THE TEMPORAL DYNAMICS OF VOLITIONAL EMOTION REGULATION

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DANKSAGUNG

SUMMARY

Happiness, anger, surprise, irritation… if we note down the emotions that we go through on a given day, the list will most probably be quite long. A surge of studies on the bidirectional interaction between emotion and cognition suggests that we need emotional appraisals in order to lead a successful life and maintain our personal, social and economic integrity (Bechara, 2005; Damasio, 1994; Fox, 2008; Gross & Thompson, 2007; Walter, 2005). And yet, we seldom 'just' experience emotions, but often try to influence them to best fit our current goals. Based on the assumption that emotional reactions entail changes on various levels, and that these changes happen in- or outside of our awareness, affective science has adopted emotion regulation as one of its major research topics (Beauregard, Levesque, & Paquette, 2004; Gross, 1999; Ochsner, 2007). In fact, neural (e.g. amygdala activation) and behavioral (e.g. feeling of negativity) correlates of emotional reactions are effectively reduced by top-down processes of explicit and implicit control (Drabant, McRae, Manuck, Hariri, & Gross, 2009; Levesque, et al., 2003; Ochsner, Ray, et al., 2004). Furthermore, evidence from studies investigating voluntary thought control suggests that control strategies may have lasting and paradoxical consequences (Abramowitz, Tolin, & Street, 2001; Wegner, 2009). In a very recent investigation, lasting effects of regulation were also shown after the cognitive control of emotions: the activation timecourse of the amygdala was significantly increased immediately following regulation, and this difference was also related to the activation of the amygdala to the same stimuli a few minutes later (Walter, et al., 2009). Aside from these contextual or qualitative influences, emotional processing also differs between individuals: genetic variation within the serotonergic system for instance is

known to affect emotional reactivity both on the behavioral and on the neural level (Hariri, et al., 2005; Hariri, et al., 2002; Lesch, et al., 1996).

In the present work, the temporal dynamics of volitional emotion regulation were investigated in three studies. It was hypothesized that both the subjective experience of negativity and the amygdala activation can be attenuated by the detachment from negative emotions, which in turn leads to an immediate neural aftereffect after the offset of regulation. Furthermore, volitional emotion regulation was expected to be capable of reducing or even obliterating genetically mediated amygdala hyperreactivity to negative emotional cues.

Similar to previous investigations (Walter, et al., 2009), pictures of aversive or neutral emotional content were presented while participants were instructed to react naturally to half of the pictures, and to regulate their emotional response upon the other half of the stimuli. The first two studies of the present work were designed to further characterize the immediate aftereffect of volitional regulation in the amygdala: Study 1 included behavioral ratings of negativity at picture offset and at fixation offset in order to provide behavioral measures of experiential changes, while in Study 2, participants continued to experience or regulate their emotions during a "maintain" phase after picture offset. The primary goal of Study 3 was to evaluate whether volitional emotion regulation can reduce genetically mediated amygdala hyperreactivity to aversive emotional material in individuals with the short variant of the serotonin transporter genotype (Hariri, et al., 2005; Hariri, et al., 2002), and whether the immediate aftereffect is also influenced by the serotonin transporter genotype.

In all three studies, the amygdala was significantly activated by aversive versus neutral stimuli, while cognitive emotion regulation attenuated the activation in the amygdala and increased the activation in a frontal-parietal network of regulatory brain regions. This neural effect was complemented by the behavioral

ratings which show that the subjective experience of negativity was also reduced by detachment (Study 1). Also in all three studies, an immediate aftereffect was observed in the amygdala following the end of regulation. Moreover, the preoccupation with the previously seen pictures after the scanning session varied across the experimental conditions (Studies 2 and 3). Volitional regulation proved effective in reducing amygdala activation to negative stimuli even in 5-HTTLPR short allele carriers that show an increased reactivity to this type of cue. At the same time, functional coupling of the ventrolateral and medial orbital prefrontal cortex, the subgenual and the rostral anterior cingulate with the amygdala was higher in the s-group. However, in Study 3 the immediate aftereffect was found only in l/l-homozygote individuals following the regulation of fear.

Taken together, the results of the three studies clearly show that volitional regulation is effective in reducing behavioral and neural correlates of the experience of negative emotions (Levesque, et al., 2003; Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner, Ray, et al., 2004), even in the case of a genetically mediated hyperreactivity to such materials. Thus, it seems reasonable to assume that conscious will can effectively counteract genetic determinants of emotional behavior. Moreover, the present results suggest that the temporal dynamics of volitional emotion regulation are characterized by a paradoxical rebound in amygdala activation after regulation, and that the immediate aftereffect is a marker of the efficiency of the initial and the sustained effects of emotion regulation (Walter, et al., 2009).

In summary, the successful replication of the immediate aftereffect of emotion regulation in all three studies of this dissertation opens up exciting new research perspectives: a comparison of the short- and long-term effects of different regulatory strategies, and the investigation of these effects also in positive

emotions would complement the present results, since the neural mechanisms involved in these processes show some characteristic differences (Ochsner, 2007; Staudinger, Erk, Abler, & Walter, 2009). A comprehensive characterization of this neural marker and its implications for emotional experience might also be useful with respect to clinical applications. The detailed examination of the various time scales of emotional regulation might for instance inform the diagnostic and therapeutic interventions in affective disorders that are associated with emotional dysfunctions (Brewin, Andrews, & Rose, 2000; Johnstone, van Reekum, Urry, Kalin, & Davidson, 2007). Ultimately, we might thus come to understand the neural underpinnings of what the feelings we have today have to do with the feelings we had yesterday – and with the feelings with might have tomorrow.

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1 Introduction

When we think about the most memorable situations in our lives, they will most probably be characterized by their extraordinary emotional significance. Be it the joy at a child's birth or the mourning at the loss of a loved one, the ability to experience such joys and sorrows is a fundamental characteristic of human life. Unsurprisingly, speculations about the relation between affect or 'passions', and cognition or 'reason' are not new. However, while modern psychology clearly acknowledges the importance of emotions, philosophers from Plato to Kant have argued that 'passions' are but a source of interference. These theoretical considerations have cemented the view that actions are best guided by cognition alone; emotions on the other hand will only spoil their success. Moreover, although the intellectual fathers of the division of mental faculties emphasized that cognition, affect and will are all part of a unitary psychological experience the founding fathers of experimental psychology, such as for example Wilhelm Wundt, were not so scrupulous; and have thus studied cognition, volition and emotions largely independently (Fox, 2008). What is rather surprising given their important role in our lives is that emotions have been ignored for a long time since the founding days of empirical psychology in the second half of the 19th century. Recently though emotions have received a lot more attention, especially with the development of new neuroscientific methods in the 1990s. In fact, recent empirical work has contradicted the notion that emotions interfere with reason: rather, a lack of emotions has serious detrimental effects on personal and social functioning. Bereft of emotional appraisals, a person cannot judge the goodness

or badness of a given choice with respect to her goals and intentions. Any reaction will thus be based on a faulty assessment of the situation which lacks its most informative part, namely an appreciation of its affective value (Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Damasio, Tranel, & Damasio, 1997; Cacioppo, Berntson, & Damasio, 2002; Damasio, 1994; Walter, 2005). Their highly informative character is inextricably linked with the fact that emotions typically entail changes on a vast number of levels including thoughts, feelings, behavior and physiology. Thus, an emotional appraisal of a situation or an object will rely on the evaluation of a number of different factors, including conscious and subconscious ones. Agreeing on the idea that emotions are vital, there are still several research branches in emotion science that try to tackle the subject matter from a variety of different angles. Some researchers have concentrated more on the way things are evaluated or 'appraised' (Arnold, 1960; Lyons, 1999; Zajonc, 1980), while others have emphasized the importance of physiological (Damasio, 1994, 1999; James, 1884; Lange, 1885/1922), and especially neural processes (Damasio, 1994, 1999; Davidson, 2000; LeDoux, 1987, 2003; MacLean, 1973). Conceptual issues such as these remain a recurring difficulty in emotion science and have of yet prevented the development of a single unitary model of the temporal and causal relationships between the various components of emotions. Closely related, the techniques and methodologies used for studying emotions are quite abundant and range from self report to measuring emotions in the brain. In the past ten years however, there have been increasing efforts to formulate more holistic models of emotion (Fox, 2008; Scherer, 2001). These attempts rely on converging evidence regarding the fundamental characteristics of emotions that originate from different approaches, such as for example behavioral and neural measures of emotions.

One of the offsprings of this development is the research branch of cognitive emotion regulation. Based on the idea that cognition and emotion inform each other to ensure the most adequate reaction in a given situation, there has been a surge of psychological and neuroscientific studies investigating what goes by names such as 'rationalization', 'coping', or 'reappraisal'. In the last few years, emotion regulation has been extensively investigated using a combination of methods from cognitive neuroscience and social psychology (Beauregard, et al., 2004; Ochsner, 2007). When research on the neural signature of cognitive emotion regulation began around the year 2000, cognitive neuroscience theories usually assumed that emotions are properties of a stimulus, such as shape, size, or color. On the other hand, social psychological theories proposed that the appraisal of a stimulus with respect to one's goals and needs is what elicits an emotion. As it turns out, empirical data supports both theories. Thus, rather than assuming one or the other to be responsible for the generation of an emotional response, it is likely the interaction of both bottom-up and top-down processes that is the basis of emotion (Lazarus & Alfert, 1964; Ochsner & Barrett, 2001; Ochsner & Gross, 2008; Pessoa, 2008; Scherer, 1984, 2001). As suggested by empirical studies, top-down control of emotions is effective in reducing the behavioral and neural reactions to emotional material (Blair, et al., 2007; Drabant, et al., 2009; Hariri, Bookheimer, & Mazziotta, 2000; Ochsner, et al., 2002; Pessoa, Japee, & Ungerleider, 2005; Staudinger, et al., 2009; van Dillen, Heslenfeld, & Koole, 2009). However, the effects of top-down cognitive control may be paradoxical, and may carry on over a certain amount of time (M. C. Anderson, et al., 2004; Brewin & Beaton, 2002; Depue, Curran, & Banich, 2007; Walter, et al., 2009; Wegner, 2009). In addition, both conscious and unconscious regulatory effects are influenced by a range of variables that relate for example to the quality of the eliciting stimulus, or to individual differences (Gross, 2002; Phillips, Ladouceur, & Drevets, 2008); genetically mediated differences in the

serotonergic neurotransmission system for example influence the amount of amygdala activity in response to negative emotional material (Hariri, et al., 2005; Hariri, et al., 2002; Heinz, et al., 2005). Based on the assumption that cognition and emotion interact in a flexible manner, the present work sought to disentangle the temporal dynamics of the volitional regulation of aversive emotions in the light of individual differences in three separate studies. With respect to the temporal dynamics of volitional regulation it was hypothesized that the detachment from negative emotions leads to a reduction of both the subjective experience of negativity and the amygdala activation; and also to an immediate neural aftereffect which is coupled with the offset of regulation. Regarding the influence of individual differences, the short variant of the serotonin transporter genotype was assumed to entail an amygdala hyperreactivity to negative emotional cues; it was also assumed that volitional emotion regulation is capable of reducing or even obliterating this hyperreactivity.

An overview of the theoretical and empirical considerations that pertain to the central topics of this thesis is given in the following Chapter 2. To serve the understanding of the research objective of the present work, which is the exploration of the temporal dynamics of volitional emotion regulation, we first need to examine its core concept, namely emotion. Thus, in the first part of Chapter 2, a definition of the term emotion is given by the discussion of the most prominent approaches to emotion science with respect to the present work. Following the introduction of biological, physiological and cognitive models of emotions, the most frequently used methods for the empirical study of emotions and their results are discussed, focusing especially on the results from affective neuroscience studies. In the second part of Chapter 2, the focus is shifted to the implicit, and (most importantly) the explicit regulation of emotions. Laying out a

framework for emotion regulation, the goals and processes of regulatory processes are discussed with regard to their experiential, behavioral and (neuro)physiological consequences. Subsequently, the immediate and the aftereffects of regulatory processes are explained in more detail. Here, the focus is on the paradoxical behavioral aftereffects of thought suppression, and the paradoxical aftereffects of emotion regulation in the amygdala. In the third part of Chapter 2, empirical and theoretical implications of individual differences are discussed with respect to emotional processing and emotional regulation. The effects of the serotonin transporter genotype on behavioral measures, but most importantly on the neural sensitivity to negative emotional stimulation are explicated. Based on this theoretical framework, the research objective of this thesis is developed: here, the main focus is to investigate the nature of the neural and behavioral correlates and aftereffects of volitional emotion regulation. The three studies designed to elaborate these objectives will be introduced and discussed in Chapter 3.

2 Theoretical Background

2.1 Emotions

2.1.1 Approaches to emotion science

In general theories of affect, moods are conceived as longer-lasting, unspecific and low-intensity affective states, while emotions are characterized by an orchestrated reaction to a particular elicitor which can be quite intense (Fox, 2008; Ochsner, 2007; Scherer, 2001). Aside from the different temporal characteristics of moods and emotions, they also differ with respect to their function, their elicitors, and their autonomic and neural responses. In the present work, I will focus on the behavioral, experiential, physiological, and neural correlates of the short-term affective experiences subsumed under the term 'emotion'. But what exactly are the characteristic features of an emotion? While most theorists agree that emotions are multi-componential phenomena, the number of components, and their exact role in the emotion generative process are still a matter of discussion (Fox, 2008). Since the characteristic changes that accompany an emotional response are manifold, a number of different research branches have aimed at defining emotions from different angles. The most influential approaches with respect to the present work will be discussed in the following sections.

Biological theories of emotion

Understanding emotions as adaptive response tendencies, biological theories have put forward that emotions are a result of evolution, since they offered advantageous solutions to recurring environmental demands such as for example finding food and an adequate mate, protecting and nurturing offspring, or identifying and avoiding dangerous, life-threatening events (Ekman, 1992; Tooby & Cosmides, 1990). However, assuming emotions to be biologically given does not necessarily imply that they are also hard-wired and inflexible. In contrast, it is commonly assumed that we are born with a primary emotional system which is then modified and shaped by learning and culture (e.g. Ekman, 1999). This innate emotional system is a genetically coded response system which can be triggered by biologically or evolutionary relevant events or objects. In his seminal work with rats, Jaak Panksepp (1998) could show that rats exhibit a classic fear response when they perceive the odor of a cat even when they have never encountered a cat before in their lives. Similarly, young monkeys readily acquire fear from snakes, while no learning effect occurs for a bunch of flowers (Mineka, Davidson, Cook, & Keir, 1984). Thus, biological relevance initiates a selective learning process more easily, while this learning process is less readily initiated by stimuli that are less relevant (Fox, 2008). Taken together, these results suggest that we are equipped with diverse automatic responses to stimuli that were either harmful or rewarding to our predecessors. The main function of emotions was and still is the facilitation of the rapid coordination of physiological, cognitive and motor processes triggered by emotionally salient events (Ohman, 1986; Ohman & Mineka, 2001). In order to serve their purpose, the different components of an emotional response are tightly coupled, and manifest as an embodied process (Scherer, 2001).

Physiological theories of emotion

Results from empirical investigations as well as our own everyday experience of emotions have highlighted the importance of bodily states in their generation. In the late 19th century, William James, one of the pioneers of scientific psychology, proposed that an emotion is the perception of the physiological changes that take place once we notice an emotionally salient stimulus (James, 1884). Around the same time, Carl Lange drew the same conclusion from his empirical work (Lange, 1885/1922). Thus, in the sense of the James-Lange theory of emotions, we are afraid because we run away from the snake, rather than running away because we are afraid. In later years, the somatic-marker hypothesis of Antonio Damasio (Damasio, 1994, 1999) has evolved from these early conceptions. In this model, emotional experiences are caused by the perception of a wide range of physiological changes, such as for example ANS activation, hormonal changes or biochemical markers. An important addition made by Damasio is the proposal of the so-called 'as-if-loops'. By means of the as-if-loop, the brain can behave in certain ways without the physiological changes actually taking place. Thus, we can have an emotion in the absence of the respective bodily changes. Moreover, in contrast to the traditional James-Lange theory of emotions Damasio assumes that the perception of bodily changes can happen outside of conscious awareness.

Cognitive theories of emotion

Rather a lot of discussion has been concerned with the question whether emotion generation and experience require cognitive appraisals, or whether they are independent of cognition. Starting in Greek philosophy, Aristotle has defined emotions as combinations of a feeling of pleasure or pain with a belief (Solomon, 1999). This very early definition already highlights the notion that

emotions may rely on the cognitive appraisal of the significance of an object or event. Similarly, the James-Lange theory and the theory of Walter Cannon and Philip Bard have underscored that the subjective feeling state is vital for affective experiences (Fox, 2008). However, while the James-Lange theory assumes that the subjective feeling state arises from the perception of a certain physiological state, the Cannon-Bard theory suggests that the physiological state and subjective feeling state of an emotion are elicited simultaneously and independently. In the 1950s and 1960s cognitive appraisals have been incorporated in contemporary models of emotion (Arnold, 1960; Arnold & Gasson, 1954). Schachter and Singer (1962) hypothesized that the subjective feeling state is caused by the cognitive appraisal of a set of physiological changes in the context of the current environment. In their view, a person will try to find a reasonable explanation for a physiological response, which in turn elicits a specific feeling state. The emotion that is experienced depends on the way a person evaluates or appraises the significance of events and objects around her. Thus, emotions are elicited by the evaluation of a situation in relation to current goals and needs rather than by the situation itself (Fox, 2008; Lazarus, 1966). Emphasizing the role of cognitive evaluation, these models can explain why the same stimulus will lead to different reactions in different people, which is not so readily achieved in the framework of other models that assume a more hard-wired, biological causation of emotional responses.

Gross's consensual process model of emotion

Drawing on empirical evidence from a number of studies using different approaches such as the ones described above, James J. Gross (Gross, 1998a, 1998b, 1999, 2002) developed his consensual process model of emotion, which relates conceptions expressed by various researchers (Arnold, 1960; Buck, 1985;

Ekman, 1972; Frijda, 1986; Scherer, 1984; Tomkins, 1984). In his model, an emotional response is triggered by an affectively salient event or object, i.e. an emotional cue. In the case that this cue is attended and evaluated in a specific way, it initiates a set of responses that facilitate an appropriate response.
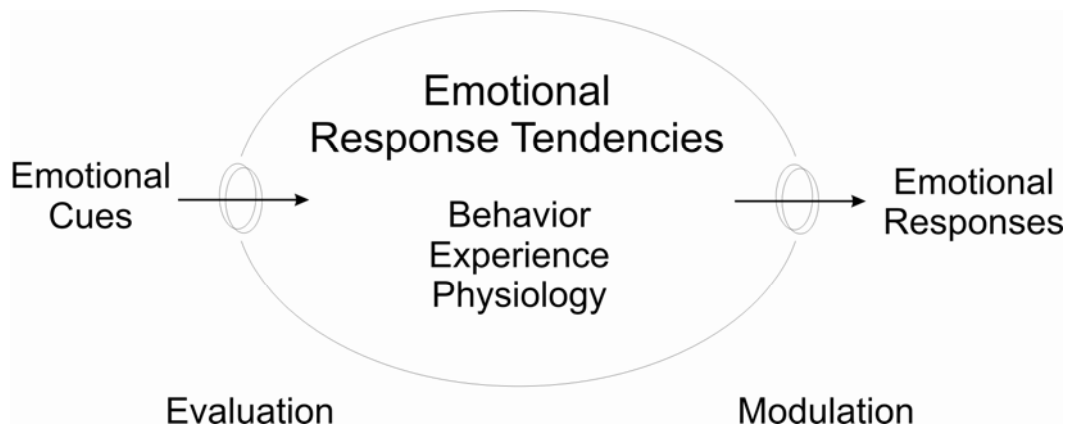
Figure 1:   James Gross's Process Model of Emotion

    Adapted from Gross (1998a)

The response systems triggered after evaluation include behavioral, experiential, and physiological systems. Critically, an emotional response only occurs after a modulation which gives final shape to the emotion. Thus, the consensual process model of emotion consolidates both an initial evaluation and a subsequent re-evaluation, which are both subject to regulatory processes. Weighting the consequences of such a complex generative model it becomes clear that individual differences play an important role at every step of this process: the inputs depend largely on an individual's everyday experience, while the evaluations, response tendencies, and 'output filters' will be determined by the individual's personality, temperament, physiology, and experience (Gross, 1999, 2002). The effects of individual differences on the behavioral and neural consequences of emotion and emotion regulation are discussed in Chapter 2.3.

Taken together, the manifold approaches that have developed over the years underscore the complex, multifaceted nature of emotions. Thus, it comes as no surprise that there are also various ways to measure emotions; their specific experimental setup will largely depend on the background of the researcher.

2.1.2 Measuring emotions

Categorical and dimensional concepts of emotion

In addition to the conceptual issues of defining 'an emotion', there are several important theoretical implications regarding the structure of affective processes. The way an emotion is measured will thus largely depend on the assumed underlying concept of affect (e.g. Fox, 2008). The two most influential concepts of the structure of emotions will be discussed in the following.

The discrete emotions approach is based on empirical evidence that some emotions rely on distinct neural structures, and that they are directly and automatically elicited by the appropriate stimuli or appraisals (Dolan, 2002; LeDoux, 1996; Panksepp, 1998). Support for this view comes from studies which found that selective lesions to certain brain regions led to impairments in specific emotional domains. For example, a selective lesion of the amygdala led to decreased performance in fear recognition, while the recognition of disgust remained largely unaffected (Adolphs, Tranel, Damasio, & Damasio, 1994; Calder, et al., 1996). Inherent in this view is the notion that there might be some emotions that are more basic than others. This relates especially to those emotional functions that are fundamental in aiding the survival of the species, the society, or the self (Ekman, 1999; Ekman & Friesen, 1971; Fox, 2008; Frijda, 1986; Izard, 2007; Lazarus, 1991). Empirical work suggests that happiness, anger, sadness, disgust, surprise and fear are fairly universal emotional categories,

partly because their concomitant facial expressions can be reliably identified across different cultures (Ekman & Friesen, 1971; Ekman, Sorenson, & Friesen, 1969).

Avoiding the tedious chore of deciding on any exact number of emotional categories, the dimensional approach to emotions suggests that every emotional response can be specified by a limited set of qualities. Based on behavioral findings, most approaches have identified two underlying dimensions. Going by various different names, these dimensions largely correspond to the concepts of valence and arousal. For example, Russell (2003) proposed a model which identifies emotions with respect to activation/deactivation, and with respect to pleasantness/unpleasantness. In this view, both fear and sadness are negative in valence; but whereas fear is highly activating, sadness is highly deactivating. Similarly, Robert E. Thayer (1989) proposed a two-dimensional model that classifies emotions regarding tension and energy. Here, fear would be characterized by a high amount of tension with a high amount of energy, while sadness has a high amount of tension with a low amount of energy. In contrast to the above mentioned model by Russell, which suggested that valence spans from positive to negative affect, Watson and Tellegen (1985) argued that positive and negative affect are orthogonal, i.e. independent dimensions of emotion. This assumption was based on the observation that a person does not necessarily feel exceptionally happy simply because she is feeling a low level of negative affect.

As mentioned above, there is still neither a unified model of emotion, nor of affect, and it remains an open question whether dimensional or categorical approaches to emotions are more appropriate. Thus, any researcher engaging in the scientific study of emotions will have to choose one definition or the other, and pick the respective methodology accordingly.

Subjective, behavioral and physiological measures of emotion

One of the more easily accessible components of emotions is the investigation of the subjective experience or feeling. By asking someone, we can usually learn how it feels for this particular person to be happy, sad, or afraid (Barrett, Mesquita, Ochsner, & Gross, 2007). In the early days of experimental psychology, introspection was the gold standard for the investigation of emotions (James, 1890/1950). There are however some drawbacks to subjective reports, which have led to the abandonment of introspection in modern emotion research (Jack & Roepstorff, 2002). One important caveat of introspection is that we can only verbally express those correlates of emotions that we are consciously aware of. Thus, processes that are not consciously experienced, for example physiological or hormonal changes, are not covered by experimental approaches that rely solely on self report (Fox, 2008). Additionally, the tendency to come up with a reason for our own behavior will often lead to false assumptions, as suggested by studies using unconscious priming (Nisbett & Wilson, 1977). In order to make use of subjective reports while at the same time providing an objective response grid, questionnaire-based measures of emotion are widely used in psychological research. Due to their standardized items and analyses, questionnaire-based measures offer good validity as well as reliability. Additionally, they offer the opportunity to assess current, i.e. state aspects, as well as general, i.e. trait aspects of emotions, such as for instance the State-Trait-Anxiety Inventory by Spielberger and colleagues (Spielberger, Gorsuch, & Lushene, 1970). Note however that the answers given in a questionnaire may be influenced by demand characteristics: Participants may choose the answers they feel are socially desirable instead of the ones that best fit their attitudes or subjective experiences. Further useful indicators of emotions are behavioral responses, such as joyful behavior at a victory or defensive behavior to a threat.

In humans, very prominent features of behavioral displays are facial expressions. But even in very standardized environments, behavioral displays of emotions can easily be suppressed, as in keeping a 'poker face' while feeling anxious during a contract negotiation (Gross, 2002; Ochsner & Gross, 2005). Thus, taking observable behavior as an indicator for the underlying emotional state of a person is problematic and not necessarily reliable. As laid out in Chapter 2.1.1, different emotional states are also related to characteristic, but unconscious changes. In contrast to self-report measures or observable behavior, the influences of emotion on attention, perception and memory are less susceptible to voluntary manipulations by the subjects. In this regard, reaction times offer a measure of how quickly people respond to a given stimulus, and can thus provide a measure of both cognitive load and the bias induced for instance by stimulus valence. Lastly, a range of techniques are available for measuring physiological parameters such as changes in sympathetic or parasympathetic arousal, muscle contractions, or changes in skin conductance (Coan & Allen, 2007). When studying physiological correlates of emotions one has to bear in mind that they alone do not constitute the whole scope of an emotional reaction, as they tells us nothing about whether the person actually feels any emotion at that specific moment. However, one of the most important advantages of measuring physiological correlates is that they are reliably quantifiable, which is why they have become overwhelmingly popular in the scientific exploration of emotions.

2.1.3 *Affective Neuroscience*

As has been mentioned previously in Chapter 1, emotion and cognition have been viewed as separate entities for a very long time. Considering the basic anatomy of the brain however, it becomes clear that both faculties rely on a

shared neural circuitry. As cognitive neuroscience has become more and more interested in emotions in the last ten to fifteen years, the flourishing field of affective neuroscience has received a lot of attention. Today, there are increasing efforts to combine cognitive, emotional, and social neuroscientific approaches in order to accommodate the interdependent nature of these processes. Owing to the development of new neuroimaging techniques in the 1990s, it is now also possible to study how emotions and cognition interact, and how they are implemented in the human brain.

The neural circuitry of emotion

Even before the boom of affective neuroscience, Paul MacLean (1973) argued that emotional processing primarily takes place in a number of mid-brain regions. These regions, which form what Papez (1995) has termed the limbic system, comprise for example the amygdala, the hippocampus, the thalamus, and the cingulate gyrus. However, while the limbic system is undoubtedly vital, activation in these regions is neither exclusive, nor sufficient for emotional processing, at least in human subjects (Damasio, 1994; Davidson, 2003; LeDoux & Phelps, 2004; Rolls, 2000). Rather, as Richard Davidson (2003) pointed out, the claim that there are regions that process either affect or cognition should be abandoned for the sake of models that can appreciate the plentiful interactions between them. Empirical evidence clearly supports this demand, as lesions to the neocortex result both in cognitive and emotional deficits (Damasio, 1994). When studying the neural dynamics of emotional processing, most neuroscientists have used visual stimuli depicting complex scenes (e.g. the site of a plane crash), or facial expressions of emotions (e.g. fear).
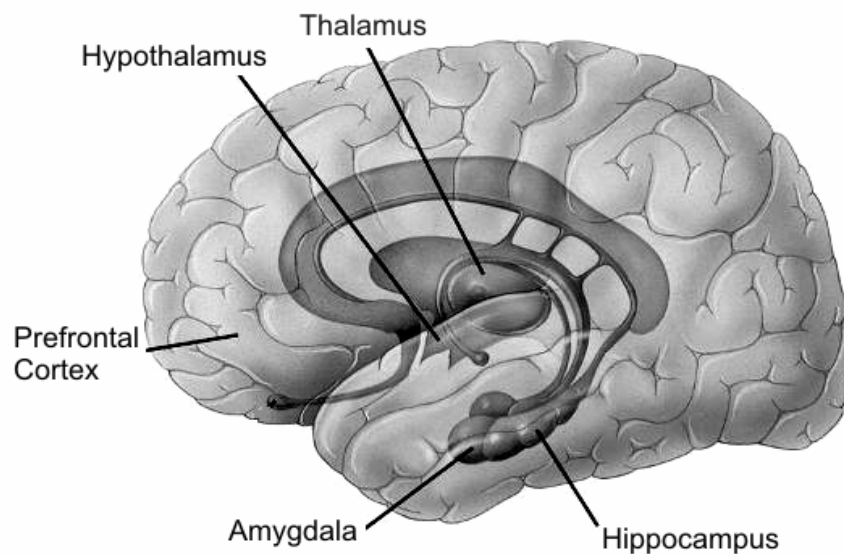
Figure 2:   The Limbic System

Adapted from www.bio1152.nicerweb.com/Locked/media/ch48/48_30LimbicSystem.jpg

Converging evidence from these studies suggests that both subcortical (e.g. the amygdala) and cortical (e.g. the prefrontal cortex) regions are inextricably linked with the processing of emotions such as fear, anger, happiness, or disgust. While the anterior cingulate cortex (ACC) and dorsomedial prefrontal cortex (dmPFC) were activated in the processing of various emotions (Murphy, Nimmo-Smith, & Lawrence, 2003), a few other regions were suggested to be more emotion-specific, such as the amygdala for fear (Adolphs, et al., 1994; Adolphs, Tranel, Damasio, & Damasio, 1995; A. K. Anderson & Phelps, 2001; Dalgleish, 2004), or the insula for disgust (Calder, et al., 2007; Calder, Lawrence, & Young, 2001; Stark, et al., 2007). In recent years, empirical evidence has somewhat watered the claim of fear specificity, as the amygdala is implicated in a variety of other emotional functions, such as reward or appetitive learning (Calder, et al., 2001; Hamann, Ely, Grafton, & Kilts, 1999; Johnsrude, Owen, White, Zhao, & Bohbot, 2000; O'Doherty, Deichmann, Critchley, & Dolan, 2002). The assumption that the

primary function of the amygdala is to signal the presence of (positively or negatively) salient emotional stimuli, however, seems to be very reasonable considering its localization and connectivity in the brain. Embedded within the medial part of the temporal lobe, the amygdala consists of thirteen single nuclei which receive input from the hippocampus, the sensory thalamus and cortex, the viscero-sensory cortex, and the entorhinal cortex. Reciprocal connections link the amygdala with the medial prefrontal cortex, the brainstem, and the polymodal association cortices (Amaral, Price, Pitkänen, & Carmichael, 1992; LeDoux, 2007). Thus, the amygdala is ideally situated to co-ordinate a wide range of cortical input, and to trigger the respective cortical output regions needed to initiate an appropriate response (Pinel, 2000; Rolls, 2000). According to LeDoux (1996, 2007), the amygdala is part of two projection paths that regulate emotional processing: the 'low road' dispatches information from the subcortical sensory systems through the sensory thalamus directly into the amygdala; and the 'high road' projects information from the respective sensory cortical areas through the thalamus into the amygdala. The low road is a phylogenetically ancient pathway which warrants the fast, automatic, superficial processing of stimulus properties, in order to initiate an immediate emotional reaction in the case of threat. In contrast, the high road requires a conscious perception and appraisal of a stimulus with respect to earlier experiences and possible reactions. However, lesion studies have raised some doubt as to the importance of the amygdala in emotion generation, since patients with lesions in the bilateral amygdala are largely unimpaired in the generation of some nonverbal behavioral expressions of emotion (A. K. Anderson & Phelps, 2001, 2002). This might be related to the specific stimulus and its context, since other structures may be equally relevant for the generation of an emotional response, such as the ventral striatum in reward (Delgado, Nystrom, Fissell, Noll, & Fiez,

2000; Knutson, Adams, Fong, & Hommer, 2001; O'Doherty, et al., 2002), or the anterior insula in disgust (Calder, et al., 2007; Murphy, et al., 2003).

Neurally, the prefrontal cortex, particularly the dorsolateral and dorsomedial regions are responsible for the volitional control of behavior (Dolan, 2002). However, non-volitional emotional control such as fear conditioning or extinction also relies on the prefrontal cortex and especially the orbitofrontal cortex (Dolan, 2007). Due to the sparse direct connections between the amygdala and the lateral PFC, regulatory influences are most likely relayed through the orbitofrontal cortex (OFC), dmPFC, and ACC, which have rich reciprocal connections with the amygdala (Ongur & Price, 2000; Price & Amaral, 1981). While costly in terms of processing speed, the stimulus evaluation taking place in cortical regions offers the possibility of changing emotional reactions, as is the case in cognitive emotion regulation (Gross, 1999) (see also Chapter 2.2). Thus, the prefrontal cortex is critically involved in a range of processes including emotional memory (Cahill, et al., 1996), the organization of goal-relevant reactions (Frijda, 1988), and emotional appraisal (Davidson & Irwin, 1999; Ochsner & Gross, 2005).

2.2   Emotion Regulation

If emotions truly represent advantageous evolutionary adaptations to recurring environmental challenges, or as Lazarus (1991) put it, "the wisdom of the ages" (p. 820), then why would anyone want to consciously alter their emotions? One important reason why we sometimes try to change the way we feel is because our emotions do not always encourage us to take the most advisable actions. For instance, while we may feel compelled to physically attack someone who hurts our feelings, we may refrain from doing so when this person is our superior.

Given that emotions figure so largely in a wide range of physical, behavioral and cognitive processes, emotion regulatory processes are a prerequisite for psychological and physical health. The research field of emotion regulation that has evolved over the last few years has built up on the grounds of two major research traditions. In the early days of psychology, the regulation of anxiety was a core concept in Freud's psychoanalytic theory (Freud, 1926). Characteristic of what Freud has called ego defenses[1] is that they do not require conscious effort (Erdelyi, 1993). In contrast, modern day theories on the behavioral and cognitive control of emotions emphasize both the importance of conscious and unconscious regulatory processes (Gross, 1999; Ochsner, 2007; Phillips, et al., 2008). Another precursory research field to modern emotion regulation research is the stress and coping tradition. Coping has been defined by Lazarus as the cognitive and behavioral efforts a person makes in response to taxing or overpowering external and/or internal demands (Lazarus & Folkman, 1984). Here, the focus is on the adaptive and conscious coping processes to situational variables. In contemporary emotion regulation research it has been made clear that regulatory processes do not only pertain to negative emotions, and that these processes leverage at both emotion expression and experience. While clinical investigations of the disturbances of emotion regulation in psychiatric disorders are of great interest, in the following I will concentrate mostly on the investigation of emotion regulation in healthy subjects.

