lobule	R	LM	0.45	30	-60	57
	Superior parietal lobule	R	LM	0.39	30	-57	66
	Superior parietal lobule	R	LM	0.45	42	-54	60
	Middle frontal gyrus	R	83	-0.49*	27	48	27
	Middle frontal gyrus	R	LM	-0.44*	33	18	24
	Superior frontal gyrus	R	LM	-0.43*	18	42	30
	Caudate	L	230	-0.53	-9	-9	15

	Caudate	L	LM	-0.46	-18	15	9
	Caudate	L	LM	-0.38*	-18	-27	18
	Caudate	L	LM	-0.41*	-12	21	0
	Anterior insula	L	LM	-0.46*	-36	27	-3
	Anterior insula	L	LM	-0.45*	-27	18	12
	Anterior insula	L	LM	-0.39*	-27	24	3
	Putamen	L	LM	-0.49*	-21	18	0
	Caudate	R	277	-0.53*	15	18	15
	Caudate	R	LM	-0.44	18	21	-3
	Anterior insula	R	LM	-0.42	30	30	3
	Anterior insula	R	LM	-0.46	39	18	9
	Anterior insula	R	LM	-0.44*	45	27	-6
	Lateral orbital gyrus	R	LM	-0.46*	36	33	-9
	Putamen	R	LM	-0.49	27	15	0
	Putamen	R	LM	-0.38*	30	3	-9
	Caudate	R	123	-0.49*	15	-12	18
	Caudate	R	LM	-0.41*	18	-33	12
	Caudate	R	LM	-0.41*	27	-33	9
	Hippocampus	R	LM	-0.39*	30	-33	-3
	Thalamus	R	LM	-0.37*	6	-27	6
	Cerebellum	L	401	-0.53	-27	-42	-30
	Cerebellum	L	LM	-0.44	-21	-54	-30
	Cerebellum	L	LM	-0.47	-15	-54	-21
	Cerebellum	L	LM	-0.45	-9	-48	-30
	Cerebellum	L	LM	-0.48	-6	-57	-30
	Cerebellum	L	LM	-0.46	-6	-66	-21
	Cerebellum	L	LM	-0.45	-6	-69	-36
	Cerebellum	R	LM	-0.39	6	-69	-33
	Cerebellum	R	LM	-0.43	9	-45	-30
	Cerebellum	R	LM	-0.40	9	-63	-18
	Cerebellum	R	LM	-0.39	9	-54	-24
	Cerebellum	R	LM	-0.47	21	-51	-24
Conjunction	Inferior parietal lobule	R	43	0.43	42	-51	60
	Superior parietal lobule	R	LM	0.42	30	-63	60
Far>Close	n.s.						

Table 5.3. Neural activity correlated with age. Condition indicates the condition being correlated with age. In the "Region" column "n.s." indicates that no clusters were identified. Side indicates whether the cluster was located on the left ("L"), right ("R"), or medially ("M"). Extent indicates the number of voxels in the cluster. Local maxima with 10 or more voxels are indicated by "LM" in the Extent column. "r" refers to the r value identified in the peak voxel. For each analysis positive correlations are listed first. Correlations that did not survive after controlling for self-reported craving are denoted with a "*".

BMI effects. BMI was examined as a predictor of neural responses for both trial types. BMI predicted diminished recruitment of the right inferior frontal gyrus (IFG; 48, 36,

-12) for the far > close contrast (Figure 5.6), even after controlling for age. No clusters were identified in whole-brain correlations between BMI and the close or far condition versus baseline.

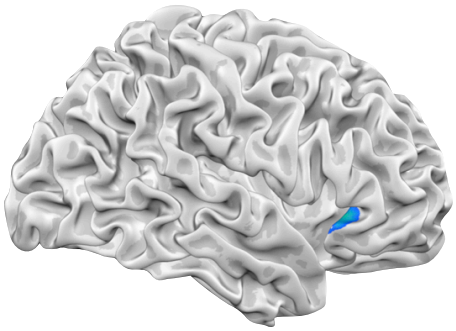

Figure 5.6. BMI predicted less recruitment of right IFG for reappraisal of appetitive stimuli.