2.2.1 A framework for emotion regulation

In everyday life, we frequently influence our emotions and moods in a variety of ways. Be it that we try to enhance our gloomy mood by watching a funny movie

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[1] Defenses refer to the regulation of very basic impulses that are often associated with negative affectivity such as aggressive or sexual impulses.

or venting our anger by working out, there are numerous self-regulatory strategies that are commonly summarized under the framework of affect regulation. Gross and Thompson (2007) put forward the suggestion that four main sets of processes are associated with affect regulation, namely defenses, coping, mood regulation, and emotion regulation. Their common aspect is that they are concerned with the attempt to minimize pain (avoidance) and maximize pleasure (approach). While defenses and coping relate to a set of processes that are focused on the reduction of negative affectivity, mood regulation summarizes the rather diffuse processes that are aimed at altering enduring emotional experiences which are not directed at a particular situation or object. In contrast, emotion regulation is concerned with altering positive and negative emotional responses that are directly associated with a particular situation or object and that are present for a limited period of time. Despite the considerable overlap between these four sets of processes the following section will give an overview over the processes involved in emotion regulation since it is the most relevant with respect to the present work (Fox, 2008).

Goals of emotion regulation

In general, an emotion might be decreased or stopped when it is based on a premature appraisal, such as mistaking a dust fluff for a spider; or when it prompts responses that are either inadvisable or conflict with other goals, such as the desire to maintain professional composure versus the urge to physically react to a provocation. Challenging evolutionary theories of emotion, there are also those instances when we might want to decrease positive emotions, or to increase or maintain negative emotions (Gross, 1999). Initiation or increase of emotions is relevant when response tendencies are low or absent; and when a particular emotion is to be replaced by another emotion. When someone delivers

good news to us while we are preoccupied with other things, we might deliberately increase our joy in order to make the other person feel good. Likewise, we might pump up our aggression before we enter a sports competition. Thus, as Gross (1999) put it, "we may define emotion regulation as the ways individuals influence which emotions they have, when they have them, and how they experience or express these emotions" (p. 542).

Emotion regulatory processes

In his seminal work on emotion regulation, James J. Gross (1998a, 1998b, 1999; Gross & Thompson, 2007) has distinguished five emotion regulatory processes that leverage either during emotion generation (antecedent-focused) or after the emotion is generated (response-focused). Antecedent-focused emotion regulatory processes include situation selection, situation modification, attentional deployment, and cognitive change, while response modulation is a response-focused regulatory strategy. In the following, the processes which are also depicted in Figure 3 will be discussed using an example: Imagine that you have just cuddled up on the couch, waiting for your favorite TV program to start. The phone rings, and you can tell by the number that it is a friend who has recently learned that she has a grave illness. By deciding whether to pick up the phone (S1) or not (S2), you can choose between putting yourself in a probably very pleasant situation, or in a probably rather unpleasant situation. Thus, emotion regulation by situation selection involves avoiding or approaching certain places, objects or people. If the person who called you does not send her number and you did pick up the phone, emotion regulation can also be achieved by active efforts to modify the situation itself (S1x-S2z); for instance by offering to return the call later. Of course, there are vast differences in the extent to which a given situation can be changed or modified that are due both to the context

and to individual differences, for example with respect to a person's assertiveness or dominance. In cases where situation selection or modification is out of the question, we can still selectively focus on different aspects of a situation (a1 –a5). In the previous example, we might distract ourselves from the conversation by watching the TV show on mute while talking to the other person on the phone. A further strategy (which is very relevant to the present work) involves cognitive changes to the meaning of a specific object or situation. Usually, there are a number of different meanings that could possibly be attached to a given situation, and these different meanings may have very different affective and physiological consequences (m1 – m3). Thus, cognitive change is very efficient in mediating both the experience and the physiological arousal associated with emotions (Gross, 1998a; Lazarus & Alfert, 1964).

In contrast to the antecedent-focused regulatory processes explained above, response-focused regulation sets in at a very late stage in the emotion generative process.
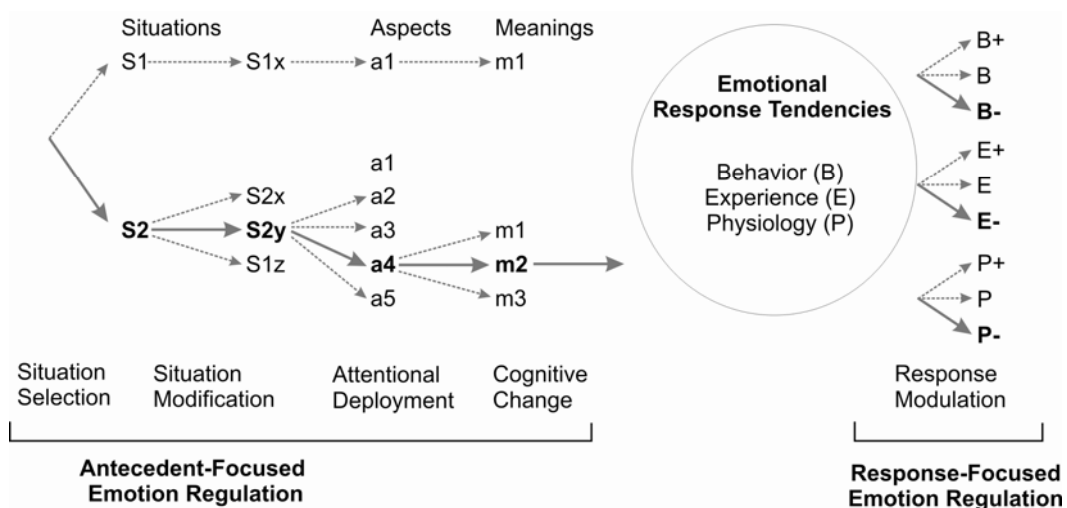
Figure 3:   James Gross's Process Model of Emotion Regulation

Adapted from Gross (1998a)

Response modulation tries to directly modify the behavioral, experiential, or physiological responses to an emotion eliciting event after the respective response tendencies have been initiated. In our example, you might try to hide your annoyance in order to safeguard your friend (and yourself) from feeling even worse. Actually, using this strategy to regulate emotions is very common in everyday life (Barrett, Ochsner, & Gross, 2007; Richards & Gross, 2000). Importantly though, the effectiveness of response modulation in reducing emotion experience varies greatly, while at the same time causing an increase in sympathetic activation (Gross & Levenson, 1993, 1997). Taken together, emotion regulation is not a singular process, but rather inherent in affective processing itself. Assuming that cognitive appraisals are critical in affective processing, neuroscientists have undertaken quite a number of attempts to gain insight into the neural underpinnings of cognitive emotion regulation. The findings of these studies have greatly improved our concepts of emotional processing and regulation, and our understanding of the interactions between emotion and cognition.

A social cognitive neuroscience model of emotion regulation

Based on the results of numerous empirical investigations, the integrative social cognitive neuroscience view of emotion regulation posits that the amygdala is critical for the perception, memory, and judgment of emotionally arousing cues. Furthermore, a growing number of studies have consistently shown that emotional appraisal systems depend on activation of the medial and lateral PFC, OFC and ACC (see Ochsner, 2007 for review). On a general account, the regions identified in emotional regulation or "hot" cognitive control, show a remarkable similarity with the regions commonly identified in "cold" cognitive control. This is not surprising given the role of the PFC and ACC in general executive control,

working memory, response inhibition, error processing and the resolution of cognitive conflict (Botvinick, Cohen, & Carter, 2004; D'Esposito, Postle, & Rypma, 2000; Jonides, Smith, Marshuetz, Koeppe, & Reuter-Lorenz, 1998; Wagner, Maril, Bjork, & Schacter, 2001; Wittfoth, Schardt, Fahle, & Herrmann, 2009). Although lateral and medial prefrontal regions are generally involved in emotional appraisal processes, there is some degree of specificity regarding the impact that different cognitive control mechanisms have on emotion generation (Beauregard, et al., 2004; Ochsner, 2007; Ochsner & Gross, 2008). Figure 4 depicts two types of neural control networks: a) the ventral system which is related to the evaluation of the emotional value of a given stimulus as well as the selection of the appropriate action; and b) the dorsal system which subserves the explicit reasoning about and description of changes in the association between a stimulus and the emotional response.
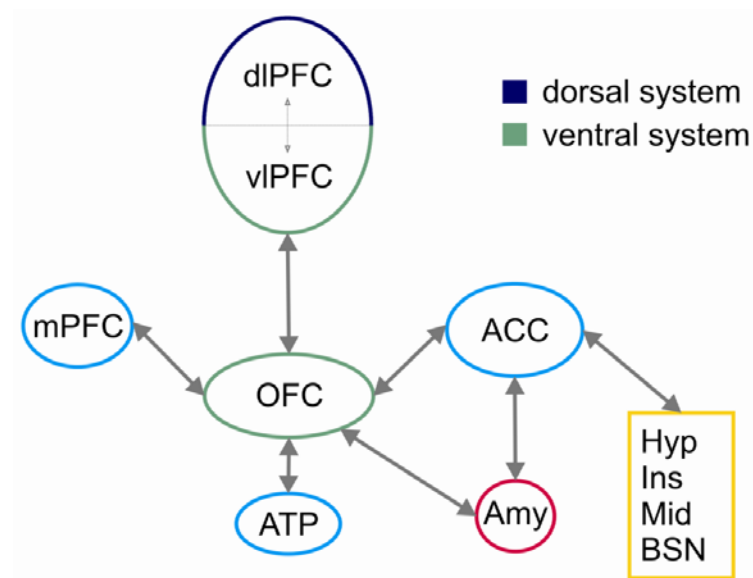
Figure 4: The neural circuitry of emotion regulation

dlPFC: dorsolateral prefrontal cortex; vlPFC: ventrolateral prefrontal cortex; mPFC: medial prefrontal cortex; OFC: orbitofrontal cortex; ATP: anterior temporal pole; ACC: anterior cingulate cortex; Amy: amygdala; Hyp: hypothalamus; Ins: insula; Mid: midbrain; BSN: brainstem nuclei

Given the comparably strong anatomical connections between the ventral system and appraisal systems such as the amygdala or the ventral striatum, the influence exerted by the first type of control process is direct, while the dorsal system indirectly influences the appraisal systems by biasing processing in the perceptional and associative systems and/or the ventral control system. Based on this distinction, cognitive change strategies can be subdivided into those strategies that are more basic and thus only recruit the ventral systems (e.g. extinction or reversal learning), and those strategies that are more complex and recruit both ventral and dorsal systems (e.g. reappraisal, detachment, or anticipation) (Beauregard, et al., 2004; Ochsner, 2007; Ochsner & Gross, 2008). It his hypothesized that the lateral PFC (Brodman areas 9 and 10) is engaged in the active maintenance of the instruction, and the selection of the respective cognitive operations. The lateral prefrontal regions then recruit the orbitofrontal cortex (Brodman area 11) in order to organize the suppression of the various dimensions of emotional responding. The OFC, by virtue of its strong anatomical connections, regulates activation in the amygdala, which in turn influences the evaluation of the emotional significance of the stimulus or situation. Back-projecting this cognitive 'reframing' to the OFC, the rostral ACC (rACC) is activated in order to modulate activity in subcortical effector regions such as the hypothalamus, insula, midbrain, or brainstem nuclei (Beauregard, et al., 2004).

Thus, converging evidence suggests that lateral prefrontal and anterior cingulate regions are generally employed in focusing on important information while ignoring irrelevant information, irrespective of whether this information is affective or not. Top-down influences from these frontal brain regions modulate activation in subcortical and posterior association cortices, thereby influencing which kinds of perceptual (visual, auditory, spatial etc.) information is

represented (Beauregard, et al., 2004; Ochsner, 2007; Ochsner & Gross, 2008). Furthermore, medial prefrontal regions that have previously been linked with metacognitive action monitoring, seem to be an integral part of the emotion regulation network (Ochsner, et al., 2005; Ochsner, Knierim, et al., 2004). In the context of emotion regulation, the medial PFC may be related to the monitoring of our own emotional state, as well as to the consideration of the impact that another person's beliefs, intentions and actions have on us (Beer & Ochsner, 2006). Having developed a model of how cognitive emotion regulation might work on the behavioral and on the neural level, what exactly happens when we volitionally attempt to alter our emotions?

2.2.2 Immediate effects of regulation

Behavioral, experiential and physiological effects of emotion regulation

Studies of the behavioral, experiential and physiological effects of emotion regulation have been conducted employing both antecedent-focused and response-focused emotion regulation strategies as exemplified above in Chapter 2.2.1. Commonly, cognitive reappraisal has been used as a means to re-interpret a potentially emotion-eliciting event in non-emotional terms before an emotion has fully developed, while the suppression of emotion-expressive behavior has been used in studies concerning the response modulation of emotion at the end of the emotion generative process (Gross, 1998a, 2002; Gross & Levenson, 1993, 1997). Aside from the obvious differences regarding their time of onset, several differences in the effects on affective, cognitive and social outcomes have been described for reappraisal versus suppression. In the 1990s, Gross and Levenson conducted a set of studies regarding the effects of suppression on emotion expression, experience, and physiology upon viewing neutral, sad, disgusting or

humorous movies. They found that the suppression of emotional facial expressions and reappraisal were both effective in decreasing facial movement, face touching, and body movement to all kinds of emotions. On the level of subjective emotion experience however, no or only modest effects were observed for suppression, while somatic activity was paradoxically increased. Reappraisal, however, was efficient in decreasing especially the experience of negative emotions, and did not increase sympathetic arousal (Gross & Levenson, 1993, 1997). Rather, a subsequent study showed that reappraisal was able to reduce the magnitude of the startle response as an index of a negative emotional state (Jackson, Malmstadt, Larson, & Davidson, 2000). In addition to being more taxing in terms of self-monitoring and –correction, suppression also had detrimental effects on cognitive resources, which is not the case for reappraisal. When asked to specify auditory and visual details of a movie, participants who engaged in suppression showed impoverished object memory, lower verbal memory performance and lower memory confidence ratings in contrast to the control group (Richards & Gross, 2000). However, participants in the reappraisal group were unimpaired regarding verbal memory performance. Considering that expressions of emotional responses are important social cues (Darwin, 1872/1955), Butler and associates (2003) set out to investigate the effects of both antecedent- and response-focused emotion regulation on social interactions. With respect to social situations, emotion regulation leverages at both the intrapersonal and the interpersonal level: since suppression is also used as a blunt instrument to mask one's true feelings (Campos, Mumme, Kermoian, & Campos, 1994), the partner is bereft of a valuable source of communicative signals, while the suppressing individual will have less cognitive resources for the detection of emotional cues from their partner. Without positive emotion expression as key element in social support and stress reduction (Uchino, Cacioppo, & Kiecolt-Glaser, 1996), the blunting of one's emotions entailed

increased physiological arousal in the interaction partner. Conversely, no physiological changes were observed in interaction partners of reappraising subjects (Butler, et al., 2003).

In conclusion, these results suggest that antecedent-focused emotion regulation strategies are more beneficial in reducing emotional responses on a multitude of levels; suppression results in decreased cognitive resources and lesser experiences of positive emotions while at the same time boosting physiological arousal irrespective of valence. In addition to physiological and cognitive costs, response-focused emotion regulation strategies also have detrimental effects on social interactions. Unsurprisingly, the changes observed during emotion regulation also have differential neural underpinnings, which will be explained in the following.

Neural effects of cognitive emotion regulation

Numerous functional imaging studies have been designed to investigate how both the voluntary and the involuntary regulation of emotions impact neural activity in the cortical (PFC, ACC, insula) and the subcortical (amygdala, hypothalamus, ventral striatum) structures involved in the evaluation of emotional significance, or in physiological and expressive processes. As mentioned previously, the neural regions identified in emotional regulation or "hot" cognitive emotion control, overlap with the regions commonly identified in "cold" cognitive control (Botvinick, et al., 2004; D'Esposito, et al., 2000; Wittfoth, Schardt, et al., 2009). Following this assumption, a number of different strategies have been employed to study the effects of top-down cognitive control on bottom-up emotional responses, which range from purely attentional control strategies to highly cognitive control strategies (compare Figure 5).
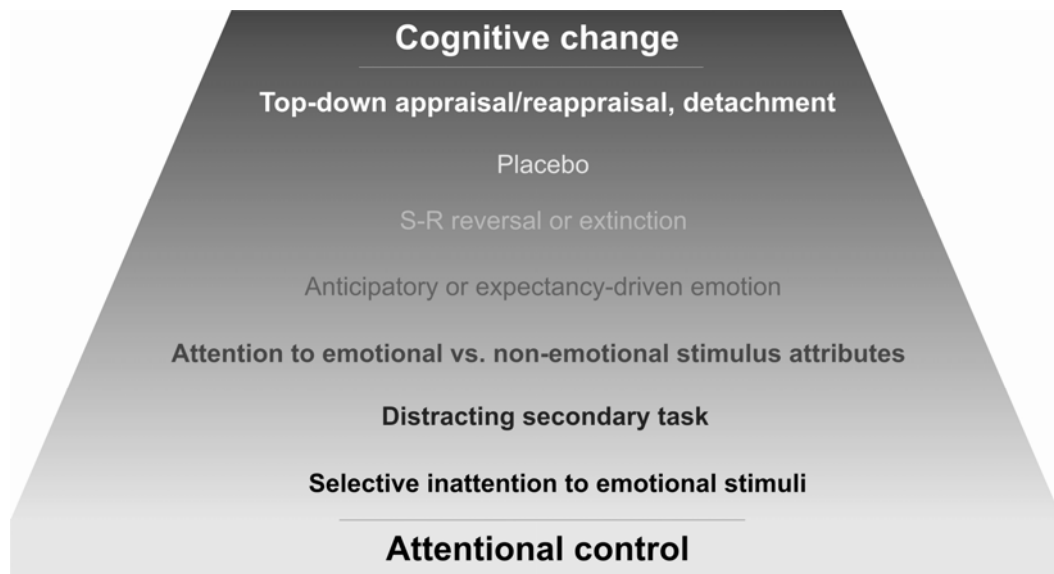
Figure 5: **Continuum of cognitive emotion regulation strategies**

Adapted from Ochsner and Gross (2005)

Moreover, the goal of regulation (i.e. up- or down-regulation) was varied, as was the valence of the to-be-regulated emotional content (i.e. positive or negative valence) (Ochsner, 2007; Ochsner & Gross, 2005).

Generally, neural and behavioral responses are facilitated by attention, while responses to unattended stimuli are inhibited (e.g. A. K. Anderson, Christoff, Panitz, De Rosa, & Gabrieli, 2003). Differences in responses to unattended versus attended cues can thus provide information about the degree of automaticity of the underlying processes. Several studies found that activation within the amygdala amongst other regions is attenuated in tasks where certain aspects a stimulus are selectively attended. For example, a reduced BOLD response in the amygdala was observed when emotional stimuli had to be evaluated regarding both emotional stimulus dimensions such as facial expression (Drabant, et al., 2009; Hariri, et al., 2000) or pleasantness (S. F. Taylor, Phan, Decker, & Liberzon, 2003) and unemotional stimulus dimensions such as artificial or natural origin

(Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003) or gender (D. G. Mitchell, et al., 2007; Pessoa, Padmala, & Morland, 2005). Moreover, cognitive load induced by complex mental operations reduces both subjective experience and limbic activation to simultaneously presented emotional stimuli. This effect has been shown for example when performing a conflict task (Ochsner, Hughes, Robertson, Cooper, & Gabrieli, 2009), evaluating distracting stimuli (Pessoa, Padmala, et al., 2005), performing arithmetic operations (van Dillen, et al., 2009) or evaluating linguistic features of words (D. G. Mitchell, et al., 2007). The modulation of limbic regions is presumably implemented by inhibitory influences of the dorsolateral prefrontal cortex. In agreement with the hypothesis that attentional load and emotional processing are inversely related, greater cognitive load was associated with greater activity in the dmPFC, dlPFC, and ACC while amygdala activation decreased as a function of the amount of cognitive load (Beauregard, et al., 2004; Ochsner, 2007; Pessoa, 2008). Taken together, these findings strongly suggest that emotional processing is reduced when cognitive resources are low.

In deliberate emotion regulation, cognition is used to control the appraisal of the meaning of an emotional stimulus. Most studies of cognitive emotion regulation made use of standardized picture sets depicting complex scenes (Lang, Bradley, & Cuthbert, 1997) or facial expressions (Ekman & Friesen, 1977; Lundqvist & Litton, 1998) in order to elicit emotions. A number of different strategies such as for example reappraisal (Ochsner, et al., 2002; Ochsner, Ray, et al., 2004; Phan, et al., 2005; Urry, et al., 2006; van Reekum, et al., 2007), detachment (Beauregard, Levesque, & Bourgouin, 2001; Eippert, et al., 2007; Kalisch, et al., 2005; Levesque, et al., 2003; Levesque, et al., 2004; Staudinger, et al., 2009; Walter, et al., 2009), or maintenance (Schaefer, et al., 2002) have been used to volitionally control emotions. All of the aforementioned strategies proved successful in modulating

both the behavioral and neural consequences of emotions. Due to the relevance in everyday life as well as affective disorders, the largest part of the empirical studies in this field have concentrated on the investigation of cognitive strategies that are successful in reducing negative effect. In correspondence with studies using passive emotional stimulation, the perception of aversive versus neutral emotional cues led to robust activations in the amygdala. The cognitive effort to decrease negative emotions was mirrored by decreased BOLD activations in the amygdala, and increased activation in dorsal and ventral lPFC regions, as well as in the parietal cortex. Concomitantly, participants felt less negative during volitional attempts to control emotions (Eippert, et al., 2007; Levesque, et al., 2003; Levesque, et al., 2004; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004). However, as mentioned previously, the goals of emotion regulation (up- or down-regulation) and the valence of the eliciting stimulus (pleasant or unpleasant) may differ from one situation to another. Thus, detachment also reduces neural activation in the ventral striatum and the subjective experience of positive emotions, i.e. reward (Staudinger, et al., 2009). By means of self-report and functional imaging it was shown that maintaining or up-regulating an initial emotional response to a negative stimulus increases the subjective experience of negativity, and the activation of the amygdala (Jackson, et al., 2000; Kim & Hamann, 2007; Ochsner, Ray, et al., 2004; Schaefer, et al., 2002; Urry, et al., 2006; van Reekum, et al., 2007).

With respect to the neural underpinnings of volitional emotion regulation, deliberate increases and decreases of emotions have been shown to rely largely on the same network. The underlying brain regions are associated with the controlled appraisal of stimulus meaning and include the left lateral PFC, dACC and dmPFC (compare Figure 6). Regarding the specific role of the lateral PFC in reappraisal, it is assumed that this region is involved in the deliberate

construction of a narrative that re-represents the meaning of a stimulus in the intended way, which is the case during both increase and decrease conditions. However, differences between increase and decrease conditions were found in the left dmPFC and right dlPFC/OFC: the dmPFC was specifically recruited during voluntary attempts to increase emotional responses, whereas the dlPFC and OFC were recruited by attempts to decrease emotions. Commonly, the dmPFC is associated with self- and other-referential thinking, as well as with processing the affective meaning of words; these functions are especially relevant when increasing an emotional response (Cato, et al., 2004; Ochsner, Ray, et al., 2004). The implication of the dlPFC and OFC in decreasing emotions fits in well with the interpretation that these regions subserve response inhibition and the updating of the motivational values of stimuli (O'Doherty, et al., 2002; Wittfoth, Schroder, et al., 2009).
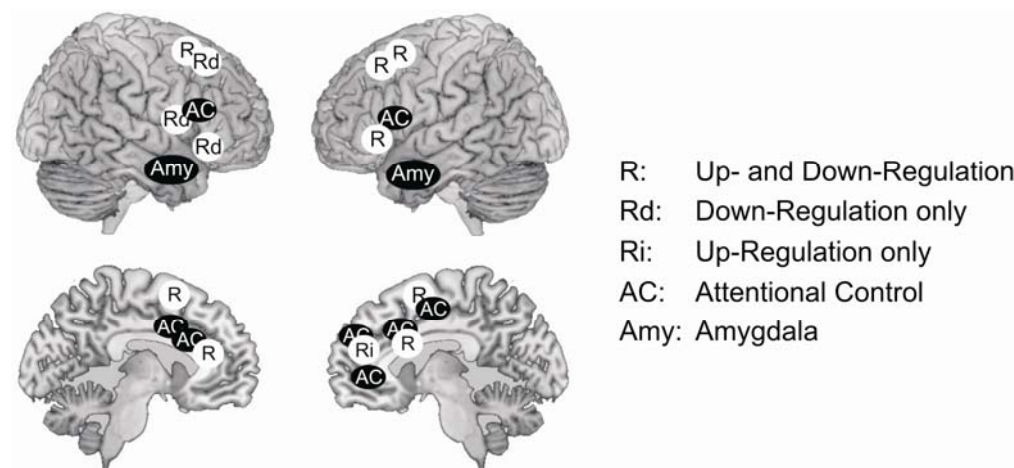
Figure 6:   Specificity of regulatory brain regions

Adapted from Ochsner (2007); black circles: implicit regulatory regions, white circles: explicit regulatory regions

In summary, converging evidence suggests that a range of volitional and non-volitional emotion regulatory strategies is effective in modulating the experiential, physiological as well as neural correlates of emotions. These strategies aim at either up- or down-regulation of emotion and are viable irrespective of emotional valence. The vital importance of the ability to regulate emotional responses is underscored by reports of dysfunctional emotional regulation and neural processing in several psychiatric conditions such as unipolar (Johnstone, et al., 2007; Killgore & Yurgelun-Todd, 2006) and bipolar depression (Caligiuri, et al., 2006; Phillips, et al., 2008), schizophrenia (S. F. Taylor, Phan, Britton, & Liberzon, 2005; L. M. Williams, et al., 2004), specific phobias (Paquette, et al., 2003), or trauma (L. M. Williams, et al., 2006).

2.2.3 Aftereffects of regulation

As pointed out in Chapter 2.2.1, the significance of emotion regulation for mental health has been acknowledged since the earliest days of psychology. But while current empirical investigations of emotional regulation are mostly concerned with the neural and behavioral mechanisms *during* emotion regulation, Sigmund Freud has described a paradoxical rebound of emotions *after* their suppression[2]; a phenomenon which he termed "the return of the repressed" (Freud, 1915). Later on, cognitive psychologists were able to show that paradoxical effects are also caused by attempts to suppress a certain thought (Abramowitz, et al., 2001; Koster, Rassin, Crombez, & Naring, 2003; Roemer & Borkovec, 1994; Wenzlaff & Wegner, 2000). However, despite the existence of consistent evidence for the momentary reduction of emotional and neural responses during cognitive emotion regulation, the existence of any potential

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[2] Suppression = the volitional, conscious effort to remove an unwanted thought from conscious attention (Wegner, 1992)

aftereffects has been largely ignored. In order to fill this void, Walter and colleagues (2009) were the first to explicitly study the behavioral and neural aftereffects of detachment using fMRI. In the following sections, I will first give a brief résumé of studies investigating the paradoxical effects of thought suppression. Subsequently, the initial functional emotion regulation study by Walter and colleagues (2009) will be reported in more detail, since it forms the basis of the experimental approach of the present work.

Paradoxical effects of suppression

Most of us will be familiar with situations where we strain to prevent from doing something and end up doing precisely that. But while stumbling over a stone with an already sprained ankle may cause momentary discomfort, ironic processes of mental control are also relevant for the development of emotional disorders, such as for example depression, post-traumatic stress disorder or obsessive compulsive disorder (Abramowitz, et al., 2001; Brewin, Andrews, & Rose, 2000; Brewin, Andrews, & Valentine, 2000; Najmi, Wegner, & Nock, 2007; Rassin, Merckelbach, & Muris, 2000; Wegner, 2009). In their seminal studies, Daniel Wegner and colleagues showed that the conscious attempt not to think about something is only partly successful, and more often than not promotes hyperaccessibility of the target thought along with other ironic processes and unwarranted consequences (Wegner & Erber, 1992; Wegner, Schneider, Carter, & White, 1987; Wegner, Shortt, Blake, & Page, 1990; Wenzlaff & Wegner, 2000). The ironic processes engendered by voluntary thought suppression have thus been dubbed the 'postsuppressional rebound' of mental control. More specifically, the instruction to suppress thinking about e.g. a "white bear" led to significant increase in target thoughts during the initial (suppression) period, *and* in a subsequent (expression) period where subjects were free to think

whatever entered their minds. In contrast, the initial expression of target thoughts did not produce any such effects. With respect to the mental control of emotional material, previous investigations of self-regulation have shown that the suppression of anxious thoughts subsequently leads to an increase in anxiety-related behavior (Janis, 1958). Similar findings were obtained by a number of more recent studies which also reported increases in the frequency of emotion-related thoughts and self-reported emotion following the attempt to avoid thinking about certain material (Harvey & Bryant, 1998a, 1998b; Koster, et al., 2003). Subsequent studies using both personally relevant (Roemer & Borkovec, 1994) and irrelevant (Clark, Ball, & Pape, 1991; Clark, Winton, & Thynn, 1993; Lavy, van den Hout, & Arntz, 1990) stimuli found similar results, which also carried on over longer time intervals (Muris & Merckelbach, 1997). As Rassin (2000) points out, however, paradoxical effects of thought suppression are not confined to thought frequency but are also apparent at the behavioral level. The suppression of pain during a cold pressor task[3] for example, was related with higher pain ratings after the task, as well as with increased sympathetic arousal in anticipation of a second cold pressor task. Similarly, the suppression of exciting thoughts resulted in heightened skin conductance levels as a measure of physiological reactivity (Wegner, et al., 1990). Based on their empirical findings, Wegner and Wenzlaff developed an ironic process model of thought suppression (Wegner, 2009; Wegner & Erber, 1992; Wegner & Erskine, 2003; Wegner & Wenzlaff, 1996), which posits that thought suppression relies on two mechanisms: a conscious, effortful "operating process", which is consigned to actively search for distractors in the environment; and an unconscious, relatively effortless "monitoring process", which monitors the occurrence of the unwanted thought. The conscious operating process has two inherent

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[3] Subjects had to immerse their hand in ice-water for as long as possible

difficulties: since thought suppression is never perfect, the unwanted target thought is bound to come into mind at some point. When this happens, the distractor which is attended at that specific moment will become associated with the unwanted thought. Thus, when the distractor is encountered again, it will trigger the unwanted thought and lead to the described paradoxical rebound effect (Muris & Merckelbach, 1997; Wegner, et al., 1987; for review see Wenzlaff & Wegner, 2000). Support to this notion was lend by an empirical study showing that a postsuppressional rebound in target thought frequency was observed when the context remained unchanged; when the context was changed however, no rebound of target thoughts was observed in subjects previously engaged in suppression (Wegner & Erber, 1992). Also, since the operating process relies on conscious processes, it is subject to the limited capacity of cognitive function. The execution of a concurrent mental operation thus leads to a less effective suppression of unwanted thoughts (Wenzlaff, Wegner, & Roper, 1988). In terms of the emotional valence of the to-be-suppressed material, several reports suggest that the success of suppression depends on the valence of the to-be-suppressed information (e.g. Wenzlaff & Wegner, 2000). For example, personal emotional issues (Petrie, Booth, & Pennebaker, 1998), distressing movies (Davies & Clark, 1998), or graphic and upsetting stimuli (Depue, et al., 2007; Edwards & Bryan, 1997) are less effectively suppressed and the postsuppressional rebound is increased compared with emotionally less agitating stimuli. However, while there is still doubt as to which aspects of emotional targets are responsible for the detrimental effects on suppression, it is clear that individual differences define a person's ability to suppress her thoughts. Correspondingly, Wegner and Zanakos (1994) developed the White Bear Suppression Inventory (WBSI) as a self-report measure for the tendency to suppress thoughts.

The neural underpinnings of thought control

Functional imaging studies of mental thought control suggest that thought suppression relies on lateral and medial prefrontal regions, which are also implicated in the cognitive control of emotions (Ochsner & Gross, 2008). In a study by Anderson and colleagues (2004), the dorsolateral and ventrolateral prefrontal cortex, as well as the ACC were more active when subjects suppressed unwanted memories, compared with a free condition. Moreover, increased activation in the bilateral dlPFC was predictive of greater success at memory inhibition (M. C. Anderson, et al., 2004). As suggested by Depue and colleagues (Depue, et al., 2007), the suppression of emotional memory involves two neural pathways that are temporally staggered: the first pathway subserves cognitive control over sensory components of memory representations and is mirrored by inhibitory influences of the right vlPFC over the thalamus and fusiform gyrus. The second pathway, which is involved in cognitive control over memory processes and emotional components, is mirrored by inhibitory influences of the right dlPFC over both the hippocampus and the amygdala. The orchestration of the timing of these suppression processes relies on modulatory influences of the OFC (BA 10). The assumption of both tonic and phasic control processes was also corroborated by a recent study reporting sustained activation in the dorsolateral PFC over the course of a thought suppression paradigm, and transient activation in the ACC that correlated with the occurrence of unwanted target thoughts during the suppression, but not the expression condition (J. P. Mitchell, et al., 2007). Again, these results correspond with the view that both PFC and ACC mediate cognitive control, and with conflict-monitoring view of the ACC (Botvinick, et al., 2004; Braver, Barch, Gray, Molfese, & Snyder, 2001; Braver, Reynolds, & Donaldson, 2003; van Veen, Cohen, Botvinick, Stenger, & Carter, 2001). Since none of the above mentioned studies has directly tested cognitive emotion regulation, they do not offer an answer to the question

whether aftereffects such as the postsuppressional rebound can also be found following intentional emotion regulation through a cognitive strategy.

The temporal dynamics of volitional emotion regulation

As mentioned above, Walter and colleagues (2009) were explicitly interested in the neural signature of emotion processing after termination of the intentional effort to regulate. Thus, their fMRI study was designed so as to find out if there is a sustained effect of detachment, mirrored for instance by a paradoxical increase of neural activation in the amygdala. To this end, two sequenced tasks were delivered, which were separated by approximately 10 minutes and allowed the investigation of amygdala activation on two different time scales. The first task involved the active regulation of emotions elicited by negative or neutral emotional pictures in a slow event-related design[4] (Lang, et al., 1997). Here, the temporal dynamics of amygdala activation were studied during both the picture presentation phase (8 seconds), and the ensuing relax period (20 seconds). Subjects were prompted either to 'permit' all upcoming emotional responses, or to 'suppress' their emotional response by adopting the position of a detached observer. The second task was a passive viewing task where all previously seen pictures were presented again very briefly (1 second) in random order, and without any instruction to regulate. In a post-scan debriefing, subjects rated their success at implementing the regulation strategy on a scale from 1 (very successful) to 9 (not at all successful). As can be seen in Figure 7, (top left), voluntary regulation of emotion by detachment was effective in reducing amygdala activation in task 1. Concomitantly, activation in a frontal-parietal regulation network was observed during emotion regulation (not shown here).

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[4] This design allows for the HRF to completely return to baseline due to a long stimulus onset asynchrony (SOA).

Investigating the temporal dynamics of amygdala activation in tasks 1 and 2, two aftereffects were found: an *immediate* aftereffect in task 1, where amygdala activation increased after the offset of regulation, and a related *sustained* aftereffect in task 2, where a decrease in amygdala signal to formerly regulated negative pictures were observed.
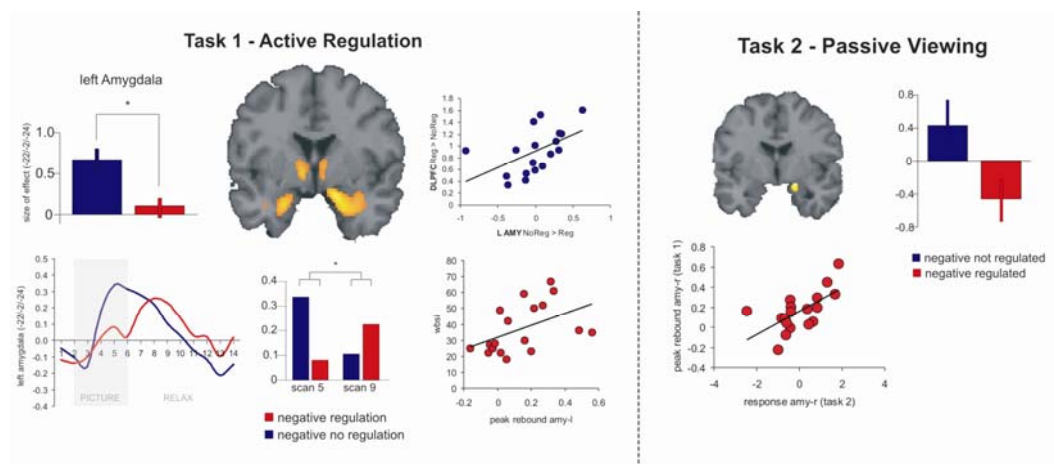
Figure 7: **Immediate and sustained aftereffects of emotion regulation in the amygdala**

Adapted from Walter et al. (2009); for Task 1, only the results for the left amygdala are shown, but amygdala activation and attenuation, as well as the immediate aftereffect are also significant in the right amygdala.

As for the *immediate* aftereffect of cognitive emotion regulation, Figure 7 shows that in the 'negative no regulation' condition, the amygdala signal increased after the onset of a negative picture and decreased back to baseline in the ensuing fixation period (blue line). The opposite pattern was found for the amygdala signal in the 'negative regulation' condition: while subjects viewed negative pictures and actively detached from emotions, the amygdala signal was significantly reduced, whereas a paradoxical increase was observed in the respective fixation period (red line). The immediate aftereffect was interpreted in terms of a paradoxical rebound effect, in analogy to rebound effects described

before e.g. in the context of thought suppression or the suppression of emotional memories (Abramowitz, et al., 2001; Wegner & Erskine, 2003; Wenzlaff & Wegner, 2000). Although the aftereffects of voluntary emotion regulation and thought suppression differ both in terms of the time scales (i.e. seconds to minutes vs. minutes to years) and affected domains (i.e. neurophysiological signals vs. frequency of thoughts), both types of regulation entail paradoxical effects delayed in time. The fact that thought suppression might indeed be related with emotion regulation was underscored by a positive correlation between WBSI scores and peak amygdala activation during regulation: subjects with greater habitual thought suppression showed an increased immediate aftereffect in the amygdala. Moreover, similar findings have been reported in thought suppression studies with psychophysiological markers where individuals with high WBSI scores showed elevated electrodermal responses after suppressing arousing thoughts (Wegner & Zanakos, 1994). Further support for the presence of neural aftereffects of cognitive emotion regulation was yielded by the analysis of task 2, where a *sustained* aftereffect of regulation was observed in the amygdala. This effect was only present for previously regulated negative, but not neutral stimuli, which suggests that it is related to the regulatory attempts in task 1 rather than a habituation of the amygdala response following stimulus repetition (Bunge, 2004; Fischer, et al., 2003; Ishai, Pessoa, Bikle, & Ungerleider, 2004; Wright, et al., 2001). Furthermore, it was also unlikely that cognitive regulation during task 2 was the cause of the sustained aftereffect, since a) the stimuli were presented very briefly (1 second) which compromises elaborate conscious processing, and b) there was no activation in the frontal-parietal regulation network previously observed in task 1 and other studies on cognitive emotion regulation (Eippert, et al., 2007; Levesque, et al., 2003; Levesque, et al., 2004; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004).

As mentioned above, the *sustained aftereffect was influenced by the immediate aftereffect* in task 1: larger immediate paradoxical increases in amygdala activation were associated with larger amygdala activation following the repeated exposure to the stimuli in task 2. This suggests that the efficiency of sustained emotion regulation is related to a surrogate physiological marker which presents itself immediately after the termination of initial regulation. Presumably, the recruitment of the dlPFC in task 1 prepared the amygdala to react less intensely at the second encounter with a formerly regulated negative stimulus. One possible interpretation is that the dlPFC initiated a remodeling of the respective stimulus-response-associations in such a way that a subsequent encounter of the same negative stimulus does not require effortful control in order to regulate amygdala activity (Bunge, 2004; Miller & Cohen, 2001). Alternatively, the meaning (i.e. appraisal) of each regulated stimulus might be initially changed during the regulation process itself. Here, the dlPFC might be involved in changing appraisals, while other neural circuits (e.g. posterior regions) might be involved in storing this specific meaning. Thus, the amount of amygdala activation would be determined by the previously stored meaning rather than by the stimulus properties themselves, an interpretation which is in line with the ideas of appraisal theories of emotions (e.g. Scherer, 2001).

2.3 Individual differences in emotional processing

2.3.1 Temperament, personality and affective style

Despite the universal nature of emotions it has become clear from the evidence presented in the previous chapters that individuals differ greatly regarding the type, strength, and duration of emotions that are elicited by any given stimulus or situation. The reactivity and the ability to regulate emotions, moods and feelings, has been related to a number of dimensions, including temperament, personality, or affective style. From the approach (excitation) – withdrawal (inhibition) point of view, temperament was defined as a set of constitutional differences in reactivity and self-regulation of affect, attention, and activity (Fox, 2008; Kagan, 1994; Rothbart & Bates, 2006). Eysenck (1953) posited that there are two major dimensions of temperament: one dimension that is related to a person's social activity and self-sufficiency and spans from introversion to extraversion, and one that is related to the range of negative emotional states and spans from neuroticism to stability. Indeed, an attentional bias towards negative emotional material has been consistently reported with higher levels of negative affectivity (e.g. J. M. Williams, Mathews, & MacLeod, 1996). Much in agreement with Eysenck's model, Cloninger (1987; Cloninger & Gilligan, 1987) suggested that behavioral inhibition (harm avoidance) and approach (novelty seeking) are elemental temperament types, while he also added the maintenance of behaviors (reward dependence) as a third dimension. In a revision of his earlier suggestions, Cloninger (1994) furthermore incorporated assertiveness, self-acceptance, cooperativeness, and self-transcendence, and translated his theoretical considerations into the seven-factor model of the Temperament and

Character Inventory, TCI. Closely related, but not exactly the same, the role of a person's personality in regard to affective experiences has been vividly discussed. A very influential contribution in the field of personality research was the five-factor model by McCrae and Costa (1985), who suggested that extraversion, neuroticism, agreeableness, conscientiousness, and openness to experience were the five core dimensions that underlie human personality. A concept that evolved from these suggestions is the concept of *traits* (Cattell, 1957), which is still very popular in modern psychology. Traits are seen as core aspects of personality that influence the way a situation is perceived and appraised, and thus also guide the way a person behaves in that situation (Fox, 2008). Moreover, Davidson (Davidson, 1998) suggested that reactions to affective situations and the regulation of affective responses are determined by the affective style of a person; that is, the degree to which an individual experiences positive and negative affect will influence both the appraisal of a situation and the reactivity to this (Davidson, 1998, 2000). These differences encompass emotion perception, production, and memory, along with differences in threshold, peak, and temporal dynamics of an emotional response.

As pointed out previously in Chapter 2.2, the ability to adjust to various situations by modulating their emotional impact is a prerequisite of mental health and social functioning. Thus, individual differences in the way that volitional regulation is implemented play an important role in determining a person's emotional reactivity. In fact, higher emotion regulation abilities are directly associated with the quality of social interactions (Lopes, Salovey, Cote, & Beers, 2005). Moreover, individuals with higher reappraisal scores are better-liked than individuals who habitually suppress their emotions (Richards & Gross, 2000). Gross and John (2003) found that high reappraisal scores were also associated with positive outcomes regarding life satisfaction, well-being, and

depression, while high suppression scores were associated with negative outcomes. Reappraisers experienced more positive emotions and less negative emotions compared with suppressors. Also, emotional expressivity, coping, and social support were significantly higher in habitual reappraisers compared with suppressors. A possible mechanism underlying the positive effects of reappraisal is implied by differential effects of these two strategies on cognitive functioning: while suppression has detrimental effects on memory performance, the use of reappraisal does not compromise memory function (Richards & Gross, 2000). Moreover, higher cognitive demands result in less apt regulation, as individuals showing greater cardiac acceleration and electrodermal activity during reappraisal also showed greater activation in the dmPFC and dACC (Urry, van Reekum, Johnstone, & Davidson, 2009).

In summary, the way we control our emotions in everyday life has significant consequences on short-term (emotions) and long-term (life satisfaction) measures of affectivity. Since trait markers influence both emotional processing and regulation, and personality traits are in turn influenced by genetic factors (Green, et al., 2008; Hahn & Blakely, 2007; Meyer-Lindenberg & Weinberger, 2006), it suggests itself that genetic factors may also modulate emotional processing and regulation. Recent advances in imaging genetics have indeed provided promising new insights into the complex interplay of genes, neural processing and behavior. For example, the neurotransmitter serotonin (5-hydroxytryptamine, 5-HT) is critically involved in emotional processing, stimulating imaging genetic studies of this neuromodulatory system (Hahn & Blakely, 2007). One well described determinant of this system is the serotonin transporter (5-HTT) which regulates 5-HT re-uptake from the synaptic cleft (Hariri & Holmes, 2006). The most relevant results regarding the influences of the 5-HTT genotype on emotions will be discussed in the next section.

2.3.2 *Emotions and the serotonin transporter*

On the molecular level, genetic regulation of 5-HTT mRNA and protein expression is influenced by a common polymorphism found in the 5-HTT linked promoter region (5-HTTLPR) of the serotonin transporter gene *SLC6A4*. In the presence of at least one short (s) allele, the level of 5-HTT mRNA and 5-HT reuptake in human lymphoblastoid cells is approximately two-fold lower compared with cells that are homozygous for the long (l) allele. Genetic variation within the serotonin transporter gene also influences psychological measures of negative emotionality. For instance, individuals with the 5-HTTLPR short genotype show significantly higher neuroticism, harm avoidance and anxiety scores compared with long homozygous individuals (Ansorge, Zhou, Lira, Hen, & Gingrich, 2004; Lesch, et al., 1996). The serotonin transporter genotype has also been implicated in the development of major depressive disorder: when carrying one or two copies of the s allele, the recurring experience of adverse life events such as for example psychosocial stress was reported to promote a higher risk for depression (Caspi, et al., 2003). Effects of the serotonin transporter genotype on complex endophenotypes are however inconsistent, as pointed out by a recent meta-analysis on the interaction of the 5-HTTLPR genotype, life stress and depression (Risch, et al., 2009), as well as by several neuroimaging studies which have failed to replicate associations between the 5-HTTLPR genotype and measures of personality and emotion (Bertolino, et al., 2005; Hariri, et al., 2005; Hariri, et al., 2002; Smolka, et al., 2007; Willis-Owen, et al., 2005). In contrast to the effects on behavior, the influence of the serotonin transporter genotype on (neuro)physiological parameters is more consistent. For example, the innate fear response as measured by the acoustic startle response is significantly elevated in short allele carriers, indicating that their physiological reaction to threat related environmental cues is increased compared to the l/l

homozygotes. Neuroimaging studies focused on the amygdala, a key region for emotional processing densely innervated by serotonergic neurons (Hariri, Drabant, & Weinberger, 2006; Hensler, 2006).
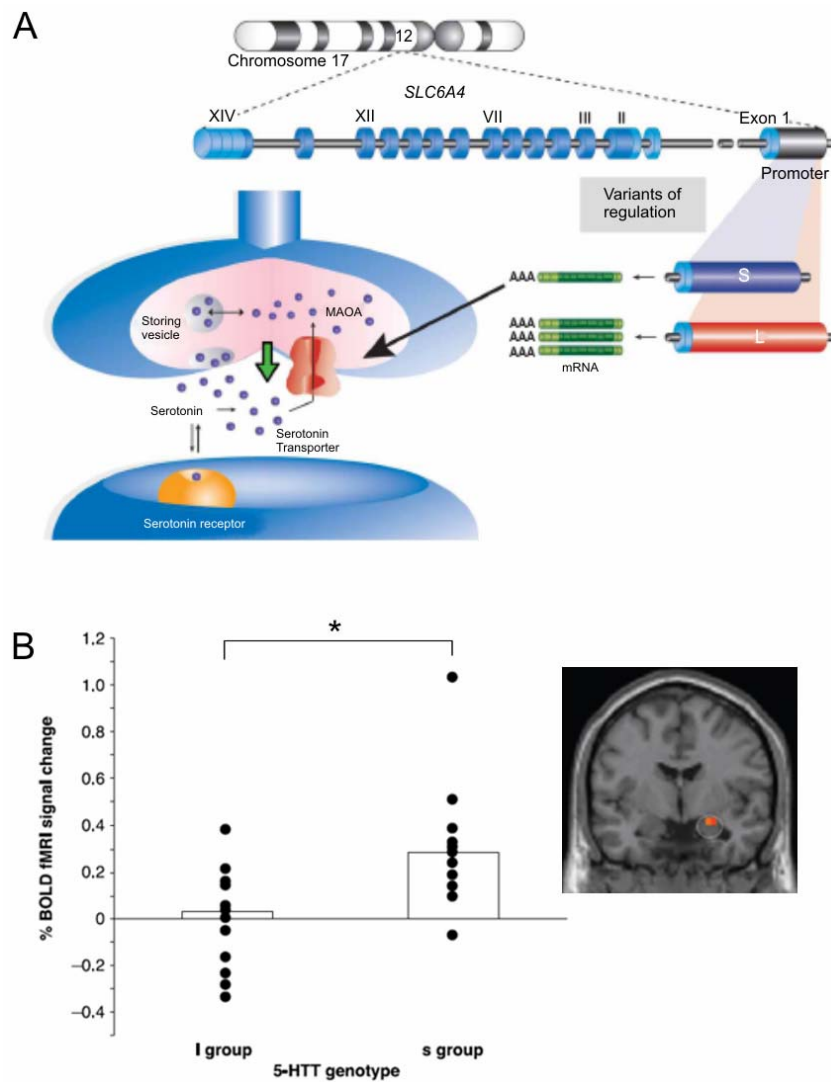
Figure 8 Effects of the 5-HTTLPR on gene expression and amygdala activation

A: A common genetic polymorphism in the human 5-HTT gene *SLC6A4* located on chromosome 17q11.1-q12 regulates 5-HTT mRNA transcription and binding, and platelet reuptake (adapted from Canli and Lesch, 2007). B: Carriers of the 5-HTTLPR short allele exhibit increased amygdala reactivity in response to negative emotional material (adapted from Hariri et al. 2002).

A number of recent studies showed that the amygdala of individuals with the short variant is more reactive during the passive viewing of aversive emotional material compared to carriers of the long variant (Bertolino, et al., 2005; Hariri, et al., 2005; Hariri, et al., 2002; Smolka, et al., 2007). Similarly, lower 5-HTT availability in the amygdala of s-carriers was related to greater BOLD signal changes to fear-related emotional material (Rhodes, et al., 2007). During passive perception, the 5-HTTLPR genotype was also related to alterations in the functional connectivity between the amygdala and the prefrontal cortex (Heinz, et al., 2005; Pezawas, et al., 2005). Additionally, structural differences between the 5-HTTLPR short and long groups were found in the amygdala, the dlPFC and vlPFC, the dmPFC and the ACC, and s-carriers exhibited significantly lower structural co-variation between the sACC and the amygdala (Canli, et al., 2005; Pezawas, et al., 2005). Taken together, these genotype-dependent dysregulations within the amygdala-prefrontal emotion network are thought to contribute to the increased negative emotionality observed in s allele carriers (Canli & Lesch, 2007; Hariri & Holmes, 2006). Consistent with this notion, in rodents a disruption in 5-HT functioning during early development entails alterations in neural structure and function, such as for example lasting emotional abnormalities (Esaki, et al., 2005; Gaspar, Cases, & Maroteaux, 2003). As pointed out by Hariri and Holmes (2006), a relative loss in serotonin transporter function related to the short variant might thus have a detrimental effect already during the development of the neural circuits involved in emotional regulation.

2.4   Aims of the current work

The main objective of the present thesis was to gain further insight into the temporal dynamics of amygdala activation during and immediately after

volitional emotion regulation. To this end, three studies were designed which address several open questions from the initial fMRI study by Walter and colleagues (2009). In all studies, participants were required either to permit or to regulate the emotions they felt in response to viewing neutral or negative pictures.

As shown in the above mentioned study (Walter, et al., 2009), voluntary emotion regulation extends beyond the period of the initial emotion regulation itself. An immediate aftereffect of volitional emotion regulation in the amygdala manifested itself as a paradoxical increase in the relax phase following negative regulation trials. However, several questions arise which cannot be answered in the framework of the initial study design. For example, from the main fMRI study, it is unclear whether the instructed volitional regulation strategy indeed works in the intended way, since there is no behavioral measure that shows that detachment also attenuated subjective experiences of negative affect. Furthermore, as picture offset and the offset of regulation both occur exactly at the same time, it cannot be excluded that the immediate aftereffect simply reflects the offset of the stimulus, or a late amygdala reaction due to voluntary regulation.

Thus, in the first part of the next chapter, two studies are reported which address the assumptions that a) the regulation task reduces the subjective experience of negativity along with the neural activation in the amygdala, and b) that the immediate aftereffect is temporally linked to the offset of regulation. In Study 1, the basic volitional regulation task used in the initial fMRI study (Walter, et al., 2009) and described in Chapter 2.2.3 was modified to contain two behavioral ratings of negativity. The first rating was acquired directly after picture offset to probe the success of the initial regulation, and the second rating was acquired at the end of the relax phase, to measure the behavioral concomitants of the

immediate aftereffect. Upon successful validation of the paradigm, another modification of the initial fMRI task was used in Study 2. Here, picture offset and the end of regulation were temporally uncoupled by introducing a delay period during which there was no picture on the screen, but participants continued permitting or regulating their emotional response to the picture.

As reported above, individual differences in the way we experience, regulate, and react to emotions have been related to a variety of factors, including genetic factors (Hariri & Holmes, 2006; Meyer-Lindenberg & Weinberger, 2006). A polymorphism within the serotonin transporter linked promoter region is associated with negative emotionality, amygdala reactivity and altered amygdala-prefrontal coupling during the perception of negative emotional material (Bertolino, et al., 2005; Hariri, et al., 2005; Hariri, et al., 2002; Heinz, et al., 2005; Pezawas, et al., 2005). However, nothing is known about the influence of volition on genetically mediated neural activity. Following this question, the second part of this thesis investigates whether individual differences in emotional reactivity are modulated by volitional emotion regulation. For this purpose, participants of Study 3 were classified with respect to their 5-HTTLPR genotype, and the neural responses during emotion perception and volitional regulation were compared between the genotype groups. Moreover, differential effects of the 5-HTTLPR genotype on the immediate aftereffect of volitional emotion regulation were explored. It was hypothesized that c) volitional emotion regulation reduces or even obliterates the amygdala hyperreactivity to the passive perception of negative emotional cues in the short allele group.

In the following chapter, the three experiments and their results will be described, and the obtained findings will be discussed.

3 Experimental Part

3.1 Introduction

The present chapter will report three experiments. All of these experiments were designed to explore the temporal dynamics of volitional emotion regulation in the amygdala described in the previous chapter and in Walter and colleagues (2009). To this end, modifications of the initial regulation task were used to address the following questions:

a) Study 1 was designed to ensure that the regulation task was also effective in reducing the experiential correlates of negative emotions by implementing an in-scan negativity rating.

b) In Study 2, the objective was to determine whether the immediate aftereffect in the amygdala pertains to the termination of the regulation strategy, or whether it is a signal that is associated with picture offset. Therefore, after each picture, participants were required to continue following the instruction given to them previously. The separation of the picture offset and the regulation offset offered the neural effects of these events to be separately investigated.

c) In Study 3, individual differences in emotional processing regarding the serotonin transporter genotype were assessed both during passive perception and active regulation of emotional pictures.

To accommodate these research objectives, the initial fMRI regulation task by Walter and colleagues (2009) was modified accordingly, while the basic idea of the task remained constant. In all three tasks, both negative and neutral pictures were presented which had to be viewed under two instructions. The 'permit' instruction asked subjects to passively view the pictures and allow emotional responses to arise naturally, while the 'suppress' instruction required participants to intentionally regulate their emotional response by adopting the position of a detached observer. Only females were studied to avoid confounding effects of gender, similar to the approaches in most other studies on cognitive emotion regulation (Drabant, et al., 2009; Eippert, et al., 2007; Goldin, McRae, Ramel, & Gross, 2008; Levesque, et al., 2003; McRae, et al., in press; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004; Schaefer, et al., 2002; Walter, et al., 2009). Moreover, female subjects were chosen based on empirical evidence that points to their increased emotional reactivity compared with males (Wager & Ochsner, 2005).

Data acquisition

Personality assessment and behavioral rating procedures

As pointed out by a bulk of studies reported in Chapter 2.3, individual differences are found regarding both the perception and the regulation of emotions. Thus, a number of personality scores were acquired in all three studies to ensure a more accurate description of the experimental groups.

Measures of depressive symptoms, anxiety, alexithymia, and habitual emotion regulation and thought suppression were acquired from the participants of all three studies. For this purpose, all participants filled out the German versions of the Beck Depression Inventory (BDI), Emotion Regulation Questionnaire (ERQ-

R), State Trait Anxiety Inventory (STAI-S/STAI-T), Toronto Alexithymia Scale (TAS-20), and the White Bear Suppression Inventory (WBS-I). The German Version of the BDI was developed by Hautzinger, Bailer, Worall and Keller (2000) and has one single scale ranging from 0 to 60, where smaller scores signify less depressive symptoms. In general, healthy female subjects are expected to reach BDI scores ≤ 16. The German ERQ by Abler and Kessler (2009) offers measures of the habitual use of suppression and reappraisal as emotion regulation strategies. The ERQ-S scale measures the tendency to suppress emotions and the ERQ-R scale measures the tendency to reappraise emotions. In a female student reference sample (N = 305), ERQ-S means were 2.92 (.93), and ERQ-R means were 4.5 (.92). The German STAI by Laux, Glanzmann, Schaffner and Spielberger (1981) has two scales, one state scale (STAI-S) and one trait scale (STAI-T). The reference population of healthy female student subjects (N=120) had means of 41.68 for the trait, and 42.09 for the state measure. In the German TAS-20 by Bach, Bach, deZwaan, Serim and Bohmer (1996) offers scales regarding problems with the identification and description of emotions, tendencies for externalization, as well as a total score of alexithymia. There are standard cutoff scores that distinguish between alexithymic subjects (> 61) and non-alexithymic subjects (< 51), with an intermediate 'grey area' for scores between 51 and 61 (G. J. Taylor, Bagby, & Parker, 1997). With the WBS-I (Wegner & Zanakos, 1994), habitual thought suppression measures were acquired. Mean values of the WBS-I total score for a female student population were between 44.8 (9.98) - 51.7 (8.53), with a maximum of 75 and higher scores representing more habitual thought suppression. For Study 3, additional personality measures were obtained because of their relevance with respect to the serotonin transporter genotype. These measures included neuroticism and harm avoidance scores, which have been previously reported to be modulated by the 5-HTTLPR (Lesch, et al., 1996). Neuroticism scores were collected from the

Neuroticism subscale of the German version of the NEO-Five Factor Inventory (NEO-FFI) by Borkenau and Ostendorf (1993). In a recent publication concerning the German norms for the NEO-FFI, young healthy females scored around 21.07 (7.3) on the Neuroticism subscale (Korner, et al., 2008). Harm avoidance was measured with the Harm Avoidance subscale of the German Version of the Temperament and Character Inventory, TCI-HA (Richter & Brandstrom, 2009). In a very recent study comparing the TCI scores of healthy controls with those of patients suffering from a personality disorder, mean harm avoidance scores of healthy controls (N=1600) were around 14.7 (6.2).

Following the scanning sessions in all three studies, a detailed debriefing was completed by all the participants. In the debriefing, subjects were asked to judge the pleasantness of every single picture, their compliance and success with implementing the instructed regulation strategy, and the amount of preoccupation with the pictures during the relax period. Pleasantness ratings were used to ensure that negative pictures were indeed more unpleasant that neutral pictures. The subjective compliance and success ratings were used to probe whether subjects performed well on the task. Moreover, the preoccupation rating was collected separately for each experimental condition (e.g. 'regulation negative', 'regulation neutral', etc.) to have a measure of possible experiential correlates of the immediate neural aftereffect in the amygdala. All ratings were carried out on 9-point Likert scales, were 1 was the lowest rating, and 9 was the highest rating for each item respectively.

The personality measures were taken on the day of the fMRI session for Studies 1 and 2, and on an additional day within one week of the fMRI session for Study 3. In Studies 1 and 2, the personality assessment and the post-scan debriefing were completed as paper-pencil versions, and in Study 3, both the post-scan debriefing and the personality assessment were completed using a personal

computer. On the day of the second appointment, blood samples were drawn for the genetic analyses after participants had filled in the personality questionnaires. Additional debriefing measures for all studies, and additional personality measures for Study 3 were also acquired which will not be reported here because they surpass the scope of the present work. The complete set of measures can however be found in Appendix B and C. The reported personality measures in the following sections are within normal range (i.e. below the indicated cut-off or within one standard deviation around the norm populations' mean value) unless otherwise indicated.

Functional magnetic resonance imaging

In all experiments participants completed an emotion regulation paradigm inside a magnetic resonance imaging (MRI) machine with a field strength of 3 Tesla (Experiments 1 & 3: Siemens Trio, Experiment 2: Siemens Allegra). All experiments were programmed and run using "Presentation", a commercially available software solution for stimulus delivery and experimental control commonly used for neuroscientific purposes (Neurobehavioral Systems, Albany, CA, USA). Functional magnetic resonance imaging (fMRI) is a means to localize neural activity in the brain during sensory, motor or cognitive tasks. It is an in-vivo and non-invasive technology based on changes in blood flow associated with neural activity. Functional imaging uses MRI scanners constructed of a coil which produces a very strong static magnetic field (B_0) and the energy of radiofrequency (RF) pulses to record local changes in blood oxygenation in dependence on time and space. Based on the biological process of changes in regional cerebral blood flow (rCBF) and cerebral blood volume (CBV), increased blood flow in the local vasculature corresponds with a local reduction in deoxyhemoglobin, while the oxygen extraction does not increase in the same

way (Plum, Posner, & Troy, 1968). Blood-oxygen-level-dependent (BOLD) imaging makes use of the fact that oxyhemoglobin is diamagnetic, while deoxyhemoglobin is paramagnetic, as these signal variations can be detected by the MRI scanner. The changes in blood oxygenation are subsumed under the term hemodynamics. The hemodynamic response function (HRF) is thought to signal the firing neurons' increased need for energy, which is satisfied by the release of oxygen from blood. The HRF begins at around 1-5 s after stimulus onset, and the peak of the HRF is reached at around 4-6 s after onset, after which it slowly returns to baseline. In fMRI, brief radiofrequency (RF) pulses emitted by additional coils, so-called gradients, are used to excite hydrogen nuclei found in different concentrations in all kinds of body tissue. Due to the fact that hydrogen nuclei are charged particles spinning at a specific frequency inside the static magnetic field B_0, they create their own magnetic dipole moments which result in very minute magnetic fields. When a body rests inside the scanner coil, all magnetic dipoles are aligned according to the static field B_0. The emission of RF pulses causes the hydrogen nuclei to be deflected from this direction, and to slowly dephase, i.e. proceed back to their original lower energy state once the RF pulse has ceased. During spin dephasing RF energy is released from the hydrogen nuclei, and this signal is detected and recorded by a receiver coil within the MRI machine. Depending on the local magnetic field, spin dephasing happens at specific frequencies which are used to decode the locus of emission of the recorded RF energy. The advantage of the technique is that functional activity of the brain can be determined from the magnetic resonance signal without the use of additional contrast enhancement. Furthermore, the time needed to acquire a sufficient amount of data is very short, and the in-plane resolution is extremely high (usually around 3-5 mm). Image acquisition is

achieved using T2*-weighted[5] gradient echo sequences. Echo planar imaging (EPI) allows for rapid image acquisitions, achieving an acquisition rate of over 30 slices per volume (= set of slices covering the whole brain or parts of the brain). Each volume is acquired in a certain amount of time which is specified in the time of repetition (TR). The number of recorded volumes depends on the length of the experiment. For any given experiment, the whole set of volumes consists of a time series of samples for every single voxel (= 3-dimensional pixel), while the number of voxels depends on the in-plane resolution and the area of the brain to be covered (Huettel, Wong, & McCarthy, 2004). The raw data is extensively processed in order to be used for statistical inferences. A rough explanation of fMRI data analysis is given in the next paragraph. Specifics about the procedures in the present studies are given in the Methods sections of each of the three experiments.

Statistical analyses

Behavioral data analysis

Behavioral data and BOLD signal time courses were analyzed using repeated measures Analyses of Variance (ANOVA). The exact procedure for any given analysis is given in the Methods section of each experiment. In general, an ANOVA tests for significant differences between different mean values, which are assessed in reference to the *Fischer*-distribution via an *F*-test. Post-hoc *F*-tests or *t*-Tests were applied in the case of significant main effects or interactions, depending on the question at hand. With *t*-Tests, differences between a pair of means are tested for significance on the basis of the *t*-distribution. The parameters associated with these procedures will be abbreviated in the

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[5] T2* refers to the time needed for the deflected magnetization to relax after a 90° radiofrequency pulse

following. ANOVA *F*-Test parameters with their respective degrees of freedom: $F(df_{factor\ levels}, df_{residual})$. Note that $df_{factor\ levels}$ = number of factor levels -1 and $df_{residual}$ = number of participants-1 / number of factor levels-1. Parameters associated with *t*-Tests: $t(df)$. Here, *t* refers to the *t*-Test parameter, with its respective degrees of freedom df = number of data-1. For both procedures, *p* refers to the significance level of the given result, i.e. the probability of the null hypothesis. Mean values are reported with either their standard deviation (*SD*) or corresponding standard error of mean (*SEM*). The statistical analysis of the behavioral data and timecourses was carried out using STATISTICA 6.0 (StatSoft, Tulsa, OK, USA).

Functional data analysis

Functional magnetic resonance imaging data were analyzed using Statistical Parametric Mapping (SPM, Wellcome Institute of Cognitive Neurology, London, UK), available as freeware online, and Matlab 6.5.1 (MathWorks, Natick, MA, USA). The first volumes acquired in each session were discarded before the analysis to allow for T1 equilibration. Functional images were slice-timed to account for acquisition delay and realigned to the first scan of the first session to correct for head motion. Images were then normalized to the Montreal Neurological Institute (MNI) EPI template and resampled in order to assure inter-subject comparability. Subsequently, the images were smoothed with an 8 mm full width at half maximum (FWHM) isotropic Gaussian kernel to increase signal-to-noise ratio. Temporal filtering was achieved using an autoregressive model (AR1), and a high-pass filter of 128 seconds removed slow signal drifts. A first-level fixed-effects model was computed for each participant. Regressors were created for the experimental conditions, and convolved with a canonical HRF implemented in SPM. Movement parameters were included in the model as regressors of no interest to account for residual motion artifacts. Random-effects

analyses were carried out in the framework of the General Linear Model (GLM) treating intersubject variability as a random factor to account for interindividual variance. Comparisons between conditions and/or groups were realized using t-Statistics for each individual voxel at individual thresholds. For the amygdala, for which specific a priori hypotheses were formulated, small volume correction was allowed at more lenient thresholds. Results are reported in MNI space indicating the x, y, and z coordinates, and Z-statistics are reported for cluster maxima.

For the investigation of the temporal dynamics of amygdala activation, regions of interest (ROIs) were defined in the amygdala. Spherical volumes of interest (VOIs) were created around the MNI coordinates of the maxima from the second level analysis of each study. Subsequently, mean 1st Eigenvariate values were extracted from all voxels included in this sphere for each subject. Mean signals were calculated for each TR of the experimental conditions by averaging the respective values from the extracted time series. External statistical validations of the immediate aftereffect were realized by repeated-measures ANOVAs comparing the effects of valence, regulation, and phase (and in the case of Study 3 also genotype). The mean signal change values from the respective TRs representing the peaks of the assumed hemodynamic response following picture onset, picture offset, and the immediate aftereffect (see Walter, et al., 2009). The validity of this approach was ensured by close visual inspections of the timecourses.

The specific parameters of the above mentioned analyses are given in the Methods descriptions of the Experiments.

3.2 Part I

As described in detail in Chapter 2.2.2, several strategies such as labeling (Hariri, et al., 2000), distraction (Erk, Abler, & Walter, 2006; Erk, Kleczar, & Walter, 2007), detachment (Beauregard, et al., 2001; Eippert, et al., 2007; Ochsner, Ray, et al., 2004; Phan, et al., 2005) or reappraising a negative event in unemotional terms (Goldin, et al., 2008; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004; Phan, et al., 2005) have proven to be effective in reducing negative feelings as well as neural responses in the amygdala. Activation in the medial and lateral prefrontal and the parietal cortex have been consistently reported during effortful emotion regulation (Beauregard, et al., 2001; Hariri, et al., 2000; Hariri, et al., 2003; Levesque, et al., 2003; Levesque, et al., 2004; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004; Phan, et al., 2005). Similar to what has been reported for behavioral data following the suppression of aversive emotional material (Harvey & Bryant, 1998a, 1998b; Koster, et al., 2003; Roemer & Borkovec, 1994), Walter and colleagues (2009) described the presence of an immediate aftereffect in the amygdala following the regulation of negative emotional stimuli. While the BOLD signal of the amygdala was higher when perceiving negative stimuli compared with regulating negative stimuli *during picture presentation*, the opposite was true *after picture presentation*. In the fixation period following the regulation of negative emotions, the amygdala signal was higher than in the fixation period following the perception of negative emotions. This immediate aftereffect of intentional regulation was associated with the habitual tendency of thought suppression and to a sustained regulation effect in a second task. Participants with higher WBSI scores showed greater immediate aftereffects, and participants with higher immediate aftereffects also showed greater amygdala signal to formerly regulated negative pictures compared with their unregulated counterparts. The immediate aftereffect was interpreted in the following way:

the increase in amygdala activation signifies a paradoxical rebound effect, analogous to similar findings in other fields, such as elevated electrodermal responses after thought suppression (Abramowitz, et al., 2001; Wenzlaff & Wegner, 2000). In respect to the immediate aftereffect of volitional emotion regulation (Walter, et al., 2009), several concerns can be raised as to whether this finding does indeed qualify as a valid effect of intentional regulation:

Firstly, it remains to be demonstrated that the regulation task reduces both the neural signature *and* the subjective experience of negativity. Secondly, empirical evidence is needed in support of the assumption that the immediate aftereffect is temporally linked to the offset of regulation and not to the offset of the stimulus. Following this rationale, the two studies were designed which will be described in the following sections. Study 1 included behavioral ratings of negativity at picture offset and at fixation offset in order to provide a behavioral measure of a) the effectiveness of regulation and b) experiential changes related to the immediate aftereffect in the amygdala. After confirming the successful implementation of intentional regulation, Study 2 was designed in order to disentangle picture offset and the offset of regulation. A "maintain" phase was introduced after picture offset during which participants continued to experience or regulate the emotion elicited by the previous stimulus. Thus, the effects following picture offset and the termination of regulation could be separately analyzed.