Discussion

While concerns about obesity in childhood and adolescence have grown in recent years, little empirical work has examined how craving for food changes during this developmental period. The present study sought to examine age-related differences in craving for food both when individuals react to the appetitive features of food and when they attempt to regulate their craving. The present results suggest that across childhood and adolescence, cognitive strategies such as reappraisal are effective at reducing self-reported craving and neural responses associated with forming affective valuations. While both conditions strongly recruited the ventral striatum at the group level, activity in this region was attenuated as a function of age for the far, but not the close, condition. When controlling for age, BMI predicted reduced recruitment of right IFG, suggesting a potential neural link between self-regulation and health outcomes. These results have implications

for both basic and applied research involving regulation of appetitive responses in development.

Craving for food across childhood and adolescence. The present study is the first to examine the neural and behavioral bases of craving for food in a developmental sample. Prior work has shown that when children and adolescents are presented with food stimuli, they show increased activation in regions associated with the experience of taste, reward processing and affective valuation including the insula, ventral striatum, vmPFC and the amygdala (Holsen et al., 2005; Hommer et al., 2012; Killgore & Yurgelun-Todd, 2005). While these patterns of recruitment are similar to what has been observed in adults, adults show attenuated responses in the ventral striatum during passive viewing of food stimuli in comparison to adolescents (Killgore & Yurgelun-Todd, 2005).

The present study informs models of age-related differences in appetitive processing in two key ways. First, results suggest that age predicts reduced self-reported craving for food, even when individuals are focusing on the "hot", appetitive features of a food. While prior work has examined age-related differences in brain regions associated with craving, such as the ventral striatum, few attempts have been made to situate such findings in the context of age-related changes in affective experience. Second, the present results indicate that age-related reductions in craving are supported by enhanced recruitment of the superior parietal cortex. Given the role of the posterior parietal cortex in selective attention and the fact that activation of this region correlates with age for cognitive control tasks (Adleman et al., 2002), these age-related increases in recruitment may represent enhanced control over attention to the appetitive features of food.

Regulation of craving in development. While prior research has examined the use of cognitive strategies to regulate craving in young children (Moore et al., 1976) and in adults (Giuliani et al., 2013; Hollmann et al., 2012; Kober et al., 2010; Wang et al., 2009), the present study is the first to examine the effects of reappraisal on craving for food across childhood, adolescence and adulthood. Results revealed that children as young as 6 years could use the far strategy to distance themselves from appetitive stimuli and reduce craving but also that older individuals reported even less craving in the far condition than did younger individuals.

Neuroimaging data revealed that across all ages, using a distancing strategy was associated with enhanced recruitment of dorsal and lateral prefrontal regions commonly implicated in reappraisal (Diekhof et al., 2011; Ochsner et al., 2012), as well as downregulation of vmPFC, which supports valuation of stimuli in a goal-dependent manner (Hare et al., 2009; Roy et al., 2012; Schoenbaum et al., 2011). While prior work has suggested that satiety reduces vmPFC responses to food stimuli in adolescents (Holsen et al., 2005), no prior work has demonstrated that cognitive strategies may also serve a modulatory effect. At the group level, both close and far trials strongly recruited the ventral striatum. Yet, only the far condition elicited age-related decreases in ventral striatal activity. Taken together, this suggests that across development, individuals are capable of using prefrontally-mediated cognitive strategies to reduce craving for food but that age predicts enhanced modulation of the ventral striatum. This finding is line with other work suggesting that the ability to exert cognitive control in the presence of appetitive stimuli improves from adolescence to adulthood in conjunction with attenuation of striatal responses (Somerville et al., 2011).

Regulation of craving and body mass index. A growing number of people in industrialized nations are overweight or obese, and more and more of these individuals are becoming overweight or obese at a younger age (Lee et al., 2010). Overweight adolescents are more likely to experience affective and behavioral problems than are their lean peers and are also more likely to grow up to become overweight or obese adults (McClure, Eddy, Kjellstrand, Snodgrass, & Martinez, 2012). Taken together, this suggests that adolescence may be a critical time for developing self-regulatory skills that can help manage both emotional and eating behaviors that may pose serious consequences in adulthood. Yet, little is known about how BMI predicts differences in regulation of craving for food across the lifespan.

Prior work has suggested that healthy adults recruit bilateral dorsal and lateral prefrontal regions when downregulating craving for food, while overweight adults only recruit lateral portions of orbitofrontal cortex (Scharmuller, Ubel, Ebner, & Schienle, 2012). The present study found that while self-reported craving for food did not vary as a function of BMI, heavier individuals failed to recruit right vlPFC as strongly during downregulation of craving than did leaner individuals. Given the role that right vlPFC plays in regulation of appetitive and aversive impulses as well as inhibition of prepotent responses more generally (Aron, Robbins, & Poldrack, 2004; Konishi et al., 1999; Lieberman et al., 2007), this suggests a potential neural mechanism for self-regulatory failures associated with overeating and weight gain in childhood and adolescence.