3.2.1 *Study 1 – Experiential and neural correlates of volitional emotion regulation and its aftereffects*

The data presented in Study 1 have been published in part in Walter, von Kalckreuth, Schardt, Stephan, Goschke, & Erk (2009).

Experimental Procedures

Subject data

Participants (n = 14) were right-handed female university students with normal or corrected-to-normal vision and without any history of neurological or psychiatric illness. Written informed consent was obtained before participation in accordance with the Declaration of Helsinki. Participants received € 20 as a reward for their participation. The study protocol was approved by the local ethics committee. The data from four participants had to be excluded due to technical problems with the synchronization between the MRI machine and Presentation. Thus, the data from 10 participants was subjected to further analyses.

Personality questionnaires

Participants filled in personality questionnaires regarding depressive symptoms (BDI), trait anxiety (STAI-Trait), habitual use of emotion regulation strategies (ERQ), alexithymia (TAS-20) and habitual thought suppression (WBS-I).

Imaging

Functional task

During imaging participants viewed an emotion regulation paradigm (Figure 9). Participants viewed 30 negative and 30 neutral pictures in a slow event-related pseudo-randomised[6] design. A total of 60 trials were presented in two sessions. The pictures were the same set previously used in Walter et al. (2009). All stimuli

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[6] no more than two consecutive trials of the same type

were taken from the International affective picture system, a standardized
stimulus set (Lang, et al., 1997), and were matched for complexity, content
(humans, nature, objects, animals), color, and brightness. Instructions detailed to
the participants that they would be viewing pictures of both neutral and
negative valence while employing one of two different strategies. Following the
word "permit", they were to look at the subsequent picture and permit
themselves to feel whichever emotional response arose naturally, without trying
to alter it. Following the word "suppress" participants were to look at the
subsequent picture while detaching from any emotional response which arose
by adopting the position of a detached observer who is not affected by the scene
presented in the picture.
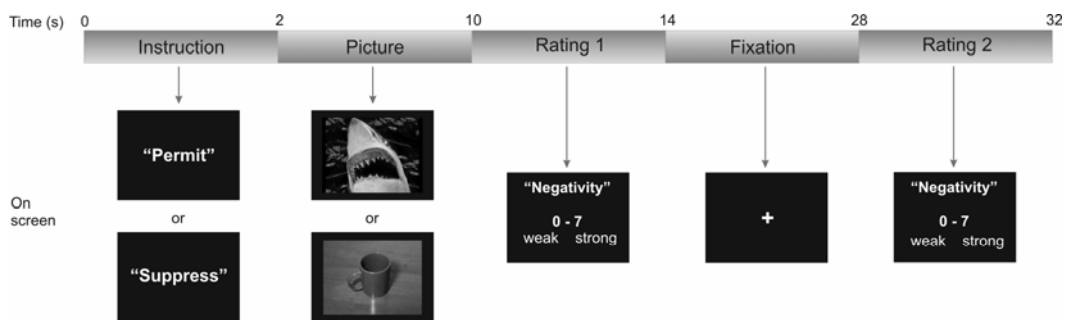
Figure 9:   Experimental Paradigm from Study 1

Half of the images of each valence were presented with the 'perception'
instruction, and the other half with the 'regulation' instruction, resulting in four
experimental conditions: 'perception negative', 'perception neutral', 'regulation
negative', and 'regulation neutral'. After the presentation of the instruction for 2
seconds, either a negative or a neutral picture appeared on screen for 8 seconds.
After picture offset, participants had to indicate the strength of their negative
affect at that moment on a scale from 0 (weak) to 7 (strong) by button press

(Ochsner, Ray, et al., 2004). During the subsequent fixation period, subjects were instructed to relax and think of nothing in particular for 14 seconds. A second rating with the same scale was acquired at the end of each trial. Participants always had 4 seconds to choose the respective negativity rating. If no response was registered during that period, the experimental paradigm continued. The total time for each trial in Study 1 thus amounted to 32 seconds.

In-scan and post-scan rating procedures

In-scan ratings required participants to indicate the strength of their negative feelings twice for each stimulus: the first rating was obtained directly after the offset of a stimulus; the second rating was obtained at the end of the relax phase. Both ratings were carried out using an 8-point Likert scale ranging from '0 – not negative at all' to '7 – extremely negative' according to the procedure reported by Ochsner and colleagues (Ochsner, Ray, et al., 2004). The first rating directly after picture offset was performed to ensure that intentional regulation through detachment induced a measurable change on the behavioral level as reported in previous studies (Beauregard, et al., 2001; Eippert, et al., 2007; Goldin, et al., 2008; Levesque, et al., 2003; Levesque, et al., 2004; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004). The second rating was included to directly test for changes in subjective feelings of negativity following the previously described immediate aftereffect of intentional regulation of negative emotions (Walter, et al., 2009). After the scanning session, a detailed debriefing (Appendix C) was carried out. From the post-scan debriefing, the ratings of stimulus pleasantness were analyzed and compared between the four experimental conditions. The assessments of the participants' compliance with the instructed regulation strategy, the general success at implementing detachment and the amount of preoccupation with the pictures during the fixation period as a measure of the

behavioral correlates of the neural aftereffect of regulation were also subjected to further analyses. All ratings were carried out on a 9-point Likert scale that ranged from '1 – lowest rating' to '9 – highest rating' respectively.

Data analysis

Behavioral data

The mean in-scan ratings of negativity were compared across conditions in a repeated-measures ANOVA with the factors 'valence' (negative, neutral), 'regulation' (perception, regulation), and 'phase' (after picture, after fixation). For the post-scan ratings of compliance and regulation success, means (*M*) and their respective standard errors (*SEM*) were calculated for the entire sample. The means of the post-scan pleasantness and preoccupation ratings were calculated for each of the four experimental conditions and entered into separate repeated-measures ANOVAs with the factors 'valence' (negative, neutral), and 'regulation' (perception, regulation). The threshold for significance was set to $p < .05$ for all analyses.

Functional image processing

Functional imaging data were acquired on a 3 Tesla Siemens Trio with a T2*-weighted gradient-echo EPI sequence. The whole brain volume was covered by 31 slices of 3 mm and a distance factor of 25 percent. An oblique slice orientation along a line between the OFC and the cerebellum was chosen in order to minimize signal dropout due to tissue borders in the medial temporal lobe (amygdala) and the orbitofrontal cortex. A set of 572 volumes was acquired in each of the two sessions. The volumes were acquired at a TR of 2 s, TE 25 ms, FA = 90°, FOV = 192 mm, with a 64 x 64 matrix. A T1-weighted MPRAGE dataset

was acquired from each subject with 92 slices, and a voxel size of 1 x 1 x 1.5 mm (256 x 256 matrix, TR = 2 s, TE = 3.39 ms). Binocular LCD video goggles (NNL, Bergen, Norway) were used for stimulus presentation. SPM2 (Statistical Parametric Mapping, Wellcome Institute of Cognitive Neurology, London, UK) and Matlab 6.5.1 (MathWorks, Natick, MA, USA) were used for pre-processing and statistical analyses of the fMRI data. The first four volumes at the beginning of each session were discarded before the analysis to allow for the T1 relaxation to reach steady state. Delays in slice acquisition and head movement were accounted for by slice-timing and realignment to the first scan of the first session respectively. Resampling the images at 2 x 2 x 2 mm, the individual data were normalized to the MNI template implemented in SPM. Spatial smoothing was achieved by applying an 8 mm FWHM isotropic Gaussian kernel. The data were high-pass filtered at 128 seconds and temporally filtered (AR1) to account for slow-cycle signal drifts and auto-correlations. The instruction, the four experimental conditions 'perception negative' (pN), 'perception neutral' (pX), 'regulation negative' (rN), 'regulation neutral' (rX), and all responses were included in a single-subject fixed effects model as boxcar regressors with their actual length (i.e. 2 seconds for the instruction, 8 seconds for picture presentation, and 4 seconds for each rating). Subsequently, a convolution of the boxcar regressors and the standard canonical HRF implemented in SPM was performed. Individual movement parameters from the realignment procedure were included in the model as regressors of no interest to account for variance attributable to motion. The *t*-contrast images of the four experimental conditions versus baseline were computed for each participant. The individual *t*-contrasts were then entered into a second-level random effects GLM with non-sphericity correction. Similar to the approach described in Study 1 and in Walter and colleagues (2009), the overall effects of perception and regulation of emotions were assessed by comparing the perception of negative versus neutral cues (pN

> pX), and the perception and regulation of negative cues (pN > rN, rN > pN). All whole brain analyses were thresholded at $p < .005$ uncorrected for multiple comparisons due to the relatively small sample size and the strong *a priori* regional hypotheses. Coordinates of cluster maxima were converted from MNI to Talairach space for labeling according to the Talairach and Tournoux atlas (Talairach & Tournoux, 1988). For reasons of accuracy however, the original unconverted MNI coordinates will be reported throughout (Chau & McIntosh, 2005), as suggested in the guidelines for reporting fMRI results by Poldrack and associates (2008).

Time series extraction and signal timecourse preparation

Regions of interest were defined in the bilateral amygdala. Spherical Volumes Of Interest (VOIs) with a radius of 8 mm were created around the MNI coordinates of the maxima from the second level contrast comparing the perception of negative versus neutral pictures (i.e. -18, -2, -20 [MNI x, y, z] and 26, -2, -20 [MNI x, y, z]). Subsequently, mean 1st Eigenvariate values were extracted from all voxels included in this sphere for each subject. Mean signals were calculated for each TR (i.e. TR 1 to 16) of the four experimental conditions by averaging the respective values from the extracted time series in the right and left amygdala respectively. A repeated-measures ANOVA with the factors 'valence' (negative, neutral), 'regulation' (perception, regulation), and 'TR' (TR 5, TR 9, scan 12) was computed to examine the immediate aftereffect of regulation. The mean signal change values from TR 5, TR 9 and TR 12 were chosen as they represent the peaks of the assumed hemodynamic response following picture onset, picture offset (and in the present case also rating onset), and the immediate aftereffect which has been previously found to occur around 6 seconds into the relaxation period (see Walter et al. 2009). A visual inspection of the timecourses validated

this approach. For the analysis of the timecourse data, the threshold of significance was set to $p < .05$.

Results

Demographics and Questionnaires

The mean age of the participants was $M = 23.9$ years (± 4.53 *SD*). Means from all personality questionnaires were within normal range i.e. below cutoff or within ± 1 *SD* around the mean of the respective reference populations (see Chapter 3.1 for reference population means).The mean BDI score was 7.3 (*SD* = 5.9, range 0-16). Habitual emotion regulation scores were $M = 2.83$ (*SD* = 1.12, range 1.5-5) for ERQ-Suppression, and $M = 4.75$ (*SD* = 1.21, range 2-6.3) for ERQ-Reappraisal. The trait anxiety measure (STAI-T) had a mean of $M = 41.5$ (*SD* = 8.71, range 28-57). Alexithymia as measured with the TAS-20 had a mean of $M = 48.8$ (*SD* = 8.88, range 40-64). Habitual thought suppression as measured by the WBS-I had a mean of $M = 43.1$ (*SD* = 15.45, range 21-65).

Behavioral ratings

In-scan negativity, post-scan pleasantness, and preoccupation ratings were assessed regarding the influence of stimulus valence and cognitive emotion regulation (Table 1). Task performance was assessed in terms of compliance with and success at detaching from emotional responses in the regulation condition. The subjective experience of negativity during the scanning session was significantly influenced by valence, regulation and phase. Aversive stimuli induced significantly more negativity than neutral stimuli (main effect 'valence', $F(1,9) = 45.28$, $p < .0001$). Detachment was effective in reducing subjective experiences of negativity (main effect of 'regulation' ($F(1,9) = 36.05$, $p < .001$).

Table 1:   **In-scan and post-scan ratings from Study 1**

In-Scan Rating	*M*	*SEM*	Post-Scan Rating	*M*	*SEM*
Negativity			*Pleasantness*		
Perception Negative			Perception Negative	2.15	0.10
After Picture	4.80	0.51	Regulation Negative	2.55	0.09
After Fixation	2.47	0.60	Perception Neutral	5.93	0.19
Regulation Negative			Regulation Neutral	6.15	0.19
After Picture	2.18	0.35			
After Fixation	1.66	0.42	*Compliance*	7.90	0.28
Perception Neutral					
After Picture	0.42	0.14	*Regulation Success*	5.40	0.43
After Fixation	0.23	0.12			
Regulation Neutral			*Preoccupation*		
After Picture	0.33	0.11	Perception Negative	3.60	0.70
After Fixation	0.26	0.09	Regulation Negative	3.90	0.74
			Perception Neutral	1.50	0.22
			Regulation Neutral	1.70	0.37

Mean ratings of negativity decreased from the first rating after picture presentation to the second rating after the fixation (main effect 'phase', $F(1,9)$ = 13.02, $p < .006$). The decrease was strongest for unregulated negative pictures, and lesser for regulated negative pictures; negativity ratings for both regulated and unregulated neutral pictures decreased only marginally from the first to the second in-scan rating (interaction 'valence' x 'regulation' x 'phase', $F(1,9)$ = 19.32, $p < .002$). The findings from the post-scan debriefing complemented these results. After the scanning session, negative stimuli were also judged as more unpleasant than neutral stimuli (main effect of 'valence', $F(1,9)$ = 392.98, $p < .0001$), and regulated pictures were judged as more pleasant than unregulated stimuli (main effect of 'regulation', $F(1,9)$ = 10.32, $p < 0.02$). High ratings of compliance with (M = 7.90, SEM = .28) and success at implementing detachment (M = 5.40, SEM = .43) indicated that participants performed well on the task. Regarding the behavioral aftereffects of regulation, participants were more preoccupied with negative than neutral stimuli during the subsequent fixation phase (main effect 'emotion', $F(1,9)$ = 11.24, $p < .009$). However, the previous regulation of emotions had no effects on preoccupation ($p > .64$).
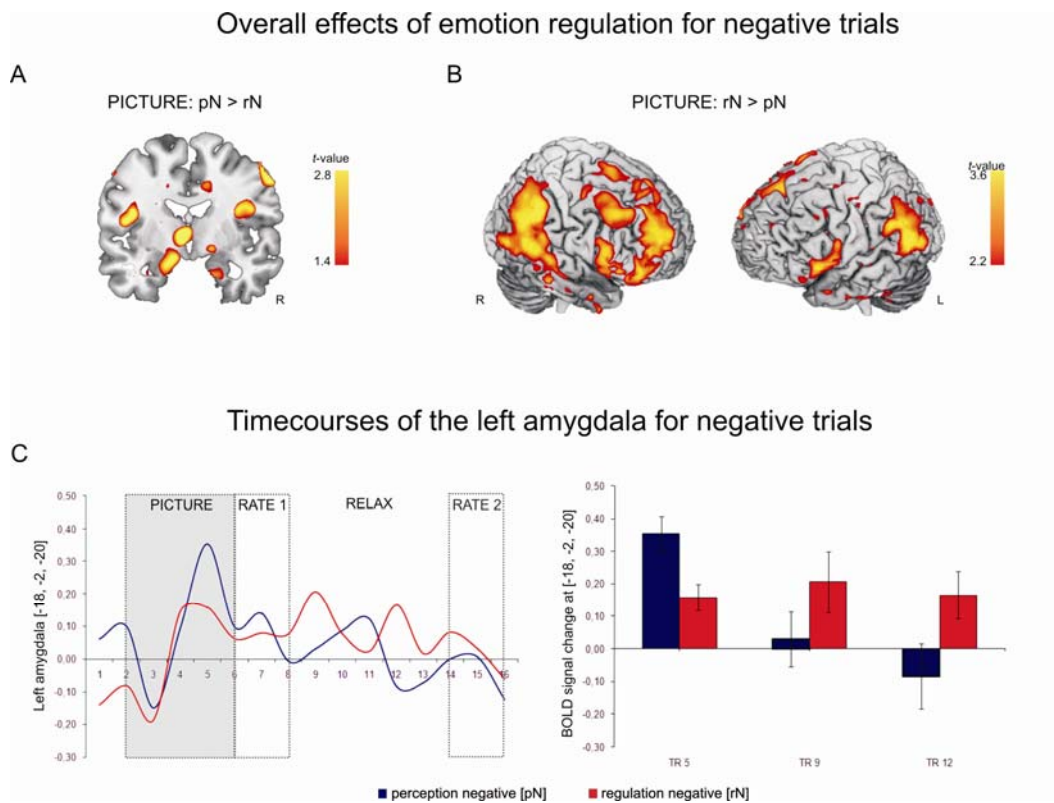
Figure 10: Results from Study 1

> A: Results from the categorical analysis show significant amygdala signal attenuation during regulation. B: A network of dorsolateral and ventrolateral prefrontal, and inferior and superior parietal regions was recruited during detachment. C: Timecourses and BOLD signal change from the left amygdala show an immediate aftereffect of regulation during the relax phase at TR 9 and TR 12.

Overall BOLD activation following the perception and regulation of negative and neutral stimuli

For the investigation of the neural correlates of valence and regulation, brain activations were compared between the perception negative and the perception neutral condition, and between the regulation negative and the perception negative condition. The perception of negative stimuli activated a network including the left amygdala, dorsal and ventral ACC, medial OFC, ventrolateral PFC and thalamus in comparison with neutral stimuli ($p < .005$ uncorrected for

multiple comparisons) (Figure 10 A). A network comprised of the dorsolateral and ventrolateral PFC along with the inferior parietal lobule was recruited during emotion regulation, while the left amygdala and left thalamus were effectively down-regulated by detachment (Figure 10 B).

Temporal dynamics of amygdala activation

The extracted signal timecourses from the amygdala were plotted for the right and left ROIs and statistically compared regarding the influence of valence, regulation, and time to assess whether an immediate aftereffect was present following regulated negative trials (Figure 10 C). The above mentioned results from the whole-brain analysis were corroborated in this analysis: negative stimuli elicited significantly larger BOLD signals compared with neutral stimuli in the left amygdala (main effect of 'valence', $F(1,9) = 14.27$, $p < .005$). In the right amygdala, no overall effect of the negative condition could be observed due to the comparably high activation in the neutral condition ($p = .17$). However, an immediate aftereffect was present in the bilateral amygdala, as signaled by a significant interaction of the factors 'TR x regulation' (left: $F(2,18) = 6.24$, $p < .009$; right: $F(2,18) = 3.57$, $p < .05$). To further explore these effects, separate post-hoc analyses of variance for the negative and the neutral conditions were carried out for the left and right amygdala ROI signal data respectively. The results of these analyses showed that the immediate aftereffect in the left amygdala was only present for regulated negative (interaction of 'TR x regulation', $F(2,18) = 6.23$, $p < .009$) but not for neutral trials ($p = .20$). In the right amygdala, the interaction of 'TR x regulation' was only marginally significant in the negative condition ($p = .07$), but clearly not significant in the neutral condition ($p > .14$). While both amygdalae showed increased activation upon the perception of a negative stimulus compared with the active regulation at TR 5, the reverse pattern was

found during the subsequent fixation at TR 9 and TR 12. Here, the BOLD signal in the bilateral amygdala was higher following the regulation of negative emotions compared with their perception. For the neutral condition, the amygdala signal remained relatively stable over time and did not differ significantly between the perception and the regulation condition.

3.2.2 Study 2 – Validation of the immediate aftereffect of regulation in the amygdala

Experimental Procedures

Participants

Fifteen female university students (all right-handed) with normal or corrected-to-normal vision took part in the study. After the exclusion of neurological or psychiatric illnesses they gave their written informed consent. Participants received course credits as a reward for their participation. The study protocol was approved by the local ethics committee, according to the guidelines laid out in the Declaration of Helsinki. Three participants were excluded due to excessive movement (> 3 mm) during the scanning session, leaving a total of 13 participants for subsequent analyses.

Personality questionnaires

Participants filled in the same personality questionnaires as in Study 1, i.e. BDI, ERQ, STAI-T, TAS-20, and WBS-I.

Imaging

Functional task

The functional task consisted of two parts; however only the results from the first part will be reported here because they are directly related to the immediate aftereffect. Part one required participants to naturally experience ('perception') or actively detach from ('regulation') emotional responses during and after the presentation of negative and neutral pictures (Walter, et al., 2009). The 30 negative and 30 neutral pictures presented in Study 2 were the same as the ones used in Study 1 and Walter et al. (2009). Participants were told that pictures of different valence were going to be presented to them, and that there would be two different strategies they would be asked to employ during picture presentation, as well as for a short period of time after the offset of the picture (maintain phase). When they saw the word 'permit', they were to look at the subsequent picture and permit themselves to feel whichever emotional response arises naturally, without trying to alter it. When they saw the word 'suppress' participants were to look at the subsequent picture while detaching from any emotional response which may arise by adopting the position of a detached observer. Participants were instructed to maintain the respective strategy (either 'permit' or 'suppress') after picture offset for as long as they saw three white dots ("…") on the screen. Thus, a given single trial was 32 seconds long: the instruction was displayed for 2 seconds, followed by 8 seconds of picture presentation. A maintain phase of 6 seconds followed, succeeded by a fixation of 12 seconds during which participants were instructed to relax (Figure 11). Half of the images of each valence were presented with the 'perception' instruction, and the other half with the 'regulation' instruction, and the picture and maintain phases were assessed separately, resulting in eight experimental conditions:

'picture perception negative', ' picture perception neutral', 'picture regulation negative', 'picture regulation neutral', 'maintain perception negative', ' maintain perception neutral', 'maintain regulation negative', and 'maintain regulation neutral'.
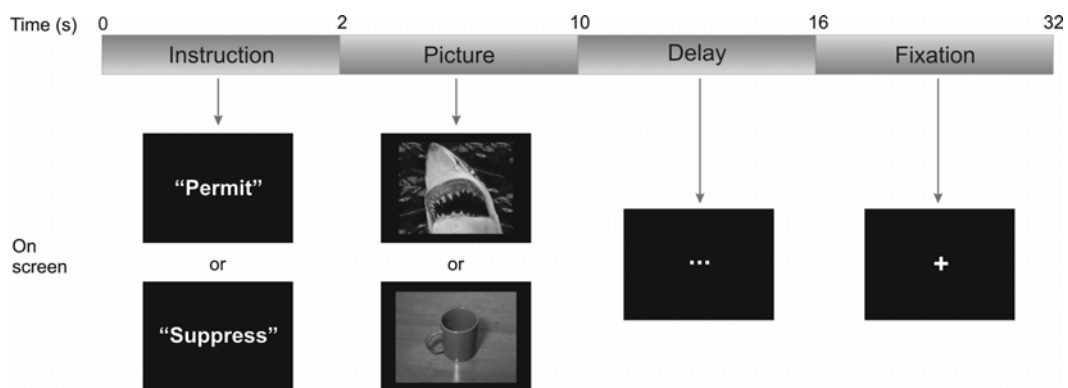
Figure 11: Experimental Paradigm from Study 2

Approximately ten minutes after the end of part 1, a "watch only" task was presented where participants were instructed to simply look at the 60 pictures again. The stimuli were presented randomly for 1 second with and inter-trial interval of 3 seconds (± 1.5 seconds). As mentioned above, the results from the latter part of the functional task will not be reported here.

Post-scan rating procedures

From the detailed debriefing (Appendix C), the ratings indicating picture pleasantness, as well as the compliance with and the success at implementing detachment as a strategy for emotion regulation will be reported in the following. Also reported are ratings of the amount of preoccupation with the pictures during the maintain phase and during the fixation. Preoccupation ratings from one subject were not recorded due to a printing mistake. All ratings

were carried out on a 9-point Likert scale that ranged from '1 – lowest rating' to '9 – highest rating' respectively.

Data analysis

Behavioral data

For the post-scan ratings of compliance and regulation success, means (*M*) and their respective standard errors (*SEM*) were calculated for the entire sample. The means of the post-scan pleasantness ratings were calculated for each of the four experimental conditions 'perception negative', 'perception neutral', 'regulation negative', and 'regulation neutral'. The resulting values were then entered into a repeated-measures ANOVA with the factors 'valence' (negative, neutral), and 'regulation' (perception, regulation). Preoccupation ratings for the maintain phase and the fixation were entered into a repeated measures ANOVA with the factors 'valence' (negative, neutral), 'regulation' (perception, regulation) and 'phase' (maintain, fixation). Results were considered to be significant at a threshold of $p < .05$.

Functional image processing

Functional imaging acquisition took place on a 3 Tesla Siemens Allegra with a gradient-echo T2*-weighted EPI sequence. For part 1 of the functional task, whole-brain images were collected in 33 slices with a slice thickness of 3 mm and a distance factor of 25 percent. In order to assure optimum signal detection in the amygdala, the slices were acquired in an oblique fashion along a line between OFC and cerebellum. 487 volumes per session were acquired with a TR of 2 seconds (TE 30 ms, FA = 80°, FOV = 192 mm, 64 x 64 matrix). During part 2 of the functional task, a total of 203 volumes with 23 slices each (slice thickness 3 mm,

distance factor 25 percent) were recorded. TR was 1.5 seconds (TE 30 ms, FA = 77°, FOV = 192 mm, 64 x 64 matrix). Additional structural T1-weighted images were acquired from each subject (160 slices, voxel size = 1 x 1 x 1.5 mm, 256 x 256 matrix, TR = 2 s, TE = 3.39 ms). Additional MR sequences were recorded (T2, CASL), the results of which are not reported here. Stimuli were presented via LCD video goggles (Resonance Technology, Northridge, CA).

SPM2 (Statistical Parametric Mapping, Wellcome Institute of Cognitive Neurology, London, UK) and Matlab 6.5.1 (MathWorks, Natick, MA, USA) were used for pre-processing and statistical analyses of fMRI data. Five volumes at the beginning of each session were discarded before analysis. Slice-timing accounted for acquisition delay, and realignment to the first scan of the first session corrected for head motion. Normalization to the MNI template was computed and images were resampled at 2 x 2 x 2 mm. For smoothing, an 8 mm FWHM isotropic Gaussian kernel was applied to increase signal-to-noise ratio. A high pass filter of 128 seconds and temporal filtering (AR1) accounted for auto-correlations and slow-cycle signal drifts. A first-level fixed-effects model was computed for each participant. Regressors were created for the instruction, as well as for the four experimental conditions, separately for the picture presentation and the maintain phase, i.e. 'picture perception negative' [pNpic], 'picture perception neutral' [pXpic], 'picture regulation negative' [rNpic], picture regulation neutral' [rXpic], and 'maintain perception negative' [pNmain], 'maintain perception neutral' [pXmain], 'maintain regulation negative' [rNmain], 'maintain regulation neutral' [rXmain]. The duration of each event corresponded to it's actual length, that is 2 seconds for the instruction, 8 seconds for the picture presentation, and 6 seconds for the maintain phase. Residual variance attributable to motion was accounted for by including movement parameters from the realignment procedure as regressors of no interest. The

resulting boxcar regressors were convolved with the standard HRF implemented in SPM. Interactions of valence, regulation and phase were assessed for the whole group in a repeated-measures GLM with non-sphericity correction treating participants as random factors. To this end, the individual *t*-contrast images of the eight experimental conditions versus baseline from each subject were used. Overall effects of perception and regulation of emotions collapsed over the picture presentation and the maintain phase were assessed by comparing the perception of negative versus neutral cues ([pNpic + pNmain] > [pXpic + pXmain]), and the perception and regulation of negative cues ([pNpic + pNmain] > [rNpic + rNmain] and vice versa). The same contrasts were also assessed for the picture presentation and the maintain phase alone (picture presentation: pNpic > pXpic, pNpic > rNpic, and rNpic > pNpic; maintain phase: pNmain > pXmain, pNmain > rNmain, and rNmain > pNmain). Direct comparisons of the picture phase and the maintain phase were computed to assess the interactions of valence, regulation and phase ([pNpic > pXpic] > [pNmain > pXmain], [pNpic > rNpic] > [pNmain > rNmain] and vice versa, [rNpic > pNpic] > [rNmain > pNmain] and vice versa). All whole brain analyses were thresholded at $p < .005$ uncorrected for multiple comparisons due to the relatively small sample size and the strong *a priori* regional hypotheses. An MNI to Talairach conversion of the coordinates of the cluster maxima was carried out before labeling (mni2tal-transform Brett, 2006). Anatomical labeling was done according to the Talairach and Tournoux atlas (Talairach & Tournoux, 1988). In the following, the original unconverted MNI coordinates will be reported (Chau & McIntosh, 2005), according to the guidelines by Poldrack et al. (2008).

Time series extraction and signal timecourse preparation

Individual time series were extracted from ROIs in the left and right amygdala. The 1st Eigenvariate values were extracted for each subject from a spherical VOI with 8 mm radius around -20, -4, -18 [MNI x, y, z] and 20, -4, -16 [MNI x, y, z]. The center coordinates of these ROIs were chosen based on the maxima of the activation in the contrast comparing the perception of negative and neutral pictures collapsed across picture presentation and maintain phase ([pNpic + pNmain] > [pXpic + pXmain]). Signals for each of the eight experimental conditions were averaged from the extracted time series in the right and left amygdala ROIs respectively. The question of whether the immediate aftereffect in the amygdala is dependent of picture offset or the offset of regulation was addressed in a repeated-measures ANOVA with the factors 'valence' (negative, neutral), 'regulation' (perception, regulation), and 'TR' (TR 5, TR 9, TR 13). To best capture the effects of picture onset, picture offset, and regulation offset, the mean signal change values from TR 5, TR 9 and TR 13 were taken from each subject. This approach was based on the assumption that the HRF reaches its peak around six to eight seconds after the occurrence of an event of interest; the visual inspection of the timecourses showed that this was indeed the case. The results of the above mentioned analyses were considered to be significant at $p < .05$.

Results

Demographics and Questionnaires

Participants had a mean age of 24.69 years (± 4.38 *SD*). Regarding the investigated personality dimensions, all means were within one standard deviation around the means of age, gender, and education matched reference

populations (see Chapter 3.1).The mean BDI score was $M = 2.31$ ($SD = 3.01$, range 0-10). The mean habitual emotion regulation scores were $M = 2.62$ ($SD = .77$, range 2-4) for ERQ-Suppression, and $M = 5.00$ ($SD = 1.00$, range 3-6) for ERQ-Reappraisal. The trait anxiety measure (STAI-T) had a mean of $M = 39.00$ ($SD = 6.43$, range 26-49). Alexithymia as measured with the TAS-20 had a mean of $M = 42.77$ ($SD = 8.61$, range 27-57). Habitual thought suppression scores from the WBS-I had a mean of $M = 48.23$ ($SD = 8.25$, range 30-58).

Table 2: Post-scan ratings from Study 2

	M	*SEM*		*M*	*SEM*
Pleasantness			*Preoccupation*		
Perception Negative	2.64	0.18	**Perception Negative**		
Regulation Negative	2.95	0.14	Maintain Phase	2.58	0.38
Perception Neutral	5.84	0.16	Fixation Phase	2.33	0.41
Regulation Neutral	5.85	0.13	**Regulation Negative**		
			Maintain Phase	2.50	0.58
Compliance	7.15	0.54	Fixation Phase	2.33	0.49
			Perception Neutral		
Regulation Success	4.92	0.49	Maintain Phase	2.41	0.67
			Fixation Phase	2.00	0.58
			Regulation Neutral		
			Maintain Phase	2.42	0.50
			Fixation Phase	2.08	0.57

Behavioral ratings

Picture pleasantness and preoccupation with pictures during the maintain and fixation periods were compared across valences and conditions. Moreover, mean compliance and regulation success ratings were computed (

Table 2). Post-scan pleasantness ratings of the pictures were generally lower for negative compared with neutral pictures (main effect 'valence' $F(1,12) = 209.75$, p <.0001), and higher for regulated compared with unregulated pictures (main effect 'regulation' $R(1,12) = 6.97$, p < .03), especially in the negative condition. The self-report ratings of the compliance with the regulation strategy and

success at implementing it were generally high (compliance: $M = 7.15$, $SEM = .54$; regulation success: $M = 4.92$, $SEM = .49$). The preoccupation with the content of the pictures was generally low (all $M < 2.58$) and did not differ with respect to valence, regulation or phase (all $p > .39$).

Overall BOLD activation following the perception and the regulation of negative and neutral stimuli

In a first step, the effects of valence and regulation were assessed collapsed across the picture perception and the maintain phase. Here, the perception of negative cues led to increased activation in the bilateral amygdala, the hippocampus, the thalamus, the ventrolateral PFC, and the fusiform gyrus during the picture presentation and the maintain phase compared with the perception of neutral pictures ($p < .005$ uncorrected for multiple comparisons). No regions showed a significant effect of down-regulation compared with the perception of negative pictures in the same time frame. During the regulation of negative emotions, the bilateral dorsolateral and ventrolateral PFC, the dorsomedial PFC, the superior and inferior parietal lobule and the precuneus were recruited.

BOLD activation during the picture presentation phase

Comparing the effects of valence and regulation during the picture phase, the perception of negative cues led to significant BOLD signal increases in the bilateral amygdala and fusiform gyrus, and the right hippocampus compared with neutral cues. Significant signal attenuations during the regulation of negative emotions were observed in the posterior middle OFC/ subgenual ACC (BA 25), the right fusiform gyrus, the left insula and the bilateral middle occipital gyrus. At a more liberal threshold ($p < .05$ uncorrected), signal attenuation was

also present in the bilateral amygdala (Figure 12 A). A largely bilateral network of regulatory regions was activated during detachment from negative emotional cues, including the dorsolateral and dorsomedial PFC, as well as the superior and (right) inferior parietal lobule. Additionally, the signal of the amygdala was significantly attenuated during regulated compared with unregulated neutral trials (Figure 12 C).

BOLD activation during the maintain phase

During the maintain phase, the bilateral sublenticular extended amygdala (SLEA), the thalamus, the hippocampus, the posterior cingulate cortex (PCC), and the left fusiform gyrus showed increased activation while continuing to feel negative emotions compared with the neutral condition. Signal attenuation due to continuing detachment from negative emotions during the maintain phase was not observed. However, the bilateral dorsolateral, ventrolateral and dorsomedial PFC, and the SMA were activated during the continuing regulation of negative emotions compared with the continuing experience of negative emotions.

Comparison of BOLD activation during the picture presentation and the maintain phase

In the last step of the categorical analysis, activation differences between the picture presentation and the maintain phase were directly compared. The bilateral amygdala, the right middle OFC/ subgenual ACC, and the right fusiform gyrus showed significantly more activation to negative pictures versus neutral pictures when the picture was still on screen compared with the subsequent maintain phase. Conversely, the bilateral SLEA, the thalamus, the temporal-parietal junction (TPJ), the PCC, as well as the right vlPFC showed

more activation during the maintain phase compared with the picture presentation for the respective contrast of negative versus neutral perception. Regulation-associated activation differences between the picture and the maintain phase were found in the bilateral ventrolateral and dorsomedial PFC, the rostral and subgenual ACC, the right thalamus and dorsolateral PFC, and the left insula. For regulated compared with unregulated negative emotion, activation in these regions was significantly larger during the maintain phase than during the picture phase.

Temporal dynamics of amygdala activation

The analysis of the temporal dynamics was performed on the mean signal change values from the left and right amygdala at TR 5, TR 9, and TR 13; mean signals were compared regarding stimulus valence, cognitive regulation, and phase, i.e. picture presentation, maintain phase, and fixation (Figure 12 B and D). BOLD signals were generally higher for negative compared with neutral trials in both the left (main effect 'valence' $F(1,12) = 23.74$, $p < .001$) and right (main effect 'valence' $F(1,12) = 8.27$, $p < .02$) amygdala. Also, an interaction of 'TR x regulation' signaled the presence of an immediate aftereffect of regulation in both the left ($F(2,24) = 4.83$, $p < .02$) and right ($F(2,24) = 7.40$, $p < .01$) amygdala. Separate analysis of the amygdala BOLD signals for negative and neutral trials in both amygdala ROIs were subsequently carried out to further explore the immediate aftereffect of regulation. In the right amygdala, the perception of both negative and neutral trials entailed greater BOLD signals at TR 5 and TR 9 compared with the respective regulation conditions, while at TR 13 the activation following the regulation of both negative and neutral trials was higher compared with the perception condition (interaction 'TR x regulation': negative $F(2,24) = 4,10$, $p < .03$; neutral $F(2,24) = 7.18$, $p < .004$). In the left amygdala, the

same pattern was observed, but the interaction of 'TR x regulation' was only significant for the neutral condition ($F(2,24) = 3.81$, $p < .04$), and bordered on significance for the negative condition ($p = .06$).
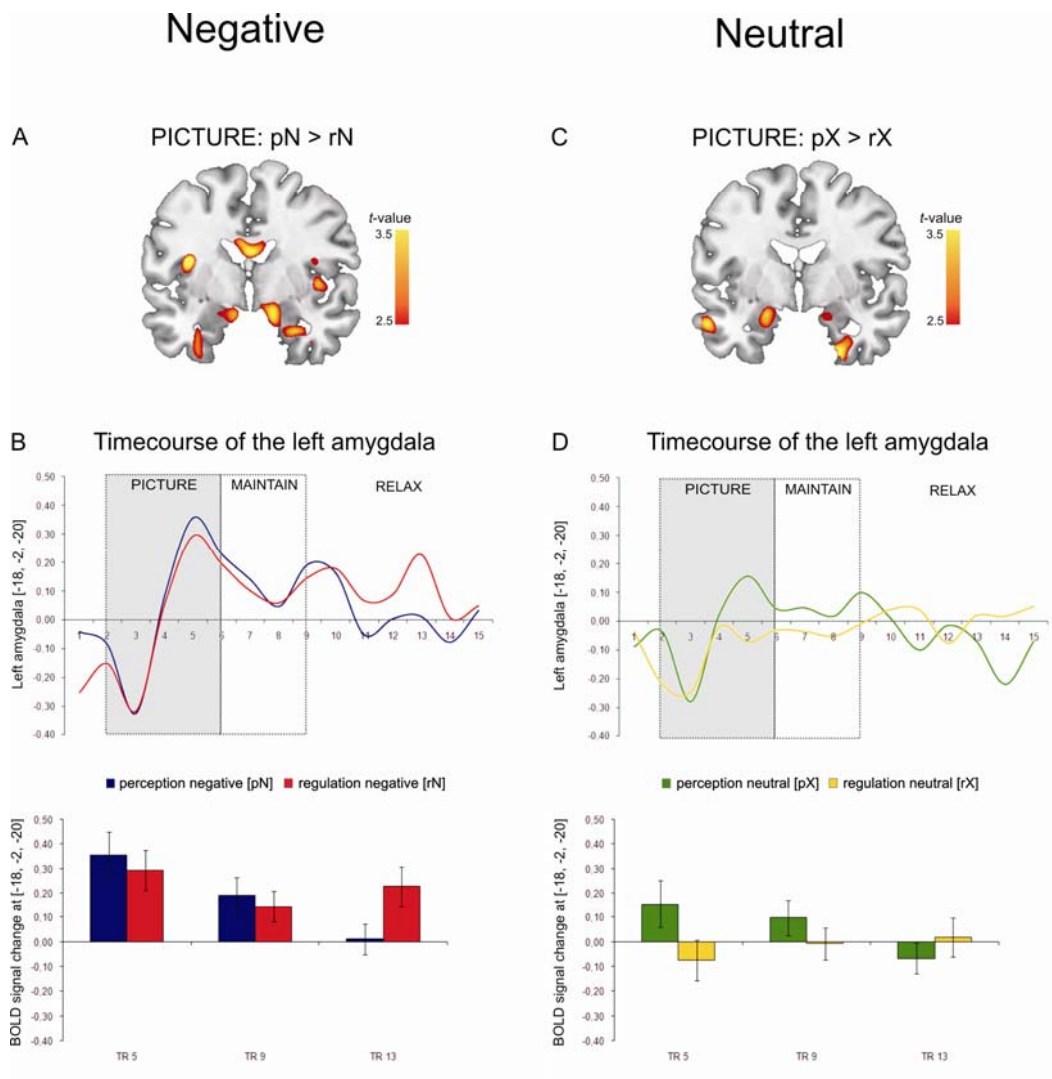
Figure 12: Results from Study 2

The categorical analysis yielded a significant amygdala signal attenuation by regulation during picture presentation for negative (A) and neutral (C). Timecourses and BOLD signal change from the left amygdala show an immediate aftereffect of regulation during the relax phase at TR 13 also for negative (B) and neutral (D) trials.

Summary

In Studies 1 and 2, functional imaging data were acquired while healthy female participants passively experienced or intentionally regulated emotional responses to negative and neutral visual stimuli. The participants of both studies showed a high compliance with the experimental manipulation and were able to successfully regulate their emotions by adopting the position of a distant observer. Consistent with the initial assumptions and the results from previous studies on detachment (Eippert, et al., 2007; Kalisch, et al., 2005; Levesque, et al., 2003), aversive stimuli were experienced as more unpleasant than neutral stimuli, and cognitive regulation was effective in reducing negative affect as mirrored by lower negativity ratings for regulated aversive stimuli both during (Study 1) and after (Studies 1 and 2) the scanning sessions. Also in line with previous findings, the amygdala was activated by negative in comparison with neutral pictures and a significant attenuation of amygdala activation was observed during intentional regulation (Eippert, et al., 2007; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004); however, signal attenuations in the amygdala were also observed for regulated compared with unregulated neutral trials in Study 2. These findings speak to the role of the amygdala in processing aversive emotional stimuli, and the efficacy of the volitional regulation of emotions in reducing experiential and neural correlates of emotions (Ochsner, 2007; Ochsner & Gross, 2008). The active detachment from emotional responses was in turn associated with increased activation in a prefrontal-parietal network comprising the dorsolateral and ventrolateral PFC and superior and inferior parietal lobule in Studies 1 and 2 (Eippert, et al., 2007; Hariri, et al., 2003; Ochsner, et al., 2005; Ochsner, Ray, et al., 2004; Phan, et al., 2005). Activations in the prefrontal and parietal cortex are consistently found in studies on the active cognitive control of emotions (Beauregard, et al., 2004), as well as in studies on cognitive control in

general (Braver, et al., 2003; Liston, Matalon, Hare, Davidson, & Casey, 2006; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004), where they are commonly associated with the implementation of control strategies and the allocation of (spatial) attention.

In accordance with the initial hypothesis derived from Walter et al. (2009), an immediate aftereffect of volitional regulation was observed in both studies: during the perception of negative emotions, the amygdala was significantly more activated than during regulation, while the opposite pattern was observed in the relax period, where the amygdala signal following regulation was significantly higher than the signal following perception. However, the paradoxical increase of amygdala activation after detachment was also present following regulated neutral trials in Study 2; in Study 1, two peaks of the amygdala signal following the regulation of negative emotions were observed: one early and one late during the relax period. Generally these findings fit in with the interpretation that the immediate aftereffect is a paradoxically increased neural signal that follows the volitional regulation of emotional material (Koster, et al., 2003; Roemer & Borkovec, 1994; Walter, et al., 2009).

3.3   Part II

3.3.1 Study 3 – Volitional emotion regulation and the serotonin transporter genotype

The data presented in Study 3 are in part reported in Schardt, Erk, Nüsser, Nöthen, Cichon, Rietschel, Treutlein, Goschke, & Walter (submitted).

Introduction

In recent years, empirical scientists have increasingly acknowledged the important role of emotions for personal integrity; social functioning and mental health (compare Chapter 2.2). A large body of literature has demonstrated that lesions in brain areas implicated in emotional appraisal severely compromise socio-affective faculties, planning, reasoning, and risk-taking. Without the ability to implicitly judge whether future outcomes are 'good' or 'bad' with respect to one's goals, the evaluation of risk and appropriateness becomes critically disturbed (M. C. Anderson, et al., 2004; Bechara, et al., 1994; Bechara, et al., 1997; Cacioppo, et al., 2002; Damasio, 1994; Walter, 2005). The action tendencies triggered by an emotional response are however not always appropriate, since the environment we live in today differs in many extents from the environment that shaped our emotions. Thus, the ability to explicitly and voluntarily down- or up-regulate what, how and when we experience emotions is vitally important (Gross, 1999; Ochsner, 2007; Phillips, et al., 2008). Both emotional reactivity and regulation are influenced by trait markers which are themselves considerably mediated by genetic factors (Green, et al., 2008; Hahn & Blakely, 2007; Meyer-Lindenberg & Weinberger, 2006). Genetic variation affects the organization of

the brain both during development as well as during adulthood on a number of different levels including structure, function, connectivity and neurotransmission (Canli & Lesch, 2007; Hariri, et al., 2006). As mentioned previously in Chapter 2.3.2, a significant amount of imaging genetics research into emotions has focused on the 5-HTTLPR which was associated with psychological measures of negative emotionality, including neuroticism, harm avoidance and anxiety (Ansorge, et al., 2004; Lesch, et al., 1996) as well altered reactivity and connectivity between the amygdala and prefrontal regions to negative emotional stimulation (Bertolino, et al., 2005; Hariri, et al., 2005; Hariri, et al., 2002; Pezawas, et al., 2005; Rhodes, et al., 2007). These genotype-dependent changes have been conceptualized as the mechanism underlying emotional dysregulations, increased negative emotionality and the risk of affective spectrum disorders (Hariri & Holmes, 2006). When an emotion eliciting situation is encountered, both the implicit as well as the explicit processes that are triggered depend on a number of different factors (MacDonald, 2008). With regard to the 5-HTTLPR mediated amygdala reactivity, the above mentioned studies have been restricted to the passive perception of negative emotions in the absence of willful actions. In turn, the willful employment of cognitive strategies is known to be effective in changing subjective and physiological responses to emotional stimuli. As mentioned previously in Chapter 2.2.2, amygdala activation is effectively reduced during e.g. labeling (Hariri, et al., 2003), cognitive reappraisal (Goldin, et al., 2008; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004) and detachment (Beauregard, et al., 2001; Levesque, et al., 2003; Levesque, et al., 2004; Staudinger, et al., 2009; Walter, et al., 2009) through top-down influences from the dorsolateral and ventrolateral prefrontal cortex, the orbitofrontal cortex and the parietal cortex. Thus, the question arises if willful emotion regulation is able to alter genetically determined differences in amygdala reactivity. This question is not only relevant within cognitive and

clinical neuroscience but also touches questions related to the power of conscious will. Actually, recent years have witnessed a number of studies trying to answer question related to the power of conscious will by conducting empirical studies of volition using neuroscientific means (Bechara, 2005; Haggard, 2008; Soon, Brass, Heinze, & Haynes, 2008; Walter, 2001; Wegner, 2004). The present work sought to investigate the neural dynamics during and immediately after willful regulation of aversive stimuli in individuals with the 5-HTTLPR short and long genotype. Since on the one hand the short allele of the serotonin transporter genotype has been associated with amygdala hyperreactivity (Hariri, et al., 2005; Hariri, et al., 2002), and on the other hand, amygdala BOLD signal is effectively attenuated through cognitive emotion regulation (Goldin, et al., 2008; Levesque, et al., 2003; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004), this region was designated the *a priori* region of interest of Study 3. The primary goal of Study 3 was to evaluate whether volition, i.e. the deliberate use of a cognitive emotion regulation strategy, can reduce the genetically mediated amygdala hyperreactivity to aversive emotional material. Thus, negative stimuli that evoked either fear or disgust were used in order to evaluate whether 5-HTTLPR short allele carriers (s-group) show increased neural activation to the perception of aversive versus neutral stimuli (Hariri, et al., 2005; Hariri, et al., 2002). Since fear stimuli are more relevant in the context of anxiety and depression amygdala hyperreactivity in the short genotype group was expected to be primarily related to the perception of fear and less to the perception of disgust (Lau, et al., 2009; Schienle, Schafer, Stark, Walter, & Vaitl, 2005). Regarding the effects of emotion regulation on 5-HTTLPR mediated amygdala hyperreactivity, two alternative assumptions arise: as prior work suggests that the dysfunctions within the amygdala-prefrontal emotion network are caused by developmental changes (Heinz, et al., 2005; Pezawas, et al., 2005), the bias towards negativity might be unspecific with respect to the

presence or absence of volition. In this case, the s-group should show increased amygdala reactivity during passive perception, and less or even no amygdala attenuation during volitional emotion regulation compared with l/l-homozygotes. On the other hand, cognitive emotion regulation might counteract the genetically determined amygdala hyperreactivity, in which equal or even larger amygdala signal reductions during the regulation of negative affect in s-carriers was expected. To address these questions, the neural responses of the two genotype groups were compared in both the presence and absence of volition. Moreover, the immediate aftereffect of volitional regulation was assessed regarding the influence of the 5-HTTLPR genotype. In the initial fMRI study by Walter et al. (2009), larger immediate aftereffects of the regulation of negative emotions were associated with more pronounced sustained aftereffects of regulation; thus, less effective regulation is thought to be related to larger paradoxical rebound signals in the amygdala. Assuming that the 5-HTTLPR s-group shows both amygdala hyperreactivity during perception and lower amygdala attenuation during regulation, the immediate aftereffect should be more pronounced in individuals with the short genotype. Alternatively, in the case that volitional regulation reduces or obliterates the amygdala hyperreactivity in the 5-HTTLPR s-group, the immediate aftereffect in s-allele carriers should be equal to or even smaller than the immediate aftereffect in 5-HTTLPR l/l-homozygote individuals.

Experimental Procedures

Participants

Forty-four right-handed female university students of central European descent with no history of neurological/psychiatric illness or substance abuse

participated in the study. Written informed consent was obtained, and subjects received € 50 for their participation. The study protocol was approved by the local ethics committee, in accordance with the Declaration of Helsinki. Five participants were excluded due to technical problems or excessive movement and two further participants were excluded following failure of valid 5-HTTLPR genotyping. A total of 37 participants (mean ± SD: age M = 22.6, SD = 2.2) were included in the analyses.

Genetic and Personality characterization

Two 9 ml samples of venous blood were taken from each participant by a trained medical doctor. EDTA anti-coagulation syringes were used to prevent clotting. Blood samples were labeled with a pseudonymized bar code and frozen at -80° C until DNA extraction.

Participants also filled in a variety of personality questionnaires (Appendix B); additional measures which surpass the scope of the present work are not reported. Reported here are depressivity (BDI), habitual emotion regulation (ERQ), neuroticism (NEO-FFI Neuroticism), trait anxiety (STAI-T), alexithymia (TAS-20), harm avoidance (TCI-Harm Avoidance) and habitual thought suppression (WBS-I). Data from the NEO-FFI Neuroticism scale for one subject were lost due to technical problems.

Imaging

Functional task

The task completed by the participants during the scanning session involved the natural experiencing of ('perception') or active detachment from ('regulation') emotional responses following the presentation of pictures in an event-related

design as used in prior studies successfully (Staudinger, et al., 2009; Walter, et al., 2009). Participants viewed fear-inducing, disgust-inducing and neutral pictures taken from a standardized stimulus set (Lang, et al., 1997), and matched for complexity, content (humans, nature, objects, animals), color, and brightness.
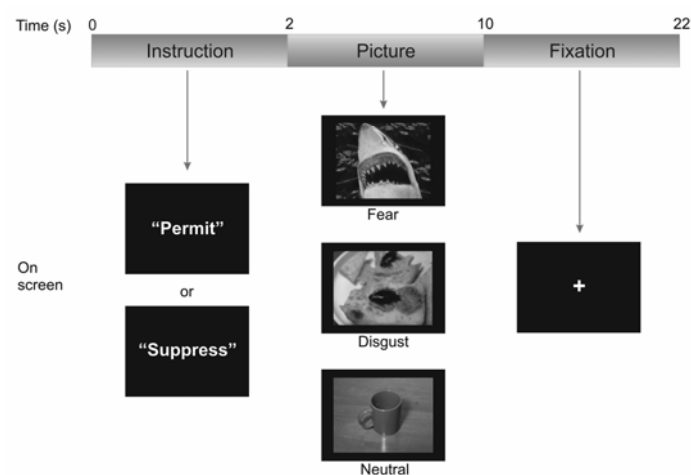
Figure 13: Experimental Paradigm from Study 3

Some additional pictures in the disgust condition were collected via the internet in order to balance picture content across conditions. During picture presentation, participants were instructed to employ one of two strategies: in the 'perception' condition, they were instructed to "look at the picture and permit yourself to feel whichever emotional response arises naturally, without trying to alter it". In the 'regulation' condition, participants were instructed to "look at the picture while detaching yourself from any emotional response which may arise by adopting the position of a detached observer who is not affected by the scene presented in the picture". Participants were trained outside the scanner until they felt confident to perform the cognitive regulation strategy during fMRI. Thirty-two pictures of each valence were presented, resulting in a total of 96

trials over the course of the experiment. Half of the trials of each valence were presented with the perception instruction, and the other half with the regulation instruction, resulting in six experimental conditions: 'perception fear', 'perception disgust', 'perception neutral', 'regulation fear', 'regulation disgust', and 'regulation neutral'. Subjects completed four sessions of 24 trials each: two sessions included unregulated and regulated fear and neutral trials, while the other two sessions included unregulated and regulated disgust and neutral trials. Trial presentation was pseudo-randomized, with no more than two consecutive trials of the same condition. Each 22-second trial began with a 2 second instruction phase, followed by 8 seconds of picture presentation and a fixation of 12 seconds during which participants were instructed to relax (Figure 13).

In-scan and post-scan rating procedures

Two different manipulation checks were carried out: first, an in-scan rating was administered verbally after each of the four sessions of the functional task. In the in-scan ratings, participants rated the overall valence and their success at implementing the regulation strategy for each block. Second, a detailed debriefing was carried out after the scanning session (Appendix C). Reported here are the ratings indicating the pleasantness of each of the previously viewed pictures, as well as the subjective assessments of the compliance with and success at regulating emotions by adopting the position of a detached observer. Furthermore, participants had to rate how much they were still preoccupied with the pictures during the fixation periods in order to provide a behavioral measure of the immediate aftereffect of regulation. All ratings were carried out on a 9-point Likert scale that ranged from '1 – lowest rating' to '9 – highest rating' respectively.

Data analysis

Behavioral data

In-scan ratings of pleasantness and regulation success were analyzed in the framework of a two-factorial repeated-measures ANOVA with respect to the within-subject factor 'valence' (fear, disgust, neutral) and the between-subject factor 'genotype' (short, long). Post-scan ratings of pleasantness and preoccupation were compared across conditions and genotypes by an ANOVA including the within-subject factors 'regulation' (perception, regulation), and 'valence' (fear, disgust, neutral), and the between-subjects factor 'genotype' (short, long). For the general compliance and regulation success ratings, means were compared between the s-group and the l-group of the 5-HTTLPR using an independent-samples *t*-Test. The threshold of significance for all analyses described above was set to $p < .05$.

Genotyping[7]

Genomic DNA was extracted from EDTA anti-coagulated venous blood samples using standard techniques. The 5-HTTLPR locus was amplified by PCR as outlined previously (Wendland, Martin, Kruse, Lesch, & Murphy, 2006) without multiplexing. In a total volume of 20μl, ~25ng of genomic DNA was amplified in the presence of 1x Promega PCR Master Mix (www.promega.com), with oligonucleotide primers 5-HTTLPR-forw (5′-FAM-TCCTCCGCTTTGGCGCCTCTTCC-3′) and 5-HTTLPR-rev (5′-VIC-TGGGGGTTGCAGGGGAGATCCTG-3′), the sequences of which are given in Wendland et al. (2006). To evaluate genotyping accuracy, 10% of the samples

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[7] This paragraph was written in part by PD Dr. Sven Cichon (life & brain Center, University of Bonn) and Dr. Jens Treutlein (Zentralinstitut für Seelische Gesundheit, Mannheim)

were analyzed in duplicate: amplification with the oligonucleotide primers of Lesch et al. (1996), stpr5 (5´-GGCGTTGCCGCTCTGAATGC-3´) and stpr3 (5´-GAGGGACTGAGCTGGACAACCAC-3´), yielded identical genotypes.

PCRs were performed in 96-well microtiter plates on a MJ Research PTC-200 cycler with 40 ng genomic DNA in a 25-μL reaction mixture containing .25 μM of each primer and 2x Promega PCR Mastermix. Cycling conditions were as follows: initial 5-minute denaturation at 95°C; 35 cycles of denaturation at 95°C for 30 seconds, annealing at 61°C for 30 seconds, extension at 72°C for 1 minute, and a final extension for 10 minutes at 72°C. Amplification products were separated on a 2.5 % agarose gel, and the long (L, 528 bp) and short (S, 484 bp) alleles of 5-HTTLPR were scored independently by two investigators.

Participants were divided into two groups, based on previous work reporting similar results for short allele homozygotes and the heterozygote group (e.g. Hariri, et al., 2005; Hariri, et al., 2002). Individuals carrying one (n = 7) or two (n = 14) short alleles were assigned to the s-group, while the l-group consisted of long allele homozygotes (n = 16).

Functional image processing

Functional imaging data were collected on a 3 Tesla Siemens Trio using a gradient-echo T2*-weighted EPI sequence. In order to minimize susceptibility artifacts in the medial temporal lobe, 31 axial slices (voxel size = 3.3 x 3.3 x 4.125 mm) were acquired parallel to a line between OFC and cerebellum (TR = 2 s, TE = 25 ms, FA = 90°, FOV = 210 cm, 64 x 64 matrix). Additional structural T1-weighted images were acquired from each subject (160 slices, voxel size = 1 x 1 x 1.5 mm, 256 x 256 matrix, TR = 2 s, TE = 3.39 ms). Stimuli were presented via binocular video goggles (NNL, Bergen, Norway) attached to the head coil and adjusted to fit the subjects' vision. Functional imaging data were collected on a 3

Tesla Siemens Trio using a gradient-echo T2*-weighted echo-planar imaging sequence. In order to minimize susceptibility artifacts in the medial temporal lobe, 31 axial slices (voxel size = 3.3 x 3.3 x 4.125 mm) were acquired parallel to a line between OFC and cerebellum to minimize susceptibility artifacts especially in the amygdala (TR = 2 s, TE = 25 ms, FA = 90°, FOV = 210 cm, 64 x 64 matrix). Additional structural T1-weighted images were acquired from each subject (160 slices, voxel size = 1 x 1 x 1.5 mm, 256 x 256 matrix, TR = 2 s, TE = 3.39 ms). Stimuli were presented via binocular video goggles (NNL, Bergen, Norway) attached to the head coil and adjusted to fit the subjects' vision. Processing of functional imaging data was carried out using SPM2 for pre-processing, and SPM5 for statistical analyses (Statistical Parametric Mapping, Wellcome Institute of Cognitive Neurology, London, UK) running on Matlab 6.5.1 (MathWorks, Natick, MA, USA). The first three volumes in each session were discarded before analysis. Functional images were slice-timed to account for acquisition delay, and realigned to the first scan of the first session of each subject to correct for head motion. Images were then normalized to the MNI template and smoothed with an 8 mm full-width at half-maximum isotropic Gaussian kernel to increase signal-to-noise ratio. Serial auto-correlations were accounted for (AR1) and a high-pass filter of 128 seconds was applied. A first-level fixed-effects model was computed for each participant. For each of the four sessions, regressors were created for the instruction phase, the experimental conditions, and the fixation period. Two sessions for each subject contained the experimental conditions 'perception fear [pF]', 'perception neutral [pX]', 'regulation fear [rF]', and 'regulation neutral [rX]'; the other two sessions contained the experimental conditions 'perception disgust [pD]', 'pX', 'regulation disgust [rD]', and 'rX'. Movement parameters were included in the model as regressors of no interest, resulting in 48 regressors for the first-level model of each subject. The respective regressors in each session were convolved with the canonical HRF implemented

in SPM. Contrasts for each of the experimental conditions versus the fixation (pF > fix, pD > fix, pX > fix, rF > fix, rD > fix, rX > fix) were computed and included in a group-level random-effects GLM model. A three-factorial 2 x 2 x 3 ANOVA ('genotype', 'regulation', 'valence') that accounts for both scan-to-scan and subject-to-subject variability was carried out. Non-sphericity correction was applied to account for unequal variances. In order to provide that the experimental manipulation was successful, the effects of valence and regulation collapsed across genotypes were analyzed in a first step ([*s-group* + *l-group*] pF > pX, [*s-group* + *l-group*] pD > pX, [*s-group* + *l-group*] pF > rF, [*s-group* + *l-group*] pD > rD, [*s-group* + *l-group*] rF > pF, [*s-group* + *l-group*] rD > pD, [*s-group* + *l-group*] pF > pD, [*s-group* + *l-group*] pD > pF). Subsequently the influence of valence and regulation was compared between genotype groups for fear (*s-group* [pF > pX] > *l-group* [pF > pX], *s-group* [pF > rF] > *l-group* [pF > rF], *s-group* [rF > pF] > *l-group* [rF > pF], *s-group* [pF > pD] > *l-group* [pF > pD] and vice versa) and disgust (*s-group* [pD > pX] > *l-group* [pD > pX], *s-group* [pD > rD] > *l-group* [pD > rD], *s-group* [rD > pD] > l-*group* [rD > pD], *s-group* [pD > pF] > *l-group* [pD > pF] and vice versa). Masking was performed with a sphere of 12 mm diameter in the center of both amygdalae ($\pm$26, -4, -16 [MNI x, y, z]). This region of interest was chosen based on the maxima reported in previous, independent studies regarding the influence of the 5-HTTLPR genotype on the perception of aversive versus neutral stimuli (Bertolino, et al., 2005; Hariri, et al., 2005; Hariri, et al., 2002; Heinz, et al., 2005; Pezawas, et al., 2005). Within the amygdala, a probability of $p < 0.05$ family-wise error (FWE) corrected for multiple comparisons was considered to be significant. Additional whole-brain analyses were thresholded at $p < 0.001$ uncorrected, using k=10 voxels spatial extent, which protects against false-positive results and thus also provides a correction for multiple comparisons (Forman, et al., 1995). As in Studies 1 and 2, the coordinates of all cluster maxima were Talairach-converted for labeling (mni2tal-transform, Brett,

2006), but will be reported in MNI space (Chau & McIntosh, 2005; Poldrack, et al., 2008).

Time series extraction

For the analysis of the amygdala timecourses and the functional connectivity analysis, individual time series were extracted from the right amygdala using the same masking procedure described above. The right amygdala was chosen as the seed region for this analysis because an influence of volitional regulation on amygdala hyperreactivity to fear was only found in the right but not in the left amygdala.

Functional connectivity

A post-hoc psycho-physiological interaction (PPI) analysis was carried out to elaborate on interactive effects of the 5-HTTLPR genotype and the volitional regulation of fear (Friston, et al., 1997). In this analysis, functional connectivity between a seed region (here: the right amygdala) and functionally connected regions is assessed through significant differences in correlations depending on different tasks (here: 'regulation' versus 'perception'). To this end, individual time series were extracted from the right amygdala using the same masking procedure described above. The right amygdala was chosen as the seed region for this analysis because an influence of volitional regulation on amygdala hyperreactivity to fear was only found in the right but not in the left amygdala. The physiological variable (amygdala ROI time-course), the psychological variable representing the regulation versus the perception of fear, and their interaction term along with the movement parameters were entered into a first-level fixed-effects model in SPM5. The resulting contrast weights of the interaction term were then entered into a second-level ANOVA to compare

amygdala coupling during the regulation of fear between the s-group and the l-group. Non-sphericity correction was applied to account for non-sphericity. Voxel level t-statistics were considered significant at an uncorrected $p < 0.005$ with an extend threshold of $k = 10$ contiguous voxels to protect against false positive results (Forman, et al., 1995). As stated above, the original MNI coordinates of cluster maxima will be reported.

Signal timecourses

From the extracted time series in the right amygdala ROI, signals were averaged for each of the six experimental conditions. These mean signal change values for each condition were then entered into a repeated-measures Analysis of Variance. The ANOVA with the within-subjects factors 'valence' (fear, disgust, neutral), 'regulation' (perception, regulation), and 'TR' (scan 5, scan 9), and the between-subjects factor 'gentoype' (short, long) and was carried out to test for the presence of an immediate aftereffect of regulation and it's interactions with valence and genotype. The mean signal change values from TR 5 and TR 9 were chosen because the HRF following picture onset and regulation offset was assumed to reach its peak with a delay of approximately six to eight seconds, as reported in Walter et al. (2009) and supported by the results from Studies 1 and 2 of the present work. Visual inspection of the timecourses validated this approach. Results were considered to be significant at a threshold of $p < .05$.

Results

Demographics and Questionnaires

Mean age and personality scores are reported in Table 3. The members of the s-group and l-group did not differ with respect to their age ($p > .41$). The overall

means of all personality questionnaires were within normal range, that is below cutoff or within ± 1 *SD* around the reference population means reported in Chapter 3.1. Furthermore, no 5-HTTLPR dependent group differences were found for BDI depression scores ($p > .96$), ERQ-Suppression scores ($p > .53$), NEO-Neuroticism scores ($p > .11$), STAI-Trait scores ($p > .20$), TAS-20 alexithymia scores ($p < .06$), TCI-Harm Avoidance scores ($p > .13$), and WBSI thought suppression scores ($p > .19$). A significant difference between the s-group and l-group was observed for habitual reappraisal, where the l-group showed higher ERQ-Reappraisal scores compared with the s-group ($t(35) = -2.42$, $p < .02$).

Behavioral ratings

The means (± *SEM*) of the in-scan and post-scan ratings are reported in Table 3 separately for the 5-HTTLPR s- and l-group. The participants' verbal ratings of the experienced negativity and success at regulating their emotions were compared between disgust and fear blocks. During the scanning session, pleasantness ratings for those blocks containing fear and neutral trials were significantly higher compared with blocks that contained disgust and neutral trials (main effect 'valence' $F(1,35) = 36.72$, $p < .001$). No effect of 5-HTTLPR genotype on in-scan pleasantness ratings was observed (main effect 'genotype' $p > .92$; interaction 'valence x genotype' $p > .18$). Ratings of the successful implementation of the regulation strategy were generally high, and did not differ between fear and disgust blocks or 5-HTTLPR genotypes (all $p > .10$). Note that since in-scan ratings were across blocks, they include overall statements regarding the combined experiences during fear-inducing and neutral, and disgust-inducing and neutral trials respectively. The ratings of picture pleasantness and preoccupation during the fixation that were collected following the fMRI sessions were analyzed regarding the effects of stimulus

valence, regulation, and 5-HTTLPR genotype. Moreover, the compliance and success ratings were compared between the two genotype groups. Both fear and disgust stimuli were perceived as negative in comparison with the neutral stimuli ('valence': $F[2,70] = 402.58$, $p < 0.0001$). Pleasantness ratings were very low for disgust and fear and intermediate for neutral stimuli. Compliance with the regulation strategy and success at implementing detachment was generally very high and did not differ between the s-group and the l-group (both $p > .15$). Reports of preoccupation with the previous picture during the fixation period differed significantly between the three valence conditions and were highest during fear-inducing trials (main effect 'valence' $F(2,70) = 21.12$, $p < .001$). Moreover, 5-HTTLPR long allele homozygotes reported more preoccupation with regulated stimuli while short allele carriers reported less preoccupation with regulated stimuli (interaction 'regulation x genotype' $F(1,35) = 7.74$, $p < .01$).

Overall BOLD signal changes during perception and volitional regulation of negative cues

The first step of the categorical analysis was the validation of the experimental manipulation across the whole sample. To this end, brain responses in the amygdala ROI and across the whole set of voxels were compared between valence and regulation conditions collapsed across the s-group and l-group. Functional imaging data revealed a significant ($p < 0.05$ FWE-corrected for multiple comparisons) main effect of valence in the bilateral amygdala. Significantly higher BOLD signal in the bilateral amygdala following both fear and disgust stimuli as compared to neutral stimuli was observed. The main effect of volitional regulation of emotions yielded effective signal attenuations in the bilateral amygdala, while signal increases ($p < .001$ uncorrected, $k = 10$) were observed in the dorsolateral (BA 9) and ventrolateral PFC (BA 46), the

orbitofrontal cortex (BA 10), the inferior parietal lobule (BA 40), and the dorsomedial prefrontal cortex (BA 8/32).

Comparison of amygdala activation between 5-HTTLPR genotype groups

Subsequently, neural responses of short allele carriers and long allele homozygotes were directly compared within the *a priori* region of interest in the bilateral amygdala ($p < 0.05$ FEW-corrected for multiple comparisons) and across the whole brain volume ($p < 0.001$ uncorrected, $k = 10$). To address whether the presence of one or two 5-HTTLPR short alleles leads to amygdala hyperreactivity, genotype groups were compared regarding the perception of fear, disgust and neutral stimuli. Subsequently, the influence of the volitional regulation of fear and disgust on amygdala reactivity was compared between short allele carriers and the group of long allele homozygotes. Amygdala hyperreactivity was observed in individuals with the 5-HTTLPR short variant. In short allele carriers, the passive viewing of pictures that induce fear led to significantly increased activation in the right amygdala compared with neutral stimuli, while amygdala activation to the perception of disgust versus neutral stimuli did not differ between the two serotonin transporter genotype groups. Moreover, the bilateral amygdala of short allele carriers showed higher activation to fear compared with disgust perception (Figure 14 B). Despite the amygdala hyperreactivity to fear and a generally reduced activation of the right inferior parietal lobule (BA 40) and supplementary motor area (BA 6) during regulation, effective signal attenuation was observed in response to detachment in individuals with the 5-HTTLPR short variant: the presence of at least one short allele was associated with a significantly larger signal reduction in the right amygdala during the regulation of fear when compared to those individuals who were homozygous for the l allele (Figure 14 A). Again, no

comparable effect was observed for the volitional regulation of disgust. The larger decrease in amygdala signal during regulation in the s-group was also observed to be valence specific at a lower threshold of $p > .05$ uncorrected for multiple comparisons: the amygdala of short allele carriers was significantly more attenuated during the regulation of fear compared with both disgust and neutral stimuli.

5-HTTLPR effects on amygdala functional connectivity during volitional regulation

In order to assess amygdala functional connectivity during the volitional regulation of fear, a psycho-physiological interaction analysis was performed (Friston, et al., 1997). Since only the right amygdala showed a 5-HTTLPR effect during both perception and regulation of fear, this region was chosen as the seed region for the psycho-physiological interaction (PPI) analysis. Generally, volitional detachment from fear modulated the functional connectivity between the right amygdala and the dorsal ACC, the medial OFC, the dorsomedial PFC as well as the bilateral vlPFC. A direct comparison between the 5-HTTLPR genotype groups showed that volitional regulation had a stronger modulatory influence on functional connectivity between the amygdala and the bilateral vlPFC, the left mOFC as well as the subgenual and rostral ACC in individuals carrying at least one short allele (Figure 15). In contrast, the l-group did not exhibit regions of increased connectivity during volitional regulation, even when lowering the threshold to an uncorrected $p < 0.05$.