Conclusions and limitations. The present results suggest that reappraisal is an effective strategy for regulating craving for food across development. However, they also suggest that both baseline reactivity and regulation success for appetitive stimuli

diminishes with age. Like Studies 2 and 3, at the group level reappraisal recruited dorsal and lateral prefrontal control regions previously observed in studies examining reappraisal in adults. In line with Study 3, the present results suggest that age predicts enhanced modulation of subcortical appraisal structures during distancing, but not during immersing. Lastly, by connecting BMI with neural markers of reappraisal, the present study suggests a potential link between self-regulation data in an experimental context and real life health outcomes.

There are several limitations to the present study that ought to be considered and improved upon in future studies. First, the number of participants representing each age in the sample is not evenly distributed. There is a particular underrepresentation of participants aged 18 years and older, which is being remedied by current efforts to recruit from this age group. Second, while the inverse correlation between BMI and right IFG observed on far trials relative to close trials is compelling, the fact that self-reported craving did not vary according to BMI makes this finding a bit difficult to interpret. On the one hand, it could be that lean and heavy participants are equally effective at regulating craving but do so using different neural mechanisms. On the other hand, it could be that heavier participants misrepresent their experienced craving in their self-report. This question is currently being addressed by bringing back participants who have completed this task and having them complete a "free eating task" to assess naturalistic eating behavior. If BMI predicts differences on this task, it would suggest that self-reported craving is not reliable for heavier participants but if no differences in eating behavior is observed, this would suggest that BMI is not actually predictive of differences in regulatory ability. Lastly, prior work has linked the ability to delay gratification to adult BMI but no

prior work has examined what the neural mediators of this effect may be. While the present data cannot speak to this issue, a subselection of participants from this sample have additionally completed Mischel's classic delay of gratification task to examine whether delay ability predicts differences in neural responses during downregulation of craving and preliminary analyses suggest that delay ability predicts enhanced modulation of the ventral striatum.

Chapter 6: General discussion

Summary and significance

Summary. Childhood and adolescence are times of emotional, social and cognitive change. The present four experiments sought to characterize one aspect of these changes by examining age-related differences in emotion regulation. Central to each experiment was the question of whether age predicts differences in bottom-up, emotional reactivity or top-down, emotion regulation. To address this issue, all four studies utilized a within-subject design that included conditions intended to elicit a naturalistic and reactive emotional response as well as a more regulated emotional response. The first three studies examined reappraisal of aversive stimuli, while the fourth study examined reappraisal of appetitive stimuli. Studies 1 and 2 focused on age-related differences in adolescence while Studies 3 and 4 expanded the age range of participants to include children. Across these studies, both common threads and significant variability were observed.

In the first experiment, participants ranging in age from 10-22 years distanced or immersed themselves from stimuli that were either negative or neutral, and social or non-social in nature. Bottom-up emotional reactivity, operationalized as the increase in negative affect reported in response to negative stimuli in the immersed condition versus neutral stimuli, did not vary as a function of age. However, regulation success, operationalized as the decrease in negative affect reported in the distanced versus immersed conditions for aversive stimuli, correlated positively with age. Age effects were stronger for social stimuli than non-social stimuli, suggesting that adult levels of regulation success are achieved at later ages for social stimuli than non-social stimuli. Additionally, young adolescents who were highly rejection sensitive were less successful at reappraising

negative social stimuli than were highly rejection sensitive older adolescents or less rejection sensitive young adolescents.

Study 2 utilized the same task design as Study 1 and sought to accomplish three goals: 1) to replicate the behavioral results observed in Study 1, 2) to examine whether reappraisal of social and non-social emotional stimuli are supported by different patterns of brain activity, and 3) to examine how age, regulation success and stimulus social content interact to predict neural recruitment during reappraisal. The results of Study 2 suggest that across adolescence, reappraisal modulates negative affect and amygdala responses to aversive stimuli. At the group level, both social content and valence predicted amygdala responses, reappraisal of social stimuli relied upon recruitment of left IFG, and reappraisal of non-social stimuli relied upon recruitment of right SFG. Like Study 1, age was found to predict regulation success but not reactivity. Additionally, age predicted decreased recruitment of right SFG, and age and reappraisal success interacted to predict recruitment of left IFG.