Table 3: **Demographic information, personality scores, in-scan and post-scan ratings from Study 3**

	s-group		l-group	
	Mean	**SD**	**Mean**	**SD**
Age	22.33	1.96	22.94	2.43
BDI	3.26	2.43	3.22	0.76
ERQ-Suppression	3.48	1.54	3.20	0.23
ERQ-Reappraisal	4.33	1.06	5.07	0.18
NEO-Neuroticism	1.58	0.57	1.89	0.13
STAI-Trait	38.43	8.54	41.94	1.81
TAS-20	41.57	11.78	49.31	2.99
TCI-Harm Avoidance	13.14	5.97	16.31	1.60
WBS-I	44.67	11.55	49.63	2.74
In-Scan Rating	*M*	*SEM*	*M*	*SEM*
Pleasantness				
Fear Blocks	4.86	0.22	4.66	0.22
Disgust Blocks	3.62	0.26	3.88	0.18
Regulation Success				
Fear Blocks	6.57	0.27	6.09	0.30
Disgust Blocks	6.05	0.33	5.91	0.31
Post-Scan Rating				
Pleasantness				
Perception Fear	3.16	0.12	3.15	0.16
Regulation Fear	3.24	0.11	3.00	0.17
Perception Disgust	2.59	0.15	2.59	0.15
Regulation Disgust	2.53	0.12	2.59	0.17
Perception Neutral	6.31	0.18	5.90	0.15
Regulation Neutral	6.16	0.16	5.90	0.16
Compliance	7.61	0.25	7.75	0.19
Regulation Success	6.23	0.30	5.56	0.35
Preoccupation				
Perception Fear	3.33	0.54	2.94	0.55
Regulation Fear	2.95	0.39	4.19	0.59
Perception Disgust	3.29	0.44	2.69	0.42
Regulation Disgust	3.05	0.41	3.69	0.51
Perception Neutral	1.81	0.25	1.75	0.27
Regulation Neutral	1.76	0.24	2.25	0.39
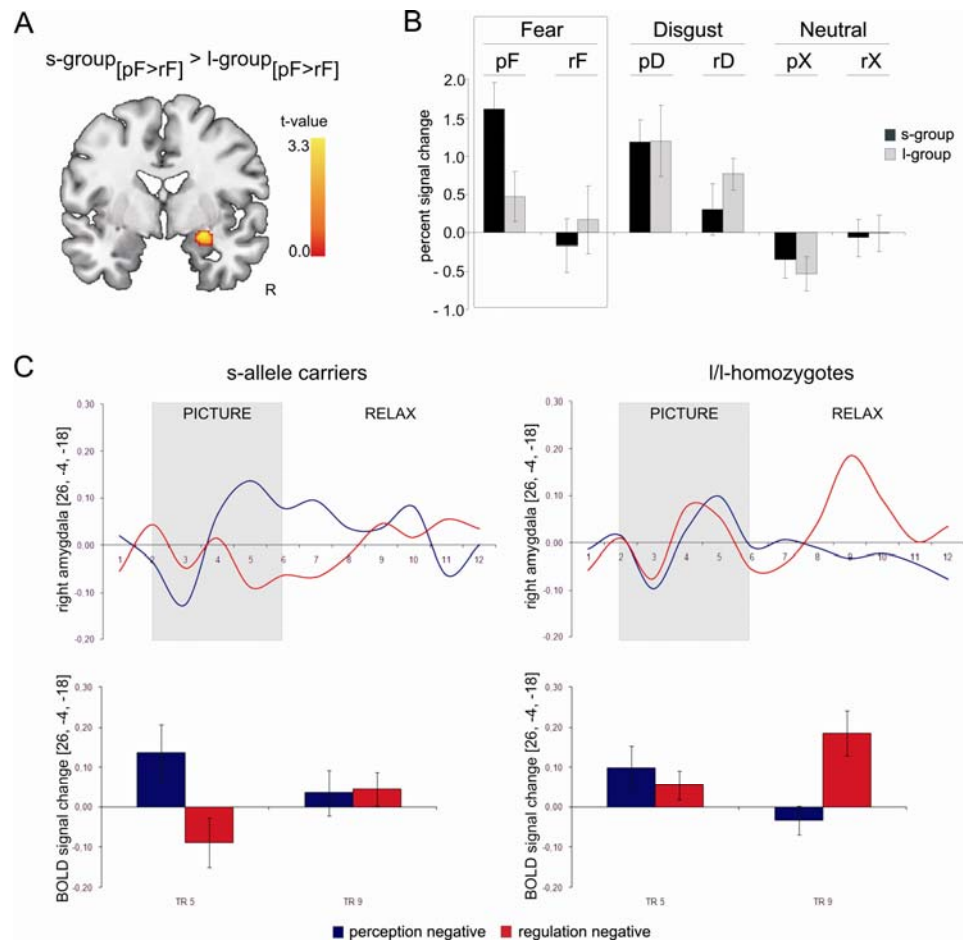
Figure 14: Results from Study 3

Amygdala hyperreactivity to fear in the 5-HTTLPR s-group was successfully obliterated by volitional regulation (A), while no hyperreactivity was observed for disgust or neutral trials (B). An immediate aftereffect of regulation was present during the relax period at TR 9 only for fear and only in the l-group (C).
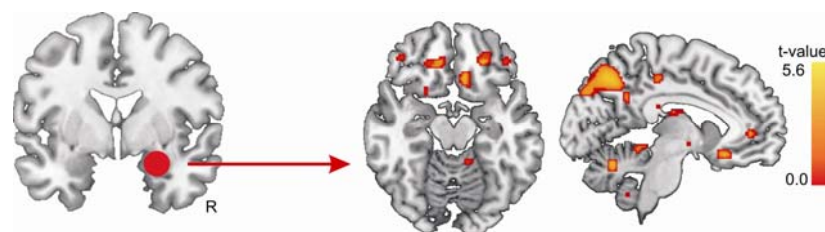
Figure 15: Increased amygdala connectivity in the s-group in Study 3

Increased functional coupling during fear regulation (rF > pF) in s-allele carriers between the right amygdala and the bilateral vlPFC, left mOFC, right premotor cortex, as well as rostral and subgenual parts of the anterior cingulate cortex.

The influence of valence, regulation, and genotype on the temporal dynamics of amygdala activation

Testing for the presence of an immediate aftereffect of the volitional regulation of negative emotions in the amygdala, an ANOVA on amygdala signal change values from TR 5 and TR 9 was carried out. Moreover, interactive effects with the 5-HTTLPR genotype were assessed by comparing the activation between the s-group and the l-group. This analysis yielded a significant main effect of the factors 'valence' ($F(1,35) = 4.94$, $p < .01$), and 'genotype' ($F(1,35) = 4.51$, $p < .04$). The mean signal change values were higher during disgust and fear than during neutral trials, and were generally lower for short allele carriers compared with the long homozygote individuals. An immediate aftereffect was also observed, mirrored by a significant interaction of 'TR x regulation' ($F(1,35) = 7.31$, $p < .01$). An interaction of 'genotype x regulation' ($F(1,35) = 6.13$, $p < .02$) arose due to the fact that only the l-group showed increased mean signal changes during regulation compared with perception, while the s-group's mean signal change values did not differ between the two conditions. Separate ANOVAs for the s- and l-group showed that an immediate aftereffect was present following the volitional regulation of fear in the l-group (interaction 'TR x regulation' $F(1,15) = 6.59$, $p < .03$), but not the s-group ($p > .11$). Corroborating these results, post-hoc correlation analyses showed that the more effective the initial signal attenuation during fear regulation was (Δ PA–SA at TR 5), the lesser was the immediate aftereffect (Δ PA–SA at TR 9; $r = -.40$, $p < .02$). No such correlation was found for disgust or neutral regulation trials (all $p > .29$).

Summary

In Study 3, individuals with the short or long variant of the 5-HTTLPR underwent functional MRI while passively perceiving or intentionally regulating

emotional responses to fear-inducing, disgust-inducing and neutral trials. The two genotype groups did not differ with respect to depression, anxiety, neuroticism, harm avoidance, and alexithymia scores, which corresponds with previous negative findings of associations between the 5-HTTLPR genotype and personality measures (Bertolino, et al., 2005; Canli, et al., 2005; Hariri, et al., 2005; Hariri, et al., 2002). Thought suppression scores were equal across genotypes, as was the habitual use of suppression. In contrast, reappraisal was less frequently used by individuals carrying the 5-HTTLPR short allele compared with l/l-homozygote individuals. Both fear-inducing and disgust-inducing trials elicited robust responses in the amygdala in comparison with neutral trials, and amygdala activation was effectively reduced during the regulation condition (Eippert, et al., 2007; Levesque, et al., 2003; Levesque, et al., 2004; Ochsner, et al., 2002; Ochsner, Ray, et al., 2004). The prefrontal-parietal regulation network previously observed in other studies (Ochsner, et al., 2002; Ochsner, Ray, et al., 2004; Staudinger, et al., 2009; Walter, et al., 2009) and in Study 1 and 2 of the present work was recruited during cognitive control of emotions also in Study 3.

Interactions between volitional regulation, valence, and 5-HTTLPR genotype were observed in the behavioral as well as functional imaging data. Heightened amygdala reactivity was found in 5-HTTLPR short allele carriers comparing the perception of fear-inducing with the perception of neutral cues (Hariri, et al., 2005; Hariri, et al., 2002; Heinz, et al., 2005). This hyperreactivity was however obliterated by the volitional regulation of fear. In short allele carriers, regulation was additionally accompanied by increased functional coupling between the amygdala and the medial and ventrolateral prefrontal cortices during volitional regulation (MacDonald, 2008; Phillips, et al., 2008; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008). As for the aftereffects of volitional regulation, signal change values from the amygdala indicated that an immediate aftereffect

was only present following the regulation of fear and only in the l-group. The l/l-homozygote individuals showed signal increases during fixation compared with picture presentation, while no such effect was observed in the s-group. These results were complemented by the fact that only 5-HTTLPR long allele homozygotes reported increased preoccupation after regulated compared with unregulated stimuli. Moreover, higher initial amygdala signal attenuation during picture presentation entailed lower immediate aftereffects during the fixation, which complements the findings from Walter and colleagues (2009) who reported that greater delayed efficacy of regulation was associated with smaller immediate aftereffects of regulation.

Taken together, the present results contrast the theoretical considerations put forward for example by Hariri and Holmes (2006) which state that 5-HTTLPR short allele carriers are characterized by general dysfunctions in emotional regulation. Moreover, no effect of the serotonin transporter genotype was observed for disgust, which should have been the case if there was a general deficit in emotional processing in the s-group. Thus, while the presence of the 5-HTTLPR short allele leads to heightened responses to fear in the amygdala, volition can modify genetically mediated effects upon brain function by altering prefrontal-amygdala connectivity.

4 General Discussion

4.1 Summary of results

The central objective of the present work was the investigation of the temporal dynamics of volitional emotion regulation in the brain. Precisely, it was assumed that a) the regulation task reduces both the subjective experience of negativity and the neural activation in the amygdala following negative cues (e.g. Ochsner, et al., 2002; Ochsner, et al., 2004), that b) the immediate aftereffect is temporally linked to the offset of regulation (Rassin, et al., 2000; Walter, et al., 2009; Wegner, 2009), and that c) volitional emotion regulation reduces or even obliterates the amygdala hyperreactivity to the passive perception of negative emotional cues in the short allele group (Hariri, et al., 2005; Hariri, et al., 2002; Ochsner, et al., 2002; Ochsner, et al., 2004).

These research objectives were addressed in three separate empirical studies. In each study, participants completed an emotion regulation task including pictures of negative and neutral valence. Upon the instruction to 'permit', participants were to look at the picture and experience all upcoming emotional responses naturally without trying to alter it. Under the instruction to 'suppress', participants should look at the picture while taking the perspective of a distant observer who is not affected by the scene (Staudinger, et al., 2009; Walter, et al., 2009).

Supporting the first assumption, the behavioral ratings obtained during the scanning session in *Study 1* showed that the subjective experience of negativity was significantly reduced immediately after picture presentation when participants had previously engaged in detachment. Detachment also attenuated the response of the amygdala and activated the dorsolateral and ventrolateral prefrontal cortex, and the inferior parietal lobule. In the bilateral amygdala, an immediate aftereffect was observed following the volitional detachment from negative emotional responses. While the experimental manipulation was thus proven successful, there was no behavioral correlate of the immediate aftereffect during the scanning session, as the reduction of the feeling of negativity from the first to the second rating was unspecific. Also, participants reported a generally increased preoccupation with negative stimuli in the post-scan rating session, which was not related to the presence or absence of regulation.

Study 2 supports and extends the findings from Study 1. Again, the volitional regulation of emotions reduced amygdala activation and increased activation in the prefrontal-parietal regulation network; the amygdala signal attenuation was larger during the picture presentation compared with the maintain phase, while the activation of the regulation network was larger during the maintain phase compared with the picture presentation. Pictures that were previously presented in the regulation condition were judged as more pleasant compared with their unregulated counterparts, which suggest a longer lasting effect of regulation. An immediate aftereffect of regulation was observed during the relax period approximately 14 seconds after picture offset and eight seconds after the offset of regulation, which supports the hypothesis that this physiological rebound signal is not simply a delayed neural signal of stimulus processing, but is indeed associated with the cessation of the cognitive control of emotions. Again, no

behavioral correlate of the immediate aftereffect was observed, as preoccupation with the previous picture did not differ between the experimental conditions.

Study 3 revealed that volitional regulation is effective in reducing amygdala activation to negative stimuli even in 5-HTTLPR short allele carriers that show an increased reactivity to this type of cue (Hariri, et al., 2005; Hariri, et al., 2002). Here, participants with the short genotype show both increased reactivity *and* increased signal attenuations in the amygdala. This effect was associated with increased functional coupling between the amygdala and the ventrolateral PFC, the medial OFC, and the subgenual and rostral ACC. An immediate aftereffect was found in l/l-homozygote individuals following the regulation of fear. The l-group was also more preoccupied with stimuli that were presented in the regulation condition. Moreover, increased initial signal reduction in the amygdala during picture presentation was associated with a lower immediate aftereffect, which fits in well with the interpretation that the s-group profited more from the volitional regulation of fear in comparison with the l-group.

In summary, the results of these three studies strongly suggest that the immediate aftereffect first observed in Walter et al. (2009) is indeed a paradoxical rebound in amygdala activation after volitional regulation. Moreover, they clearly show that volitional regulation is effective in reducing behavioral and neural correlates of the experience of negative emotions, even in the case of a genetically mediated hyperreactivity to such materials.

4.2   Effects during regulation

In all three studies of the present work, the perception of negative emotional material led to increased neural activation in (sub)cortical structures that are associated with the processing of emotionally salient stimuli including the

amygdala, thalamus, hippocampus, insula, and the fusiform gyrus (Calder, et al., 2001; Phan, Wager, Taylor, & Liberzon, 2002). Moreover, medial and ventral lateral prefrontal and cingulate regions were activated during the perception of negative emotions. These neural responses fit in well with the findings from previous studies which showed that they are critically implied in emotional processing, possibly due to their involvement in stimulus appraisals (e.g. Wager, et al., 2008). The continuing experience of negativity in the maintain phase after negative stimuli in Study 2 furthermore entailed an increased recruitment of the temporal-parietal junction (TPJ) and the PCC. The role of the TPJ in the present work was most likely related to the fact that the stimulus had to be kept in mind during the maintain phase in order to continuously feel the emotional response to it. Thus, the TPJ is possibly related to the mentalizing processes taking place during the maintain phase (Van Overwalle & Baetens, 2009) which include for example own-body imagery (Blanke, et al., 2005) and the integration and assessment of the correspondence of various input signals (Blanke & Arzy, 2005; Farrer & Frith, 2002; Spengler, von Cramon, & Brass, 2009). As shown by previous work, the PCC is sensitive to conflict at the level of the stimulus representation, and increases as a function of the salience of conflicting stimulus information (Liston, et al., 2006). Applied to the present case, the requirement to continue feeling the emotional response while the eliciting stimulus is not present any more might induce conflict, which could in turn underly the observed activation in the posterior cingulate cortex.

Also in line with the expectations raised by previous work, the voluntary regulation of emotions by detachment was highly effective in reducing amygdala activation to negative emotional cues in all three studies (Eippert, et al., 2007; Ochsner, et al., 2002; Ochsner, et al., 2004). Other regions in which activation was effectively attenuated during detachment include largely the

same subcortical and cortical regions mentioned above in the context of emotional processing, such as for example the thalamus, insula, fusiform gyrus, and the medial and ventrolateral prefrontal cortex. In line with the assumption that cognitive regulation reduces both the (neuro)physiological *and* experiential effects of emotions, the reduction of neural activation was also associated with decreased negative feelings, as mirrored by lower negativity ratings during regulation in Study 1, and the high ratings of compliance and regulation success in all three studies (Beauregard, et al., 2004; Ochsner, 2007; Ochsner & Gross, 2005, 2008).

As hypothesized, volitional emotion regulation relied on the activation of a network of prefrontal and parietal brain regions that are commonly associated with the cognitive control of emotions (Eippert, et al., 2007; Goldin, et al., 2008; Hariri, et al., 2003; Ochsner, et al., 2002; Ochsner, et al., 2004; Phan, et al., 2005), or cognitive control in general (e.g. Botvinick, Braver, Barch, Carter, & Cohen, 2001; Botvinick, et al., 2004) and include the dorsolateral and ventrolateral prefrontal cortex, the dorsomedial prefrontal cortex, the anterior cingulate cortex, the orbitofrontal cortex, and the inferior and superior parietal lobule. In the context of the present study, these regions were most probably associated with the top-down inhibitory control of amygdala function, as mirrored by the increased coupling between the amygdala and the dorsal ACC, the medial OFC, and the dorsomedial and ventrolateral PFC in Study 3. Precisely, as the dlPFC is known to play a crucial part in the implementation of associations between context and adaptive behavior (Bunge, 2004; Miller & Cohen, 2001) it seems reasonable to assume that changes in stimulus meaning during regulation are implemented in this region. The controlled appraisal of stimulus meaning is subsequently processed in the ventrolateral and dorsomedial PFC (Ochsner & Gross, 2005), while the inhibition of prepotent responses (such as the inhibition

of unpleasant feelings upon viewing an aversive picture) and the update of the motivational value of a stimulus due to its changed meaning are realized in the orbitofrontal cortex and the ACC (Kringelbach & Rolls, 2004; Ridderinkhof, et al., 2004; Rolls, Grabenhorst, Margot, da Silva, & Velazco, 2008). Aside from the role of the parietal cortex in spatial attention and attentional control in general (Farrell & Robertson, 2000; Gottlieb, 2007), and the proposed role in modulating the semantic input to the amygdala (Ochsner, et al., 2002) the activation in this region might signal additional mental processes specifically inherent to the present design. As Farrell and Robertson (2000) pointed out, attention to one's personal space depends critically on the right parietal cortex. Since detachment as used in all three studies of the present work involves a mental "stepping back from things", it can be assumed that the activation of the right inferior and superior parietal lobule that has been found in all three studies is associated with the transformation of the environmental coordinates of the self in relation to the stimulus during regulation (Colby & Goldberg, 1999).

Taken together, the findings from the present studies are in line with previous reports of the neural circuitry that underlies emotional processing and the cognitive control of emotions. In addition to the expected neural activation during the perception of or detachment from negative emotional material, a neural aftereffect of volitional regulation was observed in all three studies, which goes beyond the previous reports on the neural mechanisms of regulation. In the next section, the immediate aftereffect will be discussed in relation to the initial fMRI study on this phenomenon, and in relation to earlier work.

4.3   The immediate aftereffect of emotion regulation

Is the immediate aftereffect in the amygdala indeed related to the previous regulation of emotions?

In all three studies, an immediate aftereffect in the amygdala was found after the offset of the explicit effort to regulate. During active regulation, the amygdala signal was significantly reduced; however, the amygdala BOLD response paradoxically increased during the respective fixation. Since this effect was not observed following non-regulated items in the present studies and in the initial fMRI study by Walter and colleagues (2009), it is unlikely that it is related to the offset of the picture. Moreover, in Study 2, this assumption was refuted by the fact that the immediate aftereffect was shifted in time when the active regulation was prolonged after picture presentation. Thus, in accordance with the initial assumption, it can be concluded that the immediate aftereffect indeed pertains to regulation offset.

But if this is so, what exactly is the nature of this paradoxical neural phenomenon? One possible interpretation that arises from the studies on the paradoxical rebound effects in thought suppression is that participants might have ruminated about the pictures during the fixation. As pointed out by Wegner (2003), it is a well-known phenomenon of thought suppression that the target thought frequency increases after the end of suppression. Although both the time scales and the processes that are involved in thought suppression are different from the ones that are involved in emotional regulation, paradoxical effects that are delayed in time are observed following both processes. Contrasting this suggestion, however, there was no direct experiential correlate

of the immediate aftereffect in Study 1, since the negativity ratings that were obtained after the fixation were not influenced by valence or regulation. Moreover, in Study 2, those pictures that were previously presented in the regulation condition were later on perceived as more pleasant in the post-scan rating. Similarly, Walter and colleagues (2009) reported a sustained aftereffect ten minutes after the initial regulation. When subjects viewed the initial set of pictures again under passive viewing conditions, previously regulated pictures led to lower amygdala activations compared with previously unregulated pictures. Thus, the initial regulation of negative emotions had a lasting effect in the sense that the respective negative cues subsequently entailed lower neural reactivity. The positive relationship between these two neural measures implies that the immediate aftereffect is a surrogate physiological marker for the sustained success of emotion regulation, since greater immediate aftereffects in the first task were associated with greater amygdala activation in the second task. In line with this assumption, in Study 3 of the present work, increased initial regulation of fear during picture presentation was associated with lower amplitudes of the immediate aftereffect of regulation. Also, the s-group which showed increased amygdala signal attenuations during detachment did not report thinking about the pictures during the fixation in contrast to the l/l-homozygotes. The fact that participants thought more about regulated pictures during fixation in Study 2 might thus be related to a less effective initial regulation during the picture presentation. Although no formal statistical test can be conducted to directly compare the results across studies, the initial down-regulation of amygdala activation was indeed rather weak (i.e. present only at an uncorrected $p < 0.05$ in the whole brain analysis) compared with Studies 1 and 3, as well as other previous studies (Eippert, et al., 2007; Ochsner, et al., 2002; Ochsner, et al., 2004; Walter, et al., 2009). Since on the one hand there is no experiential correlate that is directly linked to the immediate aftereffect at the

neural level, but on the other hand, there are regulation-related differences in the post-scan pleasantness and preoccupation ratings, this might be an indication that the immediate aftereffect is especially related to the sustained effectiveness of regulation.

Taken together, these findings suggest that the immediate aftereffect of the volitional regulation of negative emotions observed in the amygdala in the initial study (Walter, et al., 2009) and in the present studies is a physiological correlate that pertains to previous explicit regulatory efforts. Moreover, the immediate aftereffect seems to be a physiological marker of the efficiency of the initial and the sustained effects of cognitive emotion regulation.

Is the immediate aftereffect in the amygdala exclusively related with volitional emotion regulation?

As mentioned previously in Chapter 3.2, the close investigation of the temporal dynamics of amygdala activation showed that there were two increases in BOLD signal after the termination of the initial regulation. In Study 1, the signal was higher following regulated negative pictures compared with unregulated negative pictures already at TR 9, approximately six seconds after picture offset (which is also the onset of the first rating). In Study 2 the amygdala signal following regulated negative pictures also showed an increase at TR 9, but it did not surpass that of the unregulated negative pictures. In contrast, no comparable effect was found in Study 3 or in the initial study (Walter, et al., 2009), where the picture presentation was directly followed by the fixation. Thus, the first amygdala signal increase in Studies 1 and 2 might signal an aftereffect that is related to the initial regulation during the picture perception, while the second increase might be associated with the specific cognitive operations that followed the picture presentation in these two studies. In this respect, the increased

amygdala BOLD signal at TR 12 in Study 1 might pertain to the end of the first rating procedure; in Study 2, the signal increase at TR 13 might be related to the end of the maintain phase. This interpretation is corroborated by the fact that both the behavioral rating of a certain aspect of an emotional stimulus (Drabant, et al., 2009; Hariri, et al., 2000) and the performance of a secondary cognitive operation (Ochsner, et al., 2009; van Dillen, et al., 2009) are in themselves regulatory strategies. Thus, although the presence of two post-regulation signal increases might at first seem to contradict our hypotheses, it may in fact underscore the association between the regulation of emotional responses and neural aftereffects in the amygdala. However, since both the selective attention to one aspect of a stimulus and the performance of a distracting cognitive task do not explicitly have the goal to down-regulate emotions, it seems reasonable to assume that the neural aftereffect in the amygdala might be related with both implicit and explicit emotion regulatory processes (Phillips, et al., 2008).

Why is there also amygdala signal reduction following neutral trials?

The above interpretation might also partly explain the significant amygdala signal reduction during and the presence of an immediate aftereffect following regulated neutral trials in Study 2. Here, different regulatory processes might take place during the picture presentation compared with the maintain phase. In contrast to the instruction to maintain an emotional response, which leads to a prolonged amygdala signal following negative pictures (Schaefer, et al., 2002), the instruction in Study 2 was to continue using a certain *strategy* of experiencing emotions (Murakami, Matsunaga, & Ohira, 2009). In the maintain phase of Study 2, no stimulus is present on the screen, while participants continue to follow the instruction to 'permit' or to 'suppress' their feelings in response to the previous stimulus. In both cases, a cognitive process is involved that has to represent the

instruction as well as the picture. Following regulated pictures, participants continue to behave as a distant observer, which is most likely associated with a mental representation of the stimulus and the (emotional) response to it (Van Overwalle & Baetens, 2009). Following unregulated pictures, participants will continue to monitor their feelings in order to comply with the instruction to permit their emotional responses; this process will probably also rely on a mental representation of the stimulus as well as the emotional responses associated with it (Blanke, et al., 2005; Farrer & Frith, 2002; Spengler, et al., 2009). Since both types of stimuli are thus associated with the need for mental representation during the maintain phase, the salience of the neutral pictures might be increased. This increase in salience might in fact be the underlying cause of the higher amygdala reactivity to unregulated compared with regulated neutral trials (LeDoux, 2007; Rolls, 2000). Due to the complex cognitive processes involved in the instruction to 'maintain', it seems reasonable to assume that the amygdala signal increase following neutral regulated trials at TR 13 in Study 2 is also associated with the termination of successful regulation at the end of the maintain phase.

4.4 Volition obliterates 5-HTTLPR mediated amygdala hyperreactivity

The results from Study 3 show that heightened amygdala reactivity attributable to the 5-HTTLPR short variant is successfully attenuated by the volitional regulation of emotion, that this effect is present for fear but not observed for disgust, and that it is mediated in s-carriers by altered functional coupling between the amygdala and the medial and ventrolateral prefrontal cortices. Both fear and disgust induced reliable activation in the amygdala amongst other

regions in comparison to emotionally neutral stimuli (Calder, et al., 2001; Phan, et al., 2002). As expected from the growing body of literature on increased amygdala reactivity to negative emotional stimuli, s-carriers in Study 3 also showed increased amygdala activation during the passive perception of fear versus neutral stimuli (Hariri, et al., 2005; Hariri, et al., 2002). However, the same s-carriers showed no amygdala hyperreaction to disgust, which suggests that the effect of the serotonin transporter genotype on amygdala activation might be modulated by the type of negative emotion evoked by a stimulus. Support for this notion also stems from the fact that the volitional regulation of fear led to a larger decrease in amygdala activation in the short genotype group. These findings speak against the assumption that emotional regulation is generally compromised in short allele carriers: the amygdala hyperreactivity to fear perception in s carriers was obliterated during volitional regulation of fear. Moreover, the present results yield evidence for a neurobiological mechanism mediating this effect in the medial and the ventrolateral prefrontal cortex. Although functional connectivity between the medial prefrontal cortex and the amygdala was previously reported to be decreased in s-carriers in an emotion paradigm without volitional regulation (Pezawas, et al., 2005), short allele carriers in Study 3 were able to effectively down-regulate their hyperreactive amygdalae. This effect was mediated by significantly stronger functional connectivity between the amygdala and the ventromedial and -lateral prefrontal cortices during volitional regulation. Recent reports have described increased connectivity between the amygdala and the dorsomedial, orbito- and ventrolateral prefrontal cortices during willful emotion regulation (Banks, Eddy, Angstadt, Nathan, & Phan, 2007; Maren & Quirk, 2004; Wager, et al., 2008). Increased connectivity with the prefrontal cortex during volitional regulation might thus signal stronger inhibitory influences on the amygdala through direct

afferent (rACC) or efferent (sACC, medial OFC) anatomical connections (Paus, 2001; Stefanacci, Suzuki, & Amaral, 1996; Stein, et al., 2007).

How do the present findings fit in with the assumption of a detrimental effect of the short allele on emotional regulation?

The present results emphasize that a clear distinction must be made between implicit, automatic processing and explicit, effortful processing with respect to the effects of the serotonin transporter genotype on neural processing (MacDonald, 2008; Phillips, et al., 2008; Satpute & Lieberman, 2006). The decreased coupling between amygdala and medial prefrontal cortex in s-carriers which has been described previously (Heinz, et al., 2005; Pezawas, et al., 2005) has been found in paradigms in which emotional regulation was not an explicit task, but which occurred instead automatically. In these paradigms, subjects either only viewed negative stimuli, or matched them without being explicitly instructed to regulate their emotions. In contrast, the task used in Study 3 contains an explicit strategy, i.e. subjects intentionally used detachment in order to down-regulate their emotions. As shown in recent studies, explicit regulation leads to increased coupling of the amygdala and ventromedial (Banks, et al., 2007) and -lateral (Wager, et al., 2008) prefrontal cortices. Thus, the present results suggest that volitional emotion regulation can compensate for hyperreactivity of the amygdala in 5-HTTLPR s-carriers, a finding which is important also with respect to the role of the will in controlling predetermined reactions (Haggard, 2008; Walter, 2001) since it suggests that willful acts can indeed compensate for genetically mediated emotional sensitivity. This interpretation is also in line with studies of serotonergic effects on cognitive task performance which demonstrated that genetic variation in the serotonin system related to negative emotionality also entailed beneficial effects on cognitive

functions (Fallgatter, et al., 2004; Strobel, et al., 2007) and the efficacy of mindfulness exercises in increasing parasympathetic dominance (Murakami, et al., 2009).

If volitional emotion regulation obliterates amygdala hyperreactivity in s-allele carriers, how can their supposed bias towards negative emotionality be explained?

One possible explanation is that s-carriers do not habitually access the full potential of volitional regulation, as suggested by the lower habitual reappraisal scores in s-carriers in the present study. An intensified experience of negativity in these individuals might critically compromise the implementation of volitional regulation, particularly when stress is frequently experienced. The repeated exposure to adverse life events depletes cognitive resources and makes successful emotion regulation more difficult (Gross, 1999), which may consequently lead to an increase of depression. At first glance, this interpretation may seem difficult to reconcile with the results of two recent meta-analyses which did not find an association between an elevated risk for depression and the serotonin transporter genotype alone or in interaction with stressful life events (Munafo, Brown, & Hariri, 2008; Risch, et al., 2009). However, while it is well acknowledged that large and homogeneously assessed samples are necessary to identify gene-environment interactions (Hoefgen, et al., 2005), the samples included in the above mentioned meta-analyses are heterogeneous with respect to ethnicity, study design, sample recruitment and assessment of stressful life events. Moreover, the sample size of 1,769 clinically depressed individuals may still be too low to identify influences of the serotonin transporter genotype on a specific subgroup. Since depression is both clinically and genetically heterogeneous, and the impact of stressful life-events on an

individual at a given point in time is hard to determine, a replication within the same study design is needed to reliably provide or refute an association between the serotonin transporter genotype, environmental factors and depression. In the present design, however, there was no direct test of the influence of the serotonin transporter genotype on depression per se; rather, quantitative measures of phenotypes of the cognitive control of emotions which may underlie the etiology of depression were examined. The relevance of successful emotion regulation with regard to mood disorders is underscored by reports of impaired volitional emotion regulation in clinically manifest depression. Whereas greater activation in the ventrolateral and –medial PFC was associated with reduced amygdala activation in healthy controls, clinically depressed individuals showed the reverse pattern where greater reappraisal effort was related to increased amygdala activation. In the present study, individuals with the risk genotype were able to effectively attenuate amygdala hyperreactivity to fear-related stimuli by means of volitional regulation. This suggests that volitional strategies may be beneficial in attenuating genotype-dependent amygdala activation, despite a less efficient automatic emotion regulation. In fact, the efficacy of cognitive behavioral therapy for depressed or depression-prone subjects might also rely on this mechanism (Johnstone, et al., 2007).

In summary, the results of Study 3 lend new insights into our understanding of the complex interplay between volition and genetic determination. They suggest that genetically predisposed neural processing may be counteracted by willful actions. Furthermore, the present findings may partly explain why short allele carriers of the 5-HTTLPR are prone to affective disorders in the presence of stressful life events, and why cognitive behavioral therapy is effective in improving volitional regulation of emotions. The present findings generate a new set of research questions concerning the neural, genetic and environmental

factors involved in affective disorders as well as effective mechanisms for coping with them. Finally, they also lend support for the notion that conscious will can effectively counteract genetic determinants of emotional behavior.

4.5 The long life of emotion regulation: implications of its immediate, delayed, and long-term effects

The results of the three studies of this dissertation along with a great number of previous studies underscore the far-reaching consequences of emotions and emotion regulation (Damasio, 1994; Davidson, 2003; Ekman, 1999; Frijda, 1986; Gross & Thompson, 2007; James, 1884; LeDoux, 1987; Scherer, 2001). On a general account, the present results are in line with the findings from previous studies on the cognitive control of emotions, which report the successful attenuation of the experiential and neural correlates of negative emotions during detachment (Beauregard, et al., 2001; Eippert, et al., 2007; Kalisch, et al., 2005; Levesque, et al., 2003; Levesque, et al., 2004). In this regard, the amygdala signal, which serves as a neural marker for the experience of emotions, is decreased when we detach ourselves from the (negative) content of a picture. At the same time, the dorsolateral and ventrolateral prefrontal cortex and the inferior parietal lobule are engaged in order to implement the volitional control of our emotions (Ochsner, et al., 2002; Ochsner, et al., 2009; Ochsner, Ray, et al., 2004). As the present results show, this is the case even when our amygdala is genetically predisposed to a heightened reactivity to negative cues, as for instance in the presence of at least one short allele of the serotonin transporter-linked promoter region. Thus, the volitional attempt to control how we feel about something by

"stepping back" and thus reducing its relevance to us is a powerful tool to exert control over our emotional reactions.

What is even more striking is that there seems to be a neural marker of the long-term effectiveness of emotion regulation as early as in the first 10 seconds after the initial regulation. In the study by Walter and colleagues (2009), and in the three studies of the present dissertation, a paradoxical increase in amygdala activation was consistently observed following the volitional regulation of emotions. Moreover, this signal also seems to be associated with other types of mental operations that might act as implicit regulatory strategies, which suggests that it is linked to the regulation of emotions both in the presence *and* absence of volition. Similar to the results from Walter et al. (2009), the present results also support the notion that the immediate aftereffect of volitional regulation is related with the long-term success of the initial attempt to control an emotional response. These findings are especially relevant with respect to a range of psychiatric disorders in which the volitional implementation of the control of emotions and thoughts often fails (Abramowitz, et al., 2001; Brewin, Andrews, & Valentine, 2000; Johnstone, et al., 2007). Thus, it would be of great interest to investigate the implications of the initial and later effects of regulation in patients suffering for example from obsessive-compulsive disorder (Ursu & Carter, 2009), post-traumatic stress disorder (Koenigs & Grafman, 2009), and especially major depression (Fales, et al., 2008; Johnstone, et al., 2007). The effect sizes observed by functional imaging during emotion regulation in combination with behavioral measures of emotional experience might serve as indicators for the severity of emotional dysfunctions, especially when using sets of stimuli that are relevant with respect to the specific disorder.