In the third study, the age range of the participants was extended to include children as young as six years. Additionally, the paradigm was changed from the one used in Studies 1-2 in two ways: 1) only social stimuli were used, and 2) to explore whether the immersed or distanced strategies were more akin to participants' naturalistic responding at different ages, a third uninstructed viewing condition was also used. At the group level, participants reported more negative affect on 'close' trials than 'look' or 'far' trials. Like Studies 1 and 2, age did not predict significant differences in self-reported negative affect or amygdala responses for 'close' negative trials (nor did it predict differences for 'look' trials). However, age predicted marginally less negative affect for 'far' trials and significant

reductions in the amygdala response. That age-related differences in amygdala modulation were observed for Study 3 but not Study 2 suggests that such age effects occur at relatively young ages.

The final study examined age-related differences in behavioral and neural responses to food stimuli. Like the other studies, the Study 4 used distancing ('close') and immersing instructions ('far') to differentiate age-related effects on reactivity and regulation. Across all ages, distancing reduced craving relative to immersing, recruited prefrontal control regions and modulated activity in brain regions associated with valuation and reward including the vmPFC. Age predicted less craving for both the immersed and distanced conditions but age-related decreases in ventral striatal recruitment were only observed for the 'far' condition.

Significance. The results of the present studies offer at least three new insights into how emotional processes develop during childhood and adolescence. The first is that even very young children are capable of using reappraisal to regulate affective responses to aversive and appetitive stimuli. While prior work has shown that children as young as three can reappraise food (Moore et al., 1976), no prior work has examined reappraisal of aversive and appetitive stimuli in this broad of an age range. Second, Studies 1-3 suggest that emotional reactivity towards aversive stimuli remains relatively constant with age while regulation success improves. This finding has significance both for the development of basic models of emotional development and also for interventions. For example, the present results suggest that therapy in adolescents may be most successful if its focus is on developing regulatory skills than on changing bottom-up emotional responses. The third implication of the present studies is that age-related differences in emotion regulation

occur via changes in recruitment of both prefrontal control regions and subcortical appraisal regions. The third and fourth studies suggest that age predicts enhanced recruitment of prefrontal control regions, in line with prior developmental work using cognitive control tasks, as well as enhanced modulation of brain regions involved in forming affective appraisals. The second study suggests that the nature of prefrontal recruitment may vary as a function of age, stimulus type, and how successful an individual is at reappraising.

Considerations for conducting research on emotion-cognition interactions in childhood and adolescence

In recent years, there has been a surge of neuroscientific research on the development of social, affective and cognitive processes in adolescence, and to a lesser degree in childhood. The emerging field of developmental cognitive neuroscience draws from a collection of partially overlapping disciplines but presents itself as an independent field of study with its own unique set of strengths and challenges. Two such challenges are how best to model and test age effects, and how to disentangle the effects of age and task performance on fMRI results.

Testing and modeling age effects. Central to all developmental science research is the question of how individuals think and act differently at different points in the lifespan. In principle, evaluating the effects of age on cognition and behavior would appear to be a rather simple task, yet in practice it rarely is. Developmental scientists must make critical decisions both when designing experiments and when analyzing data that constrain the types of interpretations that can be made about age. At the stage of experimental design, experimenters must decide whether to use a longitudinal approach, by testing the same

participants at different points in the lifespan, or a cross-sectional one, wherein different aged participants are compared to one another. While a handful of studies have used longitudinal approaches in fMRI studies (Koolschijn, Schel, de Rooij, Rombouts, & Crone, 2011; Pfeifer et al., 2011; D. J. Shaw, Grosbras, Leonard, Pike, & Paus, 2012), this approach is fairly rare for reasons of feasibility.

Within cross-sectional samples, age effects may be examined either by sampling across a continuous age range or by comparing participants from discrete age groups (e.g., adolescents versus adults). Adolescence is marked by biological, psychological and social changes that begin at different points in time and transpire at different rates. Because of its multifaceted nature, operationalizing adolescence in terms of specific ages or developmental stages poses a major challenge for developmental researchers (Galvan, 2010; Luna, Velanova, & Geier, 2010; Pfeifer & Blakemore, 2012). To illustrate this point, take the six studies that were highlighted in a recent review paper by Galvan (2010) on reward processing in adolescence. The studies described in this review drew from adolescent samples that included individuals as young as nine years of age (Ernst et al., 2005; May et al., 2004) and as old as seventeen years of age (Bjork et al., 2004; Ernst et al., 2005; Geier et al., 2010; May et al., 2004), and used age ranges as narrow as one year (Van Leijenhorst et al., 2010) and as wide as eight years (Ernst et al., 2005). Researchers may define their age groups in accordance with chronological age, school year, task performance, or a variety of other variables. While an argument could be made for why any one of these approaches is valid, using such a varied set of definitions for what defines adolescence is clearly problematic for those trying to draw broad conclusions from the existing literature. While one solution for dealing with this problem might be to adopt a