In addition to the implications for psychiatric patients, it would also seem worthwhile to investigate a number of research questions that arise from the

present results regarding healthy individuals. In a first step, the effects of different regulatory strategies in the presence and absence of volition should be compared. Such a design could for example incorporate attentional control by a cognitively taxing secondary task as an implicit control strategy (Drabant, et al., 2009; D. G. Mitchell, et al., 2007; Ochsner, et al., 2009), and reappraisal in the sense of a re-interpretation of the stimulus' meaning as an explicit control strategy (Goldin, et al., 2008; McRae, et al., in press; Ochsner, Ray, et al., 2004; van Reekum, et al., 2007). Further investigations into the nature of the immediate aftereffect should also study the down-regulation of other emotional categories, especially positive ones such as happiness or reward, and the up-regulation of both positive and negative emotions, since characteristic differences in the neural signature of these processes have been previously described (Ochsner, Ray, et al., 2004; Staudinger, et al., 2009). Moreover, replication within a design that also includes male subjects is needed to overcome the limitations of the present studies and allow for a generalization of the described effects.

To conclude, the promising replication of the initial finding of an immediate aftereffect of emotion regulation in the present work, together with the ensuing research objectives suggested above, could provide a truly comprehensive characterization of this neural marker in the amygdala. Such an empirically substantiated starting position could enable us to answer the question whether this short-lived, early signal in the brain indeed has consequences on the way we feel and behave upon the (repeated) encounter with emotionally relevant objects or events. In fact, it is especially the investigation of the various time scales of the effects of emotion regulation which may lead to a more profound understanding of the processes that are involved in emotional regulation in general, and in the development, diagnosis and ultimately also the treatment of affective disorders.

5 References

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6 Appendix

Appendix A   Activation Tables

Appendix A.1   Activation Table of Study 1

Regions	Right / Left	Brodmann's Area	Cluster size (voxels)	t-score local maximum	MNI-coordinates		
					x	y	z
Perception Negative > Perception Neutral (pN > pX)							
Amygdala	L		4950	4.22	-18	-2	-20
	R*			2.04	26	-2	-20
Pre-supplementary motor area	R	6	1115	5.53	6	8	64
Dorsal anterior cingulate cortex	R			5.46	0	16	38
Ventral anterior cingulate cortex	L	32	488	4.33	-4	40	12
Medial orbitofrontal cortex	L	11		3.89	-2	34	-22
Dorsolateral prefrontal cortex	R	9	685	6.67	56	8	40
Ventrolateral prefrontal cortex	R		750	5.67	26	18	-14
	L		4950	5.76	-26	24	-16
Thalamus	L			6.72	-4	-4	-4
	R			5.14	6	-6	-8
Cuneus	L	18			-14	-104	8
Middle occipital gyrus	L	18	4655	6.99	-42	-80	-10
	R	19	4394	6.13	44	72	-12
Perception Negative > Regulation Negative (pF > rF)							
Amygdala	L		174	4.11	-12	-10	-16
	R*			2.26	22	-2	-28
Thalamus	L		81	4.58	-4	-4	2
	R	18/19	393	4.61	20	-102	10
Lateral orbitofrontal cortex	L	11	21	3.55	-24	26	-18
Insula	L	13	60	3.69	-40	2	16
Cuneus	L	18	1483	7.12	-14	-104	8
Middle occipital gyrus	L	19		4.67	-28	-94	18
Regulation Negative > Perception Negative (rN > pN)							
Dorsolateral prefrontal cortex	R	8/9	489	4.26	44	22	44
Ventrolateral prefrontal cortex	L	45/47	162	5.05	-58	22	0
Superior frontal gyrus	R	10	3436	5.50	30	54	24
Inferior frontal gyrus	R	44/45		4.82	46	16	12
Pre-supplementary motor cortex	R	6	161	3.77	18	4	92
Frontal eye field	R	8		4.81	-2	32	54
Superior temporal gyrus	L	22	1105	6.18	-64	-56	18
Inferior parietal lobule	L	40		5.11	-64	-40	34
	R	40	3350	5.13	50	-48	32
Precuneus	R	7	459	4.77	8	-56	52

All coordinates are given in MNI space together with their *t*-scores. Whole-brain analyses were thresholded at $p <$ 0.005 (uncorrected). pN: perception Negative, pX: perception Neutral, rN: regulation Negative, rX: regulation Neutral.

Appendix A.2 Activation Table of Study 2

Regions	Right / Left	Brodmann's Area	Cluster size (voxels)	t-score local maximum	MNI-coordinates		
					x	y	z
Picture Perception + Maintain Phase							
Perception Negative > Perception Neutral ([pNpic + pNmain] > [pXpic + pXmain])							
Amygdala	L		37	3.41	-20	-4	-18
	R		1072	3.64	20	-4	-16
Hippocampus	L		101	3.39	-30	-24	-6
Thalamus	R		452	4.15	4	-8	-2
Ventrolateral prefrontal cortex	L	47	619	5.76	-30	24	-18
	R	47	165	5.55	26	24	-16
Dorsomedial prefrontal cortex	L	9	243	4.42	-6	52	26
Fusiform gyrus	R	37	482	3.92	58	-62	-14
Middle occipital gyrus	L	19	715	3.91	-56	-68	-6
Perception Negative > Regulation Negative ([pNpic + pNmain] > [rNpic +rNmain])							
No suprathreshold voxels.							
Regulation Negative > Perception Negative ([rNpic +rNmain] > [pNpic + pNmain])							
Inferior parietal lobule	L	40	37522	6.29	-62	-46	40
	R	40		5.84	56	-50	32
Superior parietal lobule	R			5.73	50	-54	46
Dorsomedial prefrontal cortex	R	9		4.71	2	40	30
Dorsolateral prefrontal cortex	R	9		5.28	48	34	30
Ventrolateral prefrontal cortex	R	10		5.69	36	54	-2
	L	47	189	3.72	-32	14	-8
Inferior frontal gyrus	R	44	138	3.49	56	0	28
Middle temporal gyrus	R	21	499	5.43	68	-22	-14
Picture Perception							
Picture Perception Negative > Picture Perception Neutral (pNpic > pXpic)							
Amygdala	L		721	4.43	16	-4	-16
	R			3.07	-16	0	-16
Hippocampus	R			3.07	28	-6	-26
Inferior frontal gyrus	R	44	92	3.63	50	10	28
Ventrolateral prefrontal cortex	R	47	96	4.48	26	24	-16
Postcentral gyrus	L	2	107	3.69	-58	-24	30
	R	3	27	3.17	66	-18	40
Fusiform gyrus	R	37	900	4.81	56	-62	-12
	L	37	639	4.32	-56	-70	-4
Cuneus	L	19	183	3.06	-12	-76	-6
Picture Perception Negative > Picture Regulation Negative (pNpic > rNpic)							
Amygdala*	L			2.46	-10	2	-16
	R			2.38	14	-4	-18
Hippocampus	L		15	6.21	-40	-22	-16
Subgenual anterior cingulate cortex	R	25	99	3.79	8	10	-16
Posterior orbitofrontal cortex		11		2.64	20	14	-20
Insula	L	13	13	2.88	-38	0	14
Fusiform gyrus	R	37	74	3.15	52	-54	-12
Middle occipital gyrus	R	18	448	3.92	20	-104	8

	L	18	571	3.73	-32	-98	4

Picture Regulation Negative > Picture Perception Negative (rNpic > pNpic)

Region	Side	BA	Voxels	Z	x	y	z
Dorsolateral prefrontal cortex	R	9/46	5995	5.04	38	46	30
Supplementary motor cortex	R	6		4.48	20	6	58
Inferior frontal gyrus	R	45	781	4.56	34	22	8
Ventrolateral prefrontal cortex	R	47		3.67	48	18	-12
Dorsomedial prefrontal cortex	L	32	217	3.80	-10	32	26
Superior temporal gyrus	L	22/39	259	4.13	-42	-58	12
Putamen	L		138	3.71	-16	-10	4
	R		98	3.66	26	-12	6
Inferior parietal lobule	R	40	2476	5.26	58	-44	42
	L	40	1309	5.41	-62	-46	38
Superior parietal lobule	L	40		3.99	-48	-52	48
Precuneus	L	7	3142	5.23	-10	-76	52
	R	7		5.01	6	-62	56

Maintain Phase

Maintain Perception Negative > maintain Perception Neutral (pNmain > pXmain)

Region	Side	BA	Voxels	Z	x	y	z
Amygdala/SLEA	L				-28	-4	-12
	R				30	-2	-14
Dorsomedial prefrontal cortex	L	32	255	4.09	-6	52	26
Ventrolateral prefrontal cortex	R	47	81	3.85	28	24	-16
	L	47	2628	5.88	-30	26	-18
Hippocampus	L			5.05	-30	-22	-8
Thalamus	L				-22	-6	14
	R		729	3.71	16	-22	14
Posterior cingulate cortex	L		90	3.43	-4	-48	18
Fusiform gyrus	L	37	66	3.19	-50	-50	-16

Maintain Perception Negative > Maintain Regulation Negative (pNmain > rNmain)
No suprathreshold voxels.

Maintain Regulation Negative > Maintain Perception Negative (rNmain > pNmain)

Region	Side	BA	Voxels	Z	x	y	z
Middle temporal gyrus	L	21	1452	4.57	-58	-32	-8
Supplementary motor cortex	R	6		5.54	30	28	58
	L	6		4.85	-38	14	56
Dorsolateral prefrontal cortex	R	9		4.87	-18	52	36
	L	9		4.74	-24	48	36
Ventrolateral prefrontal cortex	L	47/10		4.69	-44	50	2
	R	10	14707	5.70	38	50	0
Dorsomedial prefrontal cortex		32		4.53	0	42	32
Lateral orbitofrontal cortex	L	11		4.45	-20	36	-18

Picture Perception vs Maintain Phase

Picture: Negative > Neutral vs Maintain: Negative > Neutral ([pNpic > pXpic] > [pNmain > pXmain])

Region	Side	BA	Voxels	Z	x	y	z
Amygdala	R		21	3.01	14	-2	-12
	L		18	3.01	10	4	-30
Subgenual anterior cingulate	R	25	9	2.81	12	12	-14
Fusiform gyrus	R	37	37	2.94	50	-60	-10

Maintain: Negative > Neutral vs Picture: Negative > Neutral ([pNmain > pXmain] > [pNpic > pXpic])

Region	Side	BA	Voxels	Z	x	y	z
Amygdala/SLEA	L			3.77	-28	-4	-12

	R			3.39	30	-4	-10
Thalamus	R		1687	5.27	28	-12	4
	L		2368	5.96	-22	-4	16
Parahippocampal gyrus	L			4.81	-32	-34	6
Hippocampus	L			4.59	-30	-22	-6
Ventrolateral prefrontal cortex	L	47	1093	4.59	-48	30	-12
	R	10	113	3.58	44	54	-12
Middle temporal gyrus	R	21	1687	4.26	48	-26	-4
Temporo-parietal junction	L	39/40	631	4.81	-38	-52	34
	R		68	3.26	48	-22	22
Posterior cingulate cortex	L		257	3.63	-2	-42	18

Maintain: Regulation > Perception vs Picture: Regulation > Perception ([rNmain > pNmain] > [rNpic > pNpic])

Dorsolateral prefrontal cortex	R	9/46	367	3.62	48	30	16
Precentral gyrus	R	4	156	4.67	28	-18	60
Insula	L	13	77	3.58	-38	-4	14
Supplementary motor cortex	L	6	265	3.84	-4	-24	60
Dorsomedial prefrontal cortex	L	32	797	3.69	-4	56	42
Rostral anterior cingulate cortex	L	24	25	2.86	-6	52	8
Subgenual anterior cingulate	L	24	268	3.62	-8	14	-14
	R	24	603	4.79	12	12	-18
Medial orbitofrontal cortex	R	11		4.73	12	44	-16
	L	11	136	4.08	-20	36	-18
Thalamus	R		28	3.05	2	-16	6
Temporo-parietal junction	R	39/40	322	3.93	44	-64	30
Fusiform gyrus	L	37		3.89	-56	-64	-16
	R	37	788	4.37	54	-56	-16
Inferior occipital gyrus	L	18	1693	4.06	-34	-96	-4
Cuneus	L	18/19	1859	4.21	-2	-78	-8

Picture: Regulation > Perception vs Maintain: Regulation > Perception ([rNpic > pNpic] > [rNmain > pNmain])
No suprathreshold voxels.

All coordinates are given in MNI space together with their *t*-scores. Whole-brain analyses were thresholded at $p < 0.005$ (uncorrected). pN: perception Negative, pX: perception Neutral, rN: regulation Negative, rX: regulation Neutral.

Appendix A.3 Activation Tables of Study 3

Table A.3.1: Overall effects of stimulus valence and regulation (s-group + l-group,) and direct comparisons between genotype groups (s-group > l-group)

Regions	Right / Left	Brodmann's Area	Cluster size (voxels)	t-score local maximum	MNI-coordinates		
					x	y	z
s-allele carriers + l/l homozygotes							
Fear > Neutral ([pF + rF] > [pX +rX])							
Amygdala	L			3.96	-26	-8	-18
	R			3.78	28	-6	-20
Thalamus	R		185	4.84	10	-10	0
Dorsolateral prefrontal cortex	R	9/46	85	4.39	56	26	26
Precentral gyrus	R	6	20	3.59	40	-6	54
Superior temporal gyrus	L	38	15	3.51	-42	12	-22
Middle temporal / fusiform gyrus	L	37	3470	6.76	-52	-66	8
	R	39	2590	6.08	50	-60	8
Inferior parietal lobule	L	40	408	5.06	-60	-28	34
Lingual gyrus	L	18	11	3.34	-22	-78	-6
Disgust > Neutral ([pD + rD] > [pX + rX])							
Amygdala	L			3.94	-22	-2	-18
	R			5.47	22	-2	-16
Medial orbitofrontal cortex	R	11	32	3.68	4	52	-16
Dorsomedial prefrontal cortex	R	9	44	3.97	8	48	24
Pre-supplementary motor area	R	6	710	5.74	10	6	68
	L	6		4.02	-10	6	54
Precentral gyrus	L	6/4	119	4.32	-46	0	34
Insula	R	13	447	4.81	40	26	-10
Inferior parietal lobule	L	40	193	5.19	-62	-30	40
	R	3	83	3.75	62	-20	34
Fusiform gyrus	L	19	16086	9.21	-42	-64	-6
Lingual gyrus	L	18		6.76	-30	-72	-8
Perception > Regulation ([pF + pD + pX] > [rF + rD + rX])							
Amygdala	L			3.49	-28	0	-18
	R			3.54	16	-8	-14
Medial orbitofrontal cortex	L	11	533	5.33	-2	54	-12
Insula	L	13	85	4.44	-32	-14	22
Parahippocampal gyrus	R	34	83	3.73	18	-8	-18
Cuneus / lingual gyrus	R	18	21356	7.96	26	-92	-2
Regulation > Perception ([rF + rD + rX] > [pF + pD + pX])							
Dorsolateral prefrontal cortex	R	9	7497	8.55	34	40	32
Ventrolateral prefrontal cortex	R	10		8.29	38	48	4
Dorsal anterior cingulate cortex	R			5.15	4	28	40
Ventrolateral prefrontal cortex	L	10	1511	7.31	-32	46	8
Dorsolateral prefrontal cortex	L	9		4.48	-36	38	30
Insula	L	13	59	4.08	-38	14	2
Middle / inferior temporal gyrus	R	21	180	4.12	56	-28	-10
Posterior cingulate cortex	R	23	210	4.44	2	-26	28

Inferior / superior parietal lobule	L	40	1548	5.53	-56	-52	44

s-allele carriers > l/l homozygotes

Perception Fear > Perception Neutral (pF > pX)

Amygdala*	R			2.87	26	-4	-18
Dorsomedial prefrontal cortex	R	9		3.41	8	46	20
Pre-supplemental motor area	R	6	26	3.98	12	22	50
Insula / putamen	R		29	3.75	28	18	10
Thalamus	L		33	3.94	-24	-34	6
Subgenual anterior cingulate cortex	L	24	86	4.35	-4	28	0
Rostral anterior cingulate cortex	R	32	29	3.62	6	44	10
Posterior cingulate cortex	R	23	49	3.69	8	-48	26
Fusiform gyrus	L	21	76	3.88	-56	-20	-18
Precuneus	L	7	23	3.79	-10	-50	50
Inferior parietal lobule	L	39	36	3.60	-42	-60	36

Perception Fear > Perception Disgust (pF > pD)

Amygdala*	L			2.77	-28	-8	-18
	R			2.97	-26	-4	-20
Dorsomedial prefrontal cortex	R	9		3.37	2	52	22
Pre-supplemental motor area	R	6	428	5.92	12	22	52
Insula / putamen	L	13	13	3.38	-36	6	10
	R		94	4.94	28	18	10
Thalamus	L		229	4.89	-16	-28	2
Subgenual anterior cingulate cortex	L		86	4.28	-4	28	2
Rostral anterior cingulate cortex	R	32	56	3.77	8	44	10
Dorsal anterior cingulate cortex	L	24	47	4.28	-4	-2	32
	R	24	91	5.00	14	-8	44
Posterior cingulate cortex	L	31	152	3.96	-14	-30	42
Fusiform gyrus	L	20	75	4.02	-58	-10	-24
Precuneus	L	7	24	3.90	-12	-48	50

Perception Fear > Regulation Fear (pF > rF)

Amygdala*	R			3.27	26	-2	-12
Supramarginal gyrus	R	6	15	3.46	16	6	72
Middle temporal gyrus	L	21	70	3.84	-58	-18	-12
	R	21	18	3.52	58	-22	-16
Temporo-parietal junction	R	22	28	3.86	54	-32	8
Inferior parietal lobule	R	40	42	3.51	54	-38	34
Secondary sensory cortex	L	7	36	3.56	-6	-50	64
Precuneus	R	7	27	3.54	8	-58	66

Perception Disgust > Perception Neutral (pD > pX)

No suptrathreshold voxels

Perception Disgust > Perception Fear (pD > pF)

No suptrathreshold voxels.

Perception Disgust > Regulation Disgust (pD > rD)

Middle temporal gyrus	L	21	20	3.65	-50	-14	-16
	R	21	20	3.49	54	-10	-18
Supramarginal gyrus	L	40	47	4.24	-62	-54	30
	R	40	202	3.92	62	-54	30

Region	Hemisphere	BA	k	t	x	y	z
Inferior parietal lobule	R	40		3.60	58	-56	44

Fear > Neutral ([pF + rF] > [pX +rX])

Region	Hemisphere	BA	k	t	x	y	z
Amygdala*	R			2.53	26	-4	-18
Pre-supplemental motor area	R	6	127	4.30	12	22	52
Subgenual anterior cingulate cortex	L		39	3.93	-4	28	2
Dorsal anterior cingulate cortex	R	24	68	4.20	14	-8	44
Thalamus	L		18	3.77	-24	-34	6
Fusiform gyrus	L	20	17	3.52	-60	-8	-24
Precuneus	L	7	12	3.55	-12	-50	50

Disgust > Neutral ([pD + rD] > [pX + rX])
No suprathreshold voxels

Fear > Disgust ([pF + rF] > [pD + rD])

Region	Hemisphere	BA	k	t	x	y	z
Amygdala*	R			2.88	26	-4	-20
Ventrolateral prefrontal cortex	R	47	14	3.58	22	10	-14
Dorsomedial prefrontal cortex	R	9	14	3.29	4	48	20
Pre-supplemental motor area	R	6	414	6.01	12	22	52
	L	6		3.63	-4	18	70
Insula	L	13	18	3.52	-36	6	10
	R		124	5.36	30	16	8
Ventral striatum	R		28	3.67	10	6	-8
Hippocampus	L		223	5.02	-16	-28	0
	R			3.36	12	-34	-8
Thalamus	L			4.05	-24	-34	6
Subgenual anterior cingulate cortex	L		96	4.43	-4	28	2
Rostral anterior cingulate cortex	R	32	17	3.66	6	44	10
Dorsal anterior cingulate cortex	L	24	34	4.14	-4	-2	32
	R	24	137	5.32	14	-8	44
Posterior cingulate cortex	L	31	34	3.46	-8	-42	26
	R	23	13	3.40	8	-48	26
Fusiform gyrus	L	21	88	3.98	-56	-18	-20
Precuneus	L	7	118	4.02	-12	-48	50

Disgust > Fear ([pD + rD] > [pF + rF])
No suptrathreshold voxels

Perception > Regulation ([pF + pD + pX] > [rF + rD + rX])

Region	Hemisphere	BA	k	t	x	y	z
Inferior parietal lobule	R	40	144	3.76	58	-44	34
Temporo-parietal junction	R	22	35	3.75	54	-32	8

Regulation > Perception ([rF + rD + rX] > [pF + pD + pX])
No suptrathreshold voxels

All coordinates are given in MNI space together with their *t*-scores. *ROI: bilateral amygdala (x, y, z = ±26, -4, -16), significance threshold for ROI analyses $p < 0.05$ (FWE-corrected for multiple comparisons). Whole-brain analyses were thresholded at $p < 0.001$ (uncorrected) with an extent threshold of $k = 10$. pF: perception Fear, pD: perception Disgust, pX: perception Neutral, rF: regulation Fear, rD: regulation Disgust, rX: regulation Neutral.

Table A.3.2   Regions showing greater amygdala connectivity during fear regulation (rF-pF) in the whole sample (s-group + l-group) and in 5-HTTLPR short allele carriers (s-group > l-group)

Regions	Right / Left	Brodmann's Area	Cluster size (voxels)	t-score local maximum	x	y	z
s-allele carriers + l/l homozygotes							
Dorsolateral prefrontal cortex	L	9	298	4.17	-30	40	30
	L			3.79	-50	26	24
	L			3.61	-38	30	36
	L		285	4	-24	20	38
	L			3.6	-20	26	50
	L			3.59	-16	30	36
	R	9	55	3.88	34	36	36
Ventrolateral prefrontal cortex	L	10	849	4.78	-22	60	2
	L			4.43	-28	58	-4
	L		38	3.43	-38	52	12
Dorsomedial prefrontal cortex	R	9	7	3.3	10	62	28
Ventromedial prefrontal cortex	L	10		4.4	-2	56	-8
Superior frontal gyrus	R	10	10	3.25	18	66	18
Medial frontal gyrus	R	10	30	3.72	44	54	14
	R			3.53	38	60	14
Inferior frontal gyrus	L	45	76	4.02	-42	14	18
Premotor cortex	L	6	96	3.68	-14	6	56
	L			3.62	-18	6	64
	L			3.17	-14	-2	58
Insula	L	4	43	3.76	-46	-16	24
	L			3.3	-50	-8	20
Parahippocampal gyrus	R	34	38	3.79	14	-2	-20
Inferior parietal lobule	L	40	105	4.12	-48	-48	40
	L			3.33	-40	-50	22
Cuneus	L	18		5.94	-6	-80	16
	L			5.81	-8	-88	18
Thalamus	L		57447	5.97	-18	-30	4
Ventral tegmental area	R		56	3.6	14	-16	-16
Cerebellum	R		10	3.36	24	-74	-48
s-allele carriers > l/l homozygotes							
Ventrolateral prefrontal cortex	L	11	88	3.79	-40	42	-10
	L	47	18	3.12	-54	34	-6
	R	10	268	3.93	34	48	-6
	R	47	25	3.32	28	28	-4
Pre-supplemental motor area	R	6	147	3.53	32	14	56
Medial orbitofrontal cortex	L	11	45	2.99	-10	36	-16
				2.98	-18	36	-14
Dorsomedial prefrontal cortex	L	8	31	3.2	-10	32	36
Sugbenual anterior cingulate cortex	R	25	37	3.69	8	24	-14
Rostral anterior cingulate cortex	R	32	23	3.2	6	46	2
Dorsal anterior cingulate cortex	L	24	33	3.98	-14	2	36
	L	24		3.09	-10	10	30
Posterior cingulate cortex	L	29	76	3.59	-8	-42	12
Hypothalamus	L		80	3.73	-2	-2	-4
Insula	L	13	10	3.22	-40	8	10
	R	13	205	4.35	40	-12	20

	R	13		4.21	40	-26	24
Precuneus / cuneus	L	7/31	129	3.6	-14	-60	34
	L	30	31	3.17	-18	-68	12
	R	7	719	4.22	14	-58	36
	R	7		3.17	0	-74	34

All coordinates are given in MNI space together with their *t*-scores. Whole-brain analyses were thresholded at $p < 0.005$ (uncorrected) with an extent threshold of $k = 10$.

Appendix B Personality Questionnaires

Appendix B.1   BDI (Studies 1-3)

Dieser Fragebogen enthält 21 Gruppen von Aussagen. Bitte lesen Sie jede Gruppe sorgfältig durch. Suchen Sie dann die Aussage in jeder Gruppe heraus, die am besten beschreibt, wie Sie sich in dieser Woche einschließlich heute gefühlt haben, und kreuzen Sie die dazugehörige Ziffer (0,1, 2 oder 3) an. Falls mehrere Aussagen einer Gruppe gleichermaßen zutreffen, können Sie auch mehrere Ziffern markieren. Lesen Sie auf jeden Fall alle Aussagen in jeder Gruppe, bevor Sie Ihre Wahl treffen.

A)

    0   Ich bin nicht traurig.
    1   Ich bin traurig.
    2   Ich bin die ganze Zeit traurig und komme nicht davon los.
    3   Ich bin so traurig oder unglücklich, daß ich es kaum noch ertrage.

B)

    0   Ich sehe nicht besonders mutlos in die Zukunft.
    1   Ich sehe mutlos in die Zukunft.
    2   Ich habe nichts, worauf ich mich freuen kann.
    3   Ich habe das Gefühl, daß die Zukunft hoffnungslos ist, und daß die Zukunft nicht besser werden kann.

C)

    0   Ich fühle mich nicht als Versager.
    1   Ich habe das Gefühl, öfter versagt zu haben als der Durchschnitt.
    2   Wenn ich auf mein Leben zurückblicke, sehe ich bloß eine Menge Fehlschläge.
    3   Ich habe das Gefühl, als Mensch ein völliger Versager zu sein.

D)

    0   Ich kann die Dinge genauso genießen, wie früher.
    1   Ich kann die Dinge nicht mehr so genießen, wie früher.
    2   Ich kann aus nichts mehr eine echte Befriedigung ziehen.
    3   Ich bin mit allem unzufrieden oder gelangweilt.

E)

    0   Ich habe keine Schuldgefühle.
    1   Ich habe häufig Schuldgefühle.
    2   Ich habe fast immer Schuldgefühle.
    3   Ich habe immer Schuldgefühle.

F)

    0   Ich habe nicht das Gefühl, gestraft zu sein.
    1   Ich habe das Gefühl, vielleicht bestraft zu werden.
    2   Ich erwarte, bestraft zu werden.
    3   Ich habe das Gefühl, bestraft zu werden.

G)

0	Ich bin nicht von mir enttäuscht.
1	Ich bin von mir enttäuscht.
2	Ich finde mich fürchterlich.
3	Ich hasse mich.

H)

0	Ich habe nicht das Gefühl, schlechter zu sein als alle anderen.
1	Ich kritisiere mich wegen meiner Fehler und Schwächen.
2	Ich mache mir die ganze Zeit Vorwürfe wegen meiner Mängel.
3	Ich gebe mir für alles die Schuld, was schief geht.

I)

0	Ich denke nicht daran, mir etwas anzutun.
1	Ich denke manchmal an Selbstmord, aber ich würde es nicht tun.
2	Ich möchte mich am liebsten umbringen.
3	Ich würde mich umbringen, wenn ich die Gelegenheit hätte.

J)

0	Ich weine nicht öfter als früher.
1	Ich weine jetzt mehr als früher.
2	Ich weine jetzt die ganze Zeit.
3	Früher konnte ich weinen, aber jetzt kann ich es nicht mehr, obwohl ich es möchte.

K)

0	Ich bin nicht reizbarer als sonst.
1	Ich bin jetzt leichter verärgert oder gereizt als früher.
2	Ich fühle mich dauernd gereizt.
3	Die Dinge, die mich früher geärgert haben, berühren mich nicht mehr.

L)

0	Ich habe nicht das Interesse an Menschen verloren.
1	Ich interessiere mich jetzt weniger für Menschen als früher.
2	Ich habe mein Interesse an anderen Menschen zum größten Teil verloren.
3	Ich habe mein ganzes Interesse an anderen Menschen verloren.

M)

0	Ich bin so entschlussfreudig wie immer.
1	Ich schiebe Entscheidungen jetzt öfter als früher auf.
2	Es fällt mir jetzt schwerer als früher, Entscheidungen zu treffen.
3	Ich kann überhaupt keine Entscheidungen mehr treffen.

N)

0	Ich habe nicht das Gefühl, schlechter auszusehen als früher.
1	Ich mache mir sorgen, daß ich alt oder unattraktiv aussehe.
2	Ich habe das Gefühl, daß Veränderungen in meinem Aussehen eintreten, die mich hässlich machen.
3	Ich finde mich hässlich.

O)

0	Ich kann so gut arbeiten wie früher.
1	Ich muß mir einen Ruck geben, bevor ich eine Tätigkeit in Angriff nehme.
2	Ich muß mich zu jeder Tätigkeit zwingen.

3	Ich bin unfähig zu arbeiten.

P)

0	Ich schlafe so gut wie sonst.
1	Ich schlafe nicht mehr so gut wie früher.
2	Ich wache 1 bis 2 Stunden früher auf als sonst und es fällt mir schwer, wieder einzuschlafen.
3	Ich wache mehrere Stunden früher auf als sonst und kann nicht mehr einschlafen.

Q)

0	Ich ermüde nicht stärker als sonst.
1	Ich ermüde schneller als früher.
2	Fast alles ermüdet mich.
3	Ich bin zu müde, um etwas zu tun.

R)

0	Mein Appetit ist nicht schlechter als sonst.
1	Mein Appetit ist nicht mehr so gut wie früher.
2	Mein Appetit hat sehr stark nachgelassen.
3	Ich habe überhaupt keinen Appetit mehr.

S)

0	Ich habe in letzter Zeit kaum abgenommen.
1	Ich habe mehr als 2 Kilo abgenommen.
2	Ich habe mehr als 5 Kilo abgenommen.
3	Ich habe mehr als 8 Kilo abgenommen.
	Ich esse absichtlich weniger, um abzunehmen: Ja ☐ Nein ☐

T)

0	Ich mache mir keine größeren Sorgen um meine Gesundheit als sonst.
1	Ich mache mir Sorgen über körperliche Probleme wie Schmerzen, Magenbeschwerden oder Verstopfung.
2	Ich mache mir so große Sorgen über gesundheitliche Probleme, daß es mir schwer fällt, an etwas anderes zu denken.
3	Ich mache mir so große Sorgen über gesundheitliche Probleme, daß ich an nichts anderes mehr denken kann.

U)

0	Ich habe in letzter Zeit keine Veränderung meines Interesses an Sex bemerkt.
1	Ich interessiere mich weniger für Sex als früher.
2	Ich interessiere mich jetzt viel weniger für Sex als früher.
3	Ich habe das Interesse an Sex völlig verloren.

Appendix B.2   ERQ (Studies 1-3)

Wir möchten Ihnen gerne einige Fragen zu Ihren Gefühlen stellen: Uns interessiert, wie Sie Ihre Gefühle kontrollieren bzw. verändern. Die Fragen thematisieren jeweils einen der beiden Aspekte des Erlebens von Gefühlen (also was Sie fühlen) oder des Ausdrückens von Gefühlen (ob und wie Sie Ihre Gefühle verbal, gestisch oder mimisch zeigen). Manche der Fragen klingen ziemlich ähnlich. Bei genauerem Hinsehen werden Sie jedoch feststellen, dass sie sich inhaltlich deutlich unterscheiden.

Bei der Beantwortung der Fragen stehen Ihnen folgende Antwortmöglichkeiten zur Verfügung:

```
      1--------------2--------------3--------------4--------------5--------------6--------------7
   stimmt                                    neutral                                    stimmt
   vollkommen                                                              überhaupt nicht
```

1. Wenn ich mehr positive Gefühle (z.B. Freude oder Heiterkeit) empfinden möchte, ändere ich, woran ich denke.	1	2	3	4	5	6	7
2. Ich behalte meine Gefühle für mich.	1	2	3	4	5	6	7
3. Wenn ich weniger negative Gefühle (z.B. Traurigkeit oder Ärger) empfinden möchte, ändere ich, woran ich denke.	1	2	3	4	5	6	7
4. Wenn ich positive Gefühle empfinde, bemühe ich mich, sie nicht zu zeigen.	1	2	3	4	5	6	7
5. In einer stressigen Situation ändere ich meine Gedanken über die Situation so, dass es mich beruhigt.	1	2	3	4	5	6	7
6. Ich kontrolliere meine Gefühle, indem ich sie nicht ausdrücke.	1	2	3	4	5	6	7
7. Wenn ich mehr positive Gefühle empfinden möchte, ändere ich meine Gedanken über die Situation.	1	2	3	4	5	6	7
8. Ich kontrolliere meine Gefühle, indem ich meine Gedanken über meine aktuelle Situation ändere.	1	2	3	4	5	6	7
9. Wenn ich negative Gefühle empfinde, bemühe ich mich, sie nicht auszudrücken.	1	2	3	4	5	6	7
10. Wenn ich weniger negative Gefühle empfinden möchte, ändere ich meine Gedanken über die Situation.	1	2	3	4	5	6	7

Appendix B.3   NEO-FFI Neuroticism (Study 3)

Hinweise: Dieser Fragebogen umfasst 60 Aussagen, welche sich zur Beschreibung Ihrer eigenen Person eignen könnten. Lesen Sie bitte jede dieser Aussagen aufmerksam durch und überlegen Sie, ob diese Aussage auf Sie persönlich zutrifft oder nicht. Zur Bewertung jeder der 60 Aussagen steht Ihnen eine fünffach abgestufte Skala zur Verfügung.

Kreuzen Sie bitte an:

1   Starke Ablehnung, wenn Sie der Aussage auf keinen Fall zustimmen oder sie für völlig unzutreffend halten.

2   Ablehung, wenn Sie der Aussage eher nicht zustimmen oder sie für unzutreffend halten.

3   Neutral, wenn die Aussage weder richtig noch falsch, also weder zutreffend noch unzutreffend ist.

4   Zustimmung, wenn Sie der Aussage zustimmen oder sie für zutreffend halten.

5   Starke Zustimmung, wenn Sie der Aussage nachdrücklich zustimmen oder sie für völlig zutreffend halten.

6

Es gibt bei diesem Fragebogen keine ‚richtigen' oder ‚falschen' Antworten, und Sie müssen kein Experte (keine Expertin) sein, um den Fragebogen angemessen beantworten zu können. Sie erfüllen den Zweck der Befragung am besten, wenn Sie die fragen so wahrheitsgemäß wie möglich beantworten.