standardized method for assigning age categories, another is to use wide age ranges and continuous predictors of age that do not require a priori demarcation of age boundaries. The present studies adopted the latter of these approaches so as to examine childhood, adolescence and adulthood on a continuum rather than as a set of discrete categories (although age was sometimes displayed categorically for visual purposes). This approach allows the data to identify where developmental changes occur rather than the other way around, although it still requires experimenters to carefully select the minimum and maximum ages for a given age range.

A related issue for modeling age effects in developmental cognitive neuroscience is how best to test for and identify linear and non-linear age effects. One advantage to using discrete age categories is that it allows for age effects to be easily quantified and interpreted. A downside to this approach, however, is that often involves the use of narrowly defined age ranges which limits the ability to make broad generalizations about developmental effects. For example, if a group of 14-17 year olds is found to be more emotionally reactive in comparison to a group of 24-28 year olds it is unclear a) at what age emotional reactivity reaches adult levels, and b) whether adolescence peaks in adolescence or is even greater in childhood. The greatest strength of using continuous age ranges is that it allows for more fine-grained precision about the shape of age trajectories. While such approaches allow for greater flexibility and precision when examining developmental effects, they also require larger sample sizes and can pose challenges when it comes to determining whether linear or non-linear age effects best characterize the observed data. One approach is to use task performance to constrain both analytic methods and interpretations of fMRI data. For example, if errors on an inhibition task decrease linearly

with age, the most interpretable patterns of fMRI data would be those that also differ linearly as a function of age. But given that linear and quadratic predictors of age are by definition correlated, what is the best approach for determining what model best fits a given phenomenon? Two approaches to this include "extra sum-of-squares F test" and Akaike's Information Criterion, both of which compare linear and increasingly complex models to identify the model that best fits the present data using the fewest parameters (Motulsky & Christopoulos, 2004; M. S. Thomas et al., 2009). The former is appropriate for "nested models" where the simpler model is actually a version of the more complicated model (i.e., a linear model of age is a version of the quadratic form with the quadratic term set to zero) and was used in Studies 2-4.

In the present studies, age was observed to exert a primarily linear effect on improvements in reappraisal success. Yet, in Study 1, where the largest sample size was used, we found evidence for both linear and quadratic trends characterized by initially linear improvements in reappraisal success followed by a gradual tapering off in late adolescence. This developmental trajectory is similar to what has been observed in prior work examining age-related improvements in cognitive control (De Luca et al., 2003; Huizinga et al., 2006; Luciana et al., 2005; Luna et al., 2004), and fits with the notion that age-related improvements in cognitive control occur in conjunction with prefrontal structural development (Crone & van der Molen, 2007). While the developmental trajectory for reappraisal performance in Study 1 was more protracted than for what is typically observed on "cold" cognitive tasks, this is in line with other "hot" cognitive tasks (Prencipe et al., 2010). Linear age effects were similarly observed in the fMRI data collected in Studies 2-4 with age predicting differential recruitment of prefrontal regions and

enhanced modulation of subcortical appraisal structures such as the amygdala. These linear effects contrast with prior work examining developmental trajectories of emotion-cognition interactions using other tasks such as the emotional go/nogo task (EGNG) wherein participants must respond to target emotional facial expressions and withhold responses from non-target emotional facial expressions. While age predicts more or less linear improvements and changes in ventrolateral preferontal recruitment on a neutral variant of the go/nogo task, nonlinear effects are observed for task performance and subcortical recruitment when the task involves valenced stimuli (Hare et al., 2008; Somerville et al., 2011). Other tasks examining neural responses to emotional facial expressions have similarly observed quadratic effects, with amygdala responses peaking in adolescence relative to childhood or adulthood (Guyer et al., 2008; Killgore & Yurgelun-Todd, 2007; Pfeifer et al., 2011). Taken together, this suggests three things: (1) cold cognitive control improves linearly from childhood through adolescence and tracks with prefrontal development, (2) tasks assessing emotional reactivity tend to show more quadratic trends in subcortical appraisal structures such as the amygdala, and (3) tasks involving emotion-cognition interactions may show linear or quadratic age effects depending on the task at hand.