Bitte lesen Sie jede Aussage genau durch und kreuzen Sie als Antwort die Kategorie an, die Ihre Sichtweise am besten ausdrückt. Falls Sie Ihre Meinung beim Ankreuzen einmal ändern sollten, streichen Sie Ihre erste Antwort bitte deutlich durch. Bitte bewerten Sie die 60 Aussagen zügig, aber sorgfältig. Lassen Sie keine Aussage aus. Auch wenn Ihnen einmal die Entscheidung schwer fallen sollte, kreuzen Sie trotzdem immer eine Antwort an, und zwar die, welche noch am ehesten auf Sie zutrifft. Beginnen Sie bitte jetzt mit der Beantwortung!

1. Ich bin nicht leicht beunruhigt.	1	2	3	4	5
2. Ich habe gerne viele Leute um mich herum.	1	2	3	4	5
3. Ich mag meine Zeit nicht mit Tagträumereien verschwenden.	1	2	3	4	5
4. Ich versuche zu jedem, dem ich begegne, freundlich zu sein.	1	2	3	4	5
5. Ich halte meine Sachen ordentlich und sauber.	1	2	3	4	5
6. Ich fühle mich anderen oft unterlegen.	1	2	3	4	5
7. Ich bin leicht zum Lachen zu bringen.	1	2	3	4	5
8. Ich finde philosophische Diskussionen langweilig.	1	2	3	4	5
9. Ich bekomme häufiger Streit mit meiner Familie und meinen Kollegen.	1	2	3	4	5
10. Ich kann mir meine Zeit recht gut einteilen, so dass ich meine Angelegenheiten rechtzeitig beende.	1	2	3	4	5
11. Wenn ich unter starkem Stress stehe, fühle ich mich manchmal, als ob ich zusammenbräche.	1	2	3	4	5
12. Ich halte mich nicht für besonders fröhlich.	1	2	3	4	5
13. Mich begeistern die Motive, die ich in der Kunst und in der Natur finde.	1	2	3	4	5

14. Manche Leute halten mich für selbstsüchtig und selbstgefällig.	1	2	3	4	5
15. Ich bin kein sehr systematisch vorgehender Mensch.	1	2	3	4	5
16. Ich fühle mich selten einsam oder traurig.	1	2	3	4	5
17. Ich unterhalte mich wirklich gerne mit anderen Menschen.	1	2	3	4	5
18. Ich glaube, dass es Schüler oft nur verwirrt und irreführt, wenn man sie Rednern zuhören lässt, die kontroverse Standpunkte vertreten.	1	2	3	4	5
19. Ich würde lieber mit anderen zusammenarbeiten, als mit ihnen zu wetteifern.	1	2	3	4	5
20. Ich versuche, alle mir übertragenen Aufgaben sehr gewissenhaft zu erledigen.	1	2	3	4	5
21. Ich fühle mich oft angespannt und nervös.	1	2	3	4	5
22. Ich bin gerne im Zentrum des Geschehens.	1	2	3	4	5
23. Poesie beeindruckt mich wenig oder gar nicht.	1	2	3	4	5
24. Im Hinblick auf die Absichten anderer bin ich eher zynisch und skeptisch.	1	2	3	4	5
25. Ich habe eine Reihe von klaren Zielen und arbeite systematisch auf sie zu.	1	2	3	4	5
26. Manchmal fühle ich mich völlig wertlos.	1	2	3	4	5
27. Ich ziehe es gewöhnlich vor, Dinge allein zu tun.	1	2	3	4	5
28. Ich probiere oft neue und fremde Speisen aus.	1	2	3	4	5
29. Ich glaube, dass man von den meisten Leuten ausgenutzt wird, wenn man es zulässt.	1	2	3	4	5
30. Ich vertrödele eine Menge Zeit, bevor ich mit einer Arbeit beginne.	1	2	3	4	5
31. Ich empfinde selten Furcht oder Angst.	1	2	3	4	5
32. Ich habe oft das Gefühl, vor Energie zu überschäumen.	1	2	3	4	5
33. Ich nehme nur selten Notiz von den Stimmungen oder Gefühlen, die verschiedene Umgebungen hervorrufen.	1	2	3	4	5
34. Die meisten Menschen, die ich kenne, mögen mich.	1	2	3	4	5
35. Ich arbeite hart, um meine Ziele zu erreichen.	1	2	3	4	5
36. Ich ärgere mich oft darüber, wie andere Leute mich behandeln.	1	2	3	4	5
37. Ich bin ein fröhlicher, gut gelaunter Mensch.	1	2	3	4	5
38. Ich glaube, dass wir bei ethischen Entscheidungen auf die Ansichten unserer religiösen Autoritäten achten sollten.	1	2	3	4	5
39. Manche Leute halten mich für kalt und berechnend.	1	2	3	4	5
40. Wenn ich eine Verpflichtung eingehe, so kann man sich auf mich bestimmt verlassen.	1	2	3	4	5
41. Zu häufig bin ich entmutigt und will aufgeben, wenn etwas schief geht.	1	2	3	4	5
42. Ich bin kein gut gelaunter Optimist.	1	2	3	4	5
43. Wenn ich Literatur lese oder eine Kunstwerk betrachte, empfinde ich manchmal ein Frösteln oder eine Welle der Begeisterung.	1	2	3	4	5
44. In Bezug auf meine Einstellungen bin ich nüchtern und unnachgiebig.	1	2	3	4	5
45. Manchmal bin ich nicht so verlässlich oder zuverlässig, wie ich sein sollte.	1	2	3	4	5
46. Ich bin selten traurig oder deprimiert.	1	2	3	4	5
47. Ich führe ein hektisches Leben.	1	2	3	4	5
48. Ich habe wenig Interesse, über die Natur des Universums oder die	1	2	3	4	5

Lage der Menschheit zu spekulieren.					
49. Ich versuche stets rücksichtsvoll und sensibel zu handeln.	1	2	3	4	5
50. Ich bin eine tüchtige Person, die ihre Arbeit immer erledigt.	1	2	3	4	5
51. Ich fühle mich oft hilflos und wünsche mir eine Person, die meine Probleme löst.	1	2	3	4	5
52. Ich bin ein sehr aktiver Mensch.	1	2	3	4	5
53. Ich bin sehr wissbegierig.	1	2	3	4	5
54. Wenn ich Menschen nicht mag, so zeige ich ihnen das auch offen.	1	2	3	4	5
55. Ich werde wohl niemals fähig sein, Ordnung in mein Leben zu bringen.	1	2	3	4	5
56. Manchmal war mir etwas so peinlich, dass ich mich am liebsten versteckt hätte.	1	2	3	4	5
57. Lieber würde ich meine eigenen Wege gehen, als eine Gruppe anzuführen.	1	2	3	4	5
58. Ich habe oft spaß daran, mit Theorien oder abstrakten Ideen zu spielen.	1	2	3	4	5
59. Um zu bekommen, was ich will, bin ich notfalls bereit, Menschen zu manipulieren.	1	2	3	4	5
60. Bei allem, was ich tue, strebe ich nach Perfektion.	1	2	3	4	5

Appendix B.4   STAI-T (Studies 1-3)

Anleitung: Im folgenden Fragebogen finden Sie eine Reihe von Feststellungen, mit denen man sich selbst beschreiben kann. Bitte lesen Sie jede Feststellung durch und wählen Sie aus den vier Antworten diejenige aus, die angibt, wie Sie sich *im Allgemeinen* fühlen. Kreuzen Sie bitte bei jeder Feststellung das Kästchen unter der von Ihnen gewählten Antwort an. Es gibt keine richtigen oder falschen Antworten. Überlegen Sie bitte nicht lange und denken Sie daran, diejenige Antwort auszuwählen, die am besten beschreibt, wie Sie sich *im Allgemeinen* fühlen.

	überhaupt nicht	ein wenig	ziemlich	stark
21. Ich bin vergnügt.				
22. Ich werde schnell müde.				
23. Mir ist zum Weinen zumute.				
24. Ich glaube, es geht mir schlechter als anderen Leuten.				
25. Ich verpasse günstige Gelegenheiten, weil ich mich nicht schnell genug entscheiden kann.				
26. Ich fühle mich ausgeruht.				
27. Ich bin ruhig und gelassen.				
28. Ich glaube, daß mir meine Schwierigkeiten über den Kopf wachsen.				
29. Ich mache mir zuviel Gedanken über unwichtige Dinge.				
30. Ich bin glücklich.				
31. Ich neige dazu, alles schwer zu nehmen.				
32. Mir fehlt es an Selbstvertrauen.				
33. Ich fühle mich geborgen.				
34. Ich mache mir Sorgen über mögliches Missgeschick.				
35. Ich fühle mich niedergeschlagen.				
36. Ich bin zufrieden.				
37. Unwichtige Gedanken gehen mir durch den Kopf und bedrücken mich.				
38. Enttäuschungen nehme ich so schwer, dass ich sie nicht vergessen kann.				
39. Ich bin ausgeglichen.				
40. Ich werde nervös und unruhig, wenn ich an meine derzeitigen Angelegenheiten denke.				

Appendix B.5   TAS-20 (Studies 1-3)

Bitte geben Sie den Grad Ihrer Zustimmung zu den folgenden zwanzig Aussagen auf der fünfpuntigen Skala an. (1 - trifft <u>nicht</u> zu; 5 - trifft <u>absolut</u> zu)

		trifft **nicht** zu			trifft **absolut** zu	
11.	Mir ist oft unklar, welche Gefühle ich gerade habe.	1	2	3	4	5
12.	Es fällt mir schwer, die richtigen Worte für meine Gefühle zu finden.	1	2	3	4	5
13.	Ich habe körperliche Empfindungen, die sogar die Ärzte nicht verstehen.	1	2	3	4	5
14.	Es fällt mir leicht, meine Gefühle zu beschreiben.	1	2	3	4	5
15.	Ich gehe lieber Problemen auf den Grund, als sie nur zu beschreiben.	1	2	3	4	5
16.	Wenn mich etwas aus der Fassung gebracht hat, weiß ich oft nicht, ob ich traurig, ängstlich oder wütend bin.	1	2	3	4	5
17.	Ich bin oft über Vorgänge in meinem Körper verwirrt.	1	2	3	4	5
18.	Ich lasse die Dinge lieber einfach geschehen und versuche nicht herauszufinden, warum sie gerade so passiert sind.	1	2	3	4	5
19.	Einige Gefühle kann ich gar nicht richtig benennen.	1	2	3	4	5
20.	Sich mit Gefühlen zu beschäftigen finde ich sehr wichtig.	1	2	3	4	5
21.	Ich finde es schwierig zu beschreiben, was ich für andere Menschen empfinde.	1	2	3	4	5
22.	Andere fordern mich auf, meine Gefühle mehr zu beschreiben.	1	2	3	4	5
23.	Ich weiß nicht, was in mir vorgeht.	1	2	3	4	5
24.	Ich weiß oft nicht, warum ich wütend bin.	1	2	3	4	5
25.	Ich unterhalte mich mit anderen nicht so gerne über ihre Gefühle, sondern lieber darüber, womit sie sich täglich beschäftigen.	1	2	3	4	5
26.	Ich sehe mir lieber „leichte" Unterhaltungsstücke als psychologische Problemfilme an.	1	2	3	4	5
27.	Es fällt mir schwer, selbst engen Freunden gegenüber meine innersten Gefühle mitzuteilen.	1	2	3	4	5
28.	Ich kann mich jemandem sogar in Augenblicken des Schweigens sehr nahe fühlen.	1	2	3	4	5
29.	Ich finde, daß das Mir-Klarwerden über meine Gefühle wichtig ist, wenn ich persönliche Probleme lösen muß.	1	2	3	4	5
30.	Durch die Suche nach verborgenen Bedeutungen nimmt man sich das Vergnügen an Filmen oder Theaterstücken.	1	2	3	4	5

Appendix B.6 TCI-HA (Study 3)

In diesem Fragebogen werden Sie Äußerungen finden, mit denen Menschen Ihre Meinungen, Einstellungen, Interessen oder andere persönliche Gefühle ausdrücken. Jede Aussage kann mit ja oder nein beantwortet werden. Lesen Sie sich diese Aussagen durch und entscheiden Sie, was für Sie am besten zutrifft. Wir bitten Sie, dass Sie diesen Fragebogen selbständig ausfüllen und vollständig ausgefüllt zurückgeben.

Vorgehensweise:

Bitte kreuzen sie „J" für ja bzw. richtig oder „N" für nein bzw. falsch nach jeder Aussage an.

z.B.

„Ich verstehe, wie dieser Fragebogen ausgefüllt werden soll."

   J   N

Lesen Sie bitte alles sorgfältig durch und antworten Sie ohne lange zu überlegen. Bitte beantworten Sie jede Frage, auch wenn Sie sich der Antwort nicht ganz sicher sind. Bitte denken Sie daran, dass es keine richtigen oder falschen Antworten auf die Aussagen gibt. Sie beschreiben nur Ihre eigenen Einstellungen und Gefühle.

_____

2. Ich bin mir meistens sicher, dass alles gut laufen wird, sogar in Situationen, die andere beunruhigend finden.

   J   N

12. Ich fühle mich in neuen Situationen oft angespannt und beunruhigt, auch wenn andere meinen, es gäbe nichts, worüber man sich Sorgen machen müsste.

   J   N

20. Ich muss oft das, was ich gerade tue abbrechen, weil ich mir Sorgen darüber mache, was eventuell schief gehen könnte.

   J   N

22. Ich habe weniger Energie und ermüde schneller als die meisten Menschen.

   J   N

26. Meistens würde ich es bevorzugen, etwas zu tun, was ein gewisses Risiko beinhaltet (wie z. B. mit einem schnellen Auto über steile Berge und um scharfe Kurven zu fahren), anstelle für ein paar Stunden ruhig und passiv zu bleiben.

   J   N

27. Ich vermeide es oft, Fremde kennenzulernen, da ich Unbekannten gegenüber kein Vertrauen aufbringen kann.

   J   N

42. Ich glaube, dass ich in der Zukunft viel Glück haben werde.

   J   N

43. Ich erhole mich langsamer als die meisten anderen Menschen von kleineren Erkrankungen und Stress.

J   *N*

54. Wenn ich eine Gruppe Fremder treffe, bin ich schüchterner als die meisten Menschen.

J   *N*

63. Ich brauche oft ein Nickerchen oder Extrapausen, weil ich so leicht ermüde.

J   *N*

65. Ungeachtet aller zeitweiligen Probleme, die ich überwinden muss, denke ich immer, dass es sich zum Besten wendet.

J   *N*

67. Ich bleibe normalerweise in Situationen, die die meisten Menschen als gefährlich empfinden, ruhig und gelassen.

J   *N*

80. Ich würde wahrscheinlich auch dann entspannt und offen einer Gruppe von Fremden gegenübertreten, wenn ich gehört hätte, dass diese unfreundlich sind.

J   *N*

81. Gewöhnlich bin ich besorgter als die meisten Menschen, dass in der Zukunft etwas schief gehen könnte.

J   *N*

92. Ich brauche besondere Ruhe, Sicherheit und Unterstützung, um mich von kleineren Erkrankungen oder Stress zu erholen.

J   *N*

112. Wenn ich blamiert oder erniedrigt wurde, komme ich sehr schnell darüber hinweg.

J   *N*

113. Ich finde es extrem schwierig, mich auf Veränderungen meiner normalen Handlungsweisen einzustellen, da ich dann angespannt, müde und besorgt werde.

J   *N*

119. Ich bin meist auch dann noch entspannt und sorglos, wenn fast alle schon Angst haben.

J   *N*

129. Ich fühle mich in neuen Situationen oft angespannt und besorgt, selbst wenn andere darin überhaupt keine Gefahr sehen.

J   *N*

142. Ich bin sehr selbstbewusst und fühle mich in nahezu allen Situationen sehr sicher.

J   *N*

147. Ich habe mehr Energie und ermüde nicht so schnell wie die meisten Menschen.

J   *N*

149. Ich unterbreche aus Sorge oft meine Tätigkeiten, auch wenn meine Freunde mir sagen, dass alles gut laufen wird.

J   *N*

154. Meistens bevorzuge ich etwas Risikoreiches (wie z. B. Fallschirmspringen oder Drachensegeln), anstatt für ein paar Stunden ruhig und passiv zu sein.

J   *N*

157. Fremden gegenüber bin ich überhaupt nicht schüchtern.

J   *N*

164. Ich grüble nie über furchtbare Dinge, die in der Zukunft passieren könnten.

J   *N*

182. Ich erhole mich schneller als andere von leichteren Erkrankungen oder Stress.

J   *N*

188. Gewöhnlich habe ich Glück, was immer ich auch tue.

J   *N*

189. Normalerweise bin ich mir sicher, dass ich mühelos Dinge tun kann, die andere als gefährlich ansehen würden (z. B. mit dem Auto schnell über nasse und vereiste Straßen fahren).

J   *N*

202. Normalerweise kann ich den ganzen Tag in Bewegung sein, ohne mich anstrengen zu müssen.

J   *N*

209. Ich glaube, dass ich selbstbewusst und entspannt bleiben würde beim Zusammentreffen mit Fremden, auch wenn mir erzählt würde, dass sie böse auf mich wären.

J   *N*

217. Ich fühle mich meistens angespannt und besorgt, wenn ich etwas Neues, Unbekanntes tun muss.

J   *N*

225. Irgend etwas läuft oft schief, wenn ich nicht besonders vorsichtig bin.

J   *N*

231. Gewöhnlich halte ich mich von Situationen fern, in denen ich fremde Menschen treffen müsste, auch wenn mir versichert wird, dass diese Leute nett wären.

J   *N*

236. Ich fühle mich im Allgemeinen selbstsicherer und energiegeladener als andere Menschen, auch nach kleineren Erkrankungen oder Stress.

J   *N*

Appendix B.7   WBSI (Studies 1-3)

In diesem Fragebogen geht es um Gedanken. Es gibt **keine richtige oder falsche Antwort**, bitte beantworten Sie die untenstehenden Fragen **wahrheitsgemäß,** wie es für Sie am ehesten zutrifft. Bitte achten Sie darauf, daß Sie **jede einzelne Frage** beantworten, indem Sie die passende Antwort ankreuzen.

	stimmt überhaupt nicht	stimmt eher nicht	neutral/weiß nicht	stimmt teilweise	stimmt vollkommen
31. Es gibt Dinge, über welche ich lieber nicht nachdenke.					
32. Manchmal frage ich mich, warum ich gerade diese Gedanken habe, die mir durch den Kopf gehen.					
33. Manche Gedanken kann ich nicht stoppen.					
34. Manchmal kommen mir Bilder in den Sinn, die ich nicht auslöschen kann.					
35. Meine Gedanken kreisen immer wieder um ein Thema.					
36. Ich wünschte, ich könnte aufhören, über bestimmte Dinge nachzudenken.					
37. Manchmal rasen mir Gedanken so schnell durch den Kopf, dass ich wünschte, ich könnte sie stoppen.					
38. Ich versuche immer, mir Probleme aus dem Sinn zu halten.					
39. Es gibt Gedanken, die sich immer wieder plötzlich aufdrängen.					
40. Es gibt Dinge, über die ich versuche nicht nachzudenken.					
41. Manchmal würde ich am liebsten einfach aufhören zu denken.					
42. Oft mache ich etwas, um mich von meinen Gedanken abzulenken.					
43. Es gibt Gedanken, die ich versuche zu vermeiden.					
44. Viele meiner Gedanken erzähle ich niemanden.					
45. Manchmal halte ich mich mit etwas beschäftigt, damit sich keine Gedanken aufdrängen.					

Appendix C Post-scan debriefings

Appendix C.1   General questions (Study 1 and 3)

Liebe Probandin, lieber Proband,
Vielen Dank für Ihre Mitarbeit!

Zum Schluss möchten wir Sie nun noch darum bitten, zunächst einige allgemeine Fragen zu Ihren Erfahrungen und Eindrücken während der gesamten Messung zu beantworten. Hierbei geht es darum, wie gut es Ihnen im Allgemeinen gelungen ist, Ihre Emotionen zu unterdrücken, welche Strategien Sie im Allgemeinen hierzu außer der von uns vorgeschlagenen genutzt haben, und wie sehr Sie nach Verschwinden der Bilder im Allgemeinen noch gedanklich mit diesen befasst gewesen sind.

Hiernach möchten wir Sie bitten, jedes einzelne Bild aus dem Experiment, also dort wo Sie die ausgelösten Emotionen zulassen oder unterdrücken sollten, nochmals einzeln zu beurteilen. Zu jedem Bild werden Sie gebeten anzugeben, wie angenehm oder unangenehm Sie das jeweilige Bild grundsätzlich und unabhängig von der Instruktion finden, welche Instruktion vor dem jeweiligen Bild gegeben wurde und falls Sie Ihre Emotionen unterdrücken sollten, wie erfolgreich Sie bei dem jeweiligen Bild dabei waren.

Doch zunächst die allgemeinen Fragen…

1) Wie gut konnten Sie Ihre Emotionen im Experiment unterdrücken?

1	2	3	4	5	6	7	8	9
überhaupt nicht								perfekt

2) Haben Sie versucht, sich angesichts der zu unterdrückenden Bilder, wie von uns vorgeschlagen, in die Position eines neutralen Beobachters zu versetzen?

1	2	3	4	5	6	7	8	9
nie			manchmal					immer

3) Wie hilfreich erscheint Ihnen diese Technik, um sich den Bildern emotional zu entziehen?

1	2	3	4	5	6	7	8	9
nicht hilfreich								sehr hilfreich

4) Welche Strategien haben Sie benutzt, um Ihre Gefühle zu unterdrücken? Bitte geben Sie für alle unten aufgeführten Strategien ungefähre Prozentzahlen an!

- Die von uns vorgeschlagene Strategie, sich in die Position eines neutralen Betrachters zu versetzen in _____ % der Fälle

- Eine andere, nämlich…
  - Nicht richtig hingeschaut in _____ % der Fälle.
  - An etwas anderes gedacht in _____ % der Fälle.
  - Mir eine Geschichte dazu ausgedacht, die nicht so schlimm ist in _____ % der Fälle
  - Mich auf Details im Bild konzentriert in _____ % der Fälle.
  - Sonstige Strategien in _____ % der Fälle (bitte ausführen!)

    _____
    _____
    _____
    _____
    _____
    _____

Sind Sie nach Ende eines Durchgangs oder zwischendurch eingeschlafen?

Ja ☐   Nein ☐

Appendix C.2   General questions (Study 2)

Vielen Dank für Ihre Mitarbeit! Nun würden wir Sie noch bitten, abschließend die folgenden Fragen zu Ihren Erfahrungen und Eindrücken während der Messung zu beantworten.

Doch zunächst die allgemeinen Fragen…

1) Wie gut konnten Sie Ihre Emotionen im Experiment unterdrücken?

    1   2   3   4   5   6   7   8   9
    überhaupt nicht   perfekt

2) Haben Sie versucht, sich angesichts der zu unterdrückenden Bilder, wie von uns vorgeschlagen, in die Position eines neutralen Beobachters zu versetzen?

    1   2   3   4   5   6   7   8   9
    nie   manchmal   immer

3) Wie hilfreich erscheint Ihnen diese Technik, um sich den Bildern emotional zu entziehen?

    1   2   3   4   5   6   7   8   9
    nicht hilfreich   sehr hilfreich

4) Welche Möglichkeiten haben Sie benutzt, um Ihre Gefühle zu unterdrücken? Bitte geben Sie ungefähre Prozentzahlen an.

- Die von uns vorgeschlagene Strategie, sich in die Position eines neutralen Betrachters zu versetzen (_____ %)
- Eine andere
  - Nicht richtig hingeschaut (_____ %)
  - An etwas anderes gedacht (_____ %)
  - Mir eine Geschichte ausgedacht, die nicht so schlimm ist – Bitte Beispiele angeben (_____ %)
  - Ich habe mich auf Details im Bild konzentriert (_____ %)
  - Sonstiges (bitte ausführen!)

Appendix C.3   Questions regarding each stimulus category

(Study 1)

Für die Beantwortung der Fragen 5 – 12 stehen Ihnen folgende Möglichkeiten zur Verfügung:

1--------2--------3-------4-------5--------6--------7------- 8--------9

trifft **nicht** zu   trifft **völlig** zu

Die Fragen 5 und 6 betreffen **nur** die eher **EMOTIONALEN** Bilder beim „**Unterdrücken**".

5) Wie war ihr **Zustand**, nachdem die Bilder vom Bildschirm verschwunden waren?	Trifft **nicht** zu							Trifft **völlig** zu
Ich war erleichtert.	1	2	3	4	5	6	7	8	9
Ich war emotional entspannt.	1	2	3	4	5	6	7	8	9
Ich war emotional stärker beteiligt als beim Bild selbst.	1	2	3	4	5	6	7	8	9
6) Was haben sie **gedanklich** gemacht, nachdem die Bilder verschwunden waren?	Trifft **nicht** zu							Trifft **völlig** zu
Ich habe mich weiter mit den Bildern beschäftigt.	1	2	3	4	5	6	7	8	9
Ich habe weiter versucht, meine Emotionen zu unterdrücken.	1	2	3	4	5	6	7	8	9
Ich habe an andere Dinge gedacht.	1	2	3	4	5	6	7	8	9

Die Fragen 7 und 8 betreffen **nur** die eher **EMOTIONALEN** Bilder beim „**Zulassen**".

7) Wie war ihr **Zustand**, nachdem die Bilder vom Bildschirm verschwunden waren?	Trifft **nicht** zu							Trifft **völlig** zu
Ich war erleichtert.	1	2	3	4	5	6	7	8	9
Ich war emotional entspannt.	1	2	3	4	5	6	7	8	9
Ich war emotional stärker beteiligt als beim Bild selbst.	1	2	3	4	5	6	7	8	9
8) Was haben sie **gedanklich** gemacht, nachdem die Bilder verschwunden waren?	Trifft **nicht** zu							Trifft **völlig** zu
Ich habe mich weiter mit den Bildern beschäftigt.	1	2	3	4	5	6	7	8	9
Ich habe weiter versucht, meine Emotionen zu zuzulassen.	1	2	3	4	5	6	7	8	9
Ich habe an andere Dinge gedacht.	1	2	3	4	5	6	7	8	9

(same for neutral)

Appendix C.4   Questions regarding each stimulus category

(Study 2)

Für die Beantwortung der folgenden Fragen stehen Ihnen folgende Möglichkeiten zur Verfügung:

1--------2--------3-------4-------5--------6--------7------- 8--------9
trifft **nicht** zu   trifft **völlig** zu

Die Fragen 5 - 9 betreffen **nur** die eher **EMOTIONALEN** Bilder beim „**Unterdrücken**".

	Trifft **nicht** zu							Trifft **völlig** zu
5) Wie gut ist es ihnen gelungen, die durch das Bild hervorgerufenen Emotionen während der Haltephase weiter zu unterdrücken?								
Es ist mir sehr gut gelungen.	1 2 3 4 5 6 7 8 9							
Es ist mir gar nicht gelungen.	1 2 3 4 5 6 7 8 9							
6) Hat sich ihr Zustand im Vergleich zu vorher verändert, während sie die hervorgerufenen Emotionen in der Haltephase weiter unterdrücken sollten?								
Ich war emotional weniger beteiligt als beim Bild selbst.	1 2 3 4 5 6 7 8 9							
Ich war emotional stärker beteiligt als beim Bild selbst.	1 2 3 4 5 6 7 8 9							
Es gab keine Veränderung	1 2 3 4 5 6 7 8 9							
7) Was haben sie gedanklich während der Haltephase gemacht?								
Ich habe mir die Bilder vorgestellt.	1 2 3 4 5 6 7 8 9							
Ich habe an andere Dinge gedacht.	1 2 3 4 5 6 7 8 9							
8) Wie war ihr **Zustand**, nachdem sie den durch die Bilder erzeugten Eindruck nicht mehr unterdrücken sollten?								
Ich war erleichtert.	1 2 3 4 5 6 7 8 9							
Ich war emotional entspannt.	1 2 3 4 5 6 7 8 9							
Ich war emotional stärker beteiligt als beim Bild selbst.	1 2 3 4 5 6 7 8 9							
9) Was haben sie **gedanklich** gemacht, nachdem die Haltephase vorbei war?								
Ich habe mich weiter mit den Bildern beschäftigt.	1 2 3 4 5 6 7 8 9							
Ich habe weiter versucht, meine Emotionen zu unterdrücken.	1 2 3 4 5 6 7 8 9							
Ich habe an andere Dinge gedacht.	1 2 3 4 5 6 7 8 9							

Die Fragen 10 - 14 betreffen **nur** die eher **EMOTIONALEN** Bilder beim „**Zulassen**".

	Trifft **nicht** zu	Trifft **völlig** zu
10) Wie gut ist es ihnen gelungen, die durch das Bild hervorgerufenen Emotionen während der Haltephase weiter zuzulassen?		

Es ist mir sehr gut gelungen.	1	2	3	4	5	6	7	8	9
Es ist mir gar nicht gelungen.	1	2	3	4	5	6	7	8	9

11) Hat sich ihr Zustand im Vergleich zu vorher verändert, während sie die hervorgerufenen Emotionen in der Haltephase weiter zulassen sollten?

Trifft **nicht** zu   Trifft **völlig** zu

Ich war emotional weniger beteiligt als beim Bild selbst.	1	2	3	4	5	6	7	8	9
Ich war emotional stärker beteiligt als beim Bild selbst.	1	2	3	4	5	6	7	8	9
Es gab keine Veränderung	1	2	3	4	5	6	7	8	9

12) Was haben sie gedanklich während der Haltephase gemacht?

Trifft **nicht** zu   Trifft **völlig** zu

Ich habe mir die Bilder vorgestellt.	1	2	3	4	5	6	7	8	9
Ich habe an andere Dinge gedacht.	1	2	3	4	5	6	7	8	9

12) Wie war ihr **Zustand**, nachdem sie den durch die Bilder erzeugten Eindruck nicht mehr zulassen sollten?

Trifft **nicht** zu   Trifft **völlig** zu

Ich war erleichtert.	1	2	3	4	5	6	7	8	9
Ich war emotional entspannt.	1	2	3	4	5	6	7	8	9
Ich war emotional stärker beteiligt als beim Bild selbst.	1	2	3	4	5	6	7	8	9

14) Was haben sie **gedanklich** gemacht, nachdem die Haltephase vorbei war?

Trifft **nicht** zu   Trifft **völlig** zu

Ich habe mich weiter mit den Bildern beschäftigt.	1	2	3	4	5	6	7	8	9
Ich habe weiter versucht, meine Emotionen zu unterdrücken.	1	2	3	4	5	6	7	8	9
Ich habe an andere Dinge gedacht.	1	2	3	4	5	6	7	8	9

(same for neutral)

Appendix C.5   Questions regarding each stimulus category

(Study 3)

Für die Beantwortung der Fragen 5 – 12 stehen Ihnen folgende Möglichkeiten zur Verfügung:

1--------2--------3-------4-------5--------6--------7------- 8--------9

trifft **nicht** zu   trifft **völlig** zu

Die Fragen 5 und 6 betreffen **nur** die eher **Angst erregenden** Bilder beim „**Zulassen**".

5) Wie war ihr **Zustand**, nachdem die Bilder vom Bildschirm verschwunden waren?	Trifft **nicht** zu						Trifft **völlig** zu		
Ich war erleichtert.	1	2	3	4	5	6	7	8	9
Ich war emotional entspannt.	1	2	3	4	5	6	7	8	9
Ich war emotional stärker beteiligt als beim Bild selbst.	1	2	3	4	5	6	7	8	9
6) Was haben sie **gedanklich** gemacht, nachdem die Bilder verschwunden waren?	Trifft **nicht** zu						Trifft **völlig** zu		
Ich habe mich weiter mit den Bildern beschäftigt.	1	2	3	4	5	6	7	8	9
Ich habe weiter versucht, meine Emotionen zuzulassen.	1	2	3	4	5	6	7	8	9
Ich habe an andere Dinge gedacht.	1	2	3	4	5	6	7	8	9

Die Fragen 7 und 8 betreffen **nur** die eher **Angst erregenden** Bilder beim „**Unterdrücken**".

6) Wie war ihr **Zustand**, nachdem die Bilder vom Bildschirm verschwunden waren?	Trifft **nicht** zu						Trifft **völlig** zu		
Ich war erleichtert.	1	2	3	4	5	6	7	8	9
Ich war emotional entspannt.	1	2	3	4	5	6	7	8	9
Ich war emotional stärker beteiligt als beim Bild selbst.	1	2	3	4	5	6	7	8	9
7) Was haben sie **gedanklich** gemacht, nachdem die Bilder verschwunden waren?	Trifft **nicht** zu						Trifft **völlig** zu		
Ich habe mich weiter mit den Bildern beschäftigt.	1	2	3	4	5	6	7	8	9
Ich habe weiter versucht, meine Emotionen zu unterdrücken.	1	2	3	4	5	6	7	8	9
Ich habe an andere Dinge gedacht.	1	2	3	4	5	6	7	8	9

(same for disgust and neutral)

Appendix C.6   Picture ratings (Studies 1 – 2)

1	**(a) Wie unangenehm oder angenehm finden Sie das Bild im Allgemeinen?**

1

(a) Wie unangenehm oder angenehm finden Sie das Bild im Allgemeinen?

    1   2   3   4   5   6   7   8   9
    ☹   ☺   ☺

(b) Wie beruhigend oder aufregend finden Sie das Bild im Allgemeinen?

    1   2   3   4   5   6   7   8   9
beruhigend   aufregend

(c) Geben Sie an, ob sie bei diesem Bild *„unterdrücken"* oder *„zulassen"* sollten.

    □ unterdrücken   □ zulassen

(d) Sofern Sie unterdrücken ankreuzen, wie erfolgreich waren Sie dabei?

    1   2   3   4   5   6   7   8   9
überhaupt nicht   perfekt

(same for all pictures)

Appendix C.7   Picture ratings (Study 3)

1

(a) Wie unangenehm oder angenehm finden Sie das Bild im Allgemeinen?

    1   2   3   4   5   6   7   8   9
    ☹   ☺   ☺

(b) Wie beruhigend oder aufregend finden Sie das Bild im Allgemeinen?

    1   2   3   4   5   6   7   8   9
beruhigend   aufregend

(c) Welcher der folgenden Emotionen würden Sie dieses Bild zuordnen?

□ Überraschung □ Ekel □ Angst □ Ärger □ Freude □ Trauer □ Sonstige

(d) Geben Sie an, ob sie bei diesem Bild *„unterdrücken"* oder *„zulassen"* sollten.

    □ unterdrücken   □ zulassen

(d) Sofern Sie unterdrücken ankreuzen, wie erfolgreich waren Sie dabei?

    1   2   3   4   5   6   7   8   9
überhaupt nicht   perfekt

(same for all pictures)

ERKLÄRUNG

gemäß § 5 (1) Satz 5 der Promotionsordnung der Fakultät Mathematik und Naturwissenschaften der Technischen Universität Dresden

Hiermit versichere ich, dass ich die vorliegende Arbeit „The temporal dynamics of volitional emotion regulation" ohne unzulässige Hilfe Dritter und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe; die aus fremden Quellen direkt oder indirekt übernommenen Gedanken sind als solche kenntlich gemacht. Die Arbeit wurde bisher weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde vorgelegt.

Die Arbeit wurde am Institut für Allgemeine Psychologie, Biopsychologie und Methoden der Psychologie der Technischen Universität Dresden unter wissenschaftlicher Betreuung von Prof. Dr. phil. habil. Thomas Goschke angefertigt.

Die Promotionsordnung der Fakultät Mathematik und Naturwissenschaften vom 20. März 2000 erkenne ich an.

Hannover,

Dina Schardt