At present it is unknown why some emotion-cognition tasks show linear age effects and others show quadratic age effects is not immediately clear but at least two possibilities ought to be considered. First, the types of stimuli used may yield different developmental profiles. The vast majority of emotional reactivity tasks and the EGNG use emotional facial expressions, while reappraisal tasks tend to use IAPS stimuli. These two classes of stimuli differ not only in their visual features, but also in their tendency to probe emotion

perception as opposed to experience. Given this, future research ought to use emotional facial expressions as reappraisal stimuli and vice versa in developmental samples. Second, while the EGNG requires participants to recognize a facial expression in order to respond correctly, it does not require participants to alter the meaning of the stimulus over the course of several seconds the way that reappraisal tasks do. This may require a fundamentally different combination of cognitive and semantic processes than what is typically required on tasks such as the EGNG, and therefore may elicit a different pattern of age-related effects.

Disentangling age and task performance. Age predicts changes in task performance as well as neural recruitment. Given this fact, a challenge to developmental researchers is how best to disentangle what observed effects are due purely to age and what effects are driven by age-related changes in task performance. As noted in the introduction, there are several approaches to addressing this issue. On the side of task design, experimenters may opt to use tasks that afford high levels of performance across different ages or that titrate for individual participants. Both of these approaches hold performance constant so that any observed age-related differences in brain activity can be attributed solely to age rather than to task. The upside to these approaches is that they provide a stricter test of what brain activity is purely related to age and what is not. The downside to these approaches is that if performance is held constant in a domain for which there are ostensibly age-related differences in everyday life, such as emotion regulation, the effect of interest is no longer being studied. An alternative approach is to use statistical methods to separately examine the effects of age and task, such as what was done in the present studies when age was significantly correlated with task performance. This

approach can be useful in that it grants insight not only into the neural correlates of task performance and age, but also how the two may interact over time. For example, it may be that recruiting additional prefrontal control regions predicts greater task performance in younger adolescents, but not adults, as was observed in Study 2.

While developmental research examining cognitive control has made efforts to disentangle task performance and age, this is less common in research examining emotional processing or reactivity. In fact, most emotional processing paradigms that have been used in pediatric populations lack any kind of behavioral measure at all. Aside from a handful of studies examining reappraisal in developmental samples (McRae et al., 2012; Perlman et al., 2012; Pitskel et al., 2011), only two prior fMRI studies have asked children or adolescents to rate their affective responses to valenced stimuli on a trial-by-trial basis (Ernst et al., 2005; Galvan & McGlennen, 2013). While the studies by Ernst and Galvan both examined the neural bases of self-reported affect within adolescents and adults, they did not directly compare how changes in affect differed between the groups at the neural level. It will be crucial for developmental affective neuroscience to address this issue moving forward in order to disentangle whether age or age-related differences in emotional experience drive recruitment of brain regions involved in emotional processing.

Limitations and future directions

The present studies provide novel insights into how emotion regulation develops during childhood and adolescence. Yet, like any research, they have several limitations that ought to be considered. First, all of the present studies used photographic stimuli to elicit emotional responses. The results of these studies suggest that age effects can differ as a function of a stimulus's social content and valence and therefore it is worth investigating

whether other factors such as a stimulus' modality, affective intensity or personal relevance may also impact age effects. A second limitation of the present studies is that they all used reappraisal to model emotion regulation. Recent work has suggested that other types of regulatory processes, such as fear extinction, follow quadratic developmental trajectories rather than linear ones like what was observed in the present studies (Pattwell et al., 2012). Therefore, future work may seek to directly compare and contrast developmental trajectories for different types of emotion regulation. A third limitation of the present studies is that while they can inform our understanding of how well children, adolescents and adults can reappraise when they are instructed to do so, they do not inform our understanding of what those individuals do in their everyday lives. Put another way, it is unknown whether reappraisal success on a laboratory task predicts meaningful differences in emotion regulation or wellbeing outside of the laboratory. Study 4 marks a first attempt to address this issue by linking BMI with neural responses that support regulation of craving. Yet, there is still much to be done including linking reappraisal performance in the laboratory to everyday use of reappraisal using diary or experience sampling measures. Lastly, the present work suggests that with a brief training session, individuals as young as 6 years of age can use reappraisal to regulate emotional responses. However, at present it is unclear whether these brief training sessions have any enduring effects on the way children or adolescents manage their emotional experiences in everyday life. Future work ought to examine not only whether training may improve reappraisal success but also whether it may enhance physical and emotional wellbeing more broadly in pediatric populations.

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