

# The Influence of Individual Differences on Neural Correlates of Emotional and Cognitive Information Processes

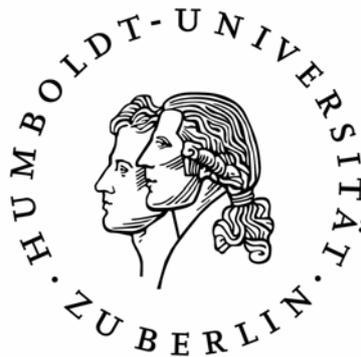
## Dissertation

zur Erlangung des akademischen Grades Doctor rerum naturalium (Dr. rer. nat.)

im Fach Psychologie

eingereicht an der Mathematisch-Naturwissenschaftlichen Fakultät II

der Humboldt-Universität zu Berlin



Von Dipl.-Psych. Katja Mériaux, MSc  
geb. 10. Januar 1976 in Erlangen

Prof. Dr. Christoph Marksches  
Präsident

Prof. Dr. Wolfgang Coy  
Dekan

Gutachterin/Gutachter:

Prof. Dr. Elke van der Meer

Prof. Dr. med. Dr. phil. Henrik Walter

Dr. Hauke R. Heekeren

Tag der Verteidigung: 29.11.2007

**TO MY PARENTS**

## **ACKNOWLEDGEMENTS**

This work in its present form would not have been possible without the adept and always motivating support of my supervisors Elke van der Meer and Hauke R. Heekeren, from whose expertise and experience I profited greatly. I also would like to thank Isabell Wartenburger for her patient help of many kinds.

Many thanks to Arno Villringer - I am glad to have had the great opportunity to work at the Berlin NeuroImaging Center.

Furthermore, my cordial gratitude goes to Kristin Prehn, Philipp Kazzner, and Thomas Dresler and special thanks to Jörn, Francisco and Charlotte.

Last but not least, I want to express my deepest gratitude to my family, for everything that has to do and does not have to do with this work.

July, 2007

## **ABSTRACT**

Modern multi-level theories claim that emotion may be generated by different ways using different processes. The dual memory model of emotion refers to these processes as schematic processing (automatic) and propositional processing (controlled). The model further integrates emotion regulatory strategies, such as re-direction of attention and emotional elaboration as essential components of emotion processing. However, research on the neurobiological correlates of the different processing modes is scarce. Hence, the present work focuses on the identification of behavioral and neural correlates of the hypothesized processing modes and how these are modulated by individual differences in affectivity and in the cognitive processing of emotions.

Individual differences in state negative affect were associated with altered activity in the insula during schematic processing of negative emotional information. This may indicate increased processing of the hedonic dimension of aversive stimuli in individuals with high state negative affect. Individual differences in state anxiety and in the cognitive processing of emotions modulated behavioral and neural correlates of propositional processing of emotional information. Specifically, in individuals with high state anxiety and with difficulties to cognitively process emotions, re-direction of attention was associated with increased cognitive effort. Findings at the neural level indicate that re-direction of attention as compared to elaboration of emotional information may represent a less effective emotion regulatory strategy in individuals with difficulties to cognitively process emotions.

## ZUSAMMENFASSUNG

Moderne Mehr-Ebenen-Ansätze gehen davon aus, dass Emotionen auf unterschiedlichen Ebenen der Informationsverarbeitung und durch unterschiedliche Prozesse erzeugt werden. Im Rahmen des ‘dual memory model of emotion’ werden diese Prozesse als schematische (automatische) und propositionale (kontrollierte) Verarbeitungsprozesse bezeichnet. Darüber hinaus integriert das Modell Strategien zur Emotionsregulation, wie Aufmerksamkeitslenkung und semantische Elaborierung emotionaler Information. Über die zugrundeliegenden neuronalen Korrelate weiß man bisher allerdings noch wenig. Die vorliegende Arbeit konzentriert sich auf die Identifizierung behavioraler und neuronaler Korrelate der schematischen und propositionalen Verarbeitungsprozesse und wie diese durch interindividuelle Differenzen in der Affektivität und in der kognitiven Verarbeitung von Emotionen moduliert werden.

Interindividuelle Differenzen im aktuellen negativen Affekt waren mit Aktivitätsveränderungen in der Insula während der schematischen Verarbeitung negativer Stimuli assoziiert. Dies kann als verstärkte Verarbeitung des hedonischen Wertes negativer Stimuli in Individuen mit hohem aktuellen negativen Affekt interpretiert werden. Interindividuelle Differenzen in der Zustandsangst und im kognitiven Verarbeiten von Emotionen modulierten behaviorale und neuronale Korrelate propositionaler Verarbeitungsprozesse. Hohe Zustandsangst und Schwierigkeiten im kognitiven Verarbeiten von Emotionen waren assoziiert mit erhöhtem kognitiven Aufwand, wenn der emotionale Gehalt der Stimuli ignoriert werden musste. Die neuronalen Befunde deuten darauf hin, dass für Individuen mit Schwierigkeiten im kognitiven Verarbeiten von Emotionen Aufmerksamkeitslenkung im Vergleich zu Elaborierung emotionaler Informationen eine weniger effektive Strategie zur Emotionsregulation darstellt.

## TABLE OF CONTENTS

<b>1</b>	<b>Introduction.....</b>	<b>1</b>
<b>1.1</b>	<b>Cognitive Theories of Emotion.....</b>	<b>3</b>
1.1.1	The Dual Memory Model of Emotion.....	4
<b>1.2</b>	<b>Neuroanatomy of Emotion .....</b>	<b>10</b>
1.2.1	The Prefrontal Cortex.....	11
1.2.2	The Anterior Cingulate Cortex.....	11
1.2.3	The Amygdala .....	13
1.2.4	The Insular Cortex .....	14
<b>1.3</b>	<b>Individual Differences in Affectivity .....</b>	<b>15</b>
1.3.1	Anxiety .....	16
1.3.2	Negative Affect.....	17
1.3.3	Impairment in the Cognitive Processing of Emotions (Alexithymia) .....	18
<b>2</b>	<b>Open questions and Hypotheses .....</b>	<b>19</b>
<b>3</b>	<b>Methods .....</b>	<b>23</b>
<b>3.1</b>	<b>Psychophysics.....</b>	<b>23</b>
<b>3.2</b>	<b>Psychometrics.....</b>	<b>23</b>
3.2.1	The Positive and Negative Affect Schedule .....	23
3.2.2	The State-Trait Anxiety Inventory .....	24
3.2.3	The Toronto Alexithymia Scale-26.....	24
<b>3.3</b>	<b>Psychophysiology .....</b>	<b>25</b>
3.3.1	Principles and Technique .....	25
<b>3.4</b>	<b>Functional Magnetic Resonance Imaging.....</b>	<b>25</b>
3.4.1	Principles and Technique .....	25
3.4.2	Data Acquisition and Analysis.....	26

4	Experiments .....	28
4.1	The influence of word valence, word arousal, and individual differences in anxiety on emotional interference .....	28
4.2	The influence of individual differences in state negative affect on neural correlates of passive viewing of aversive stimuli.....	32
4.3	The influence of individual differences in cognitive processing of emotions on neural correlates of perceptual decision-making on emotional stimuli .....	36
5	Discussion and Conclusion.....	41
	REFERENCES .....	48
	RESEARCH ARTICLES .....	61
I	Emotional Stroop Test: Effect of Word Arousal and Subject Anxiety on Emotional Interference. Dresler T, Mériaux K, Heekeren HR, van der Meer E, 2007. (Submitted).....	61
II	Insular activity during passive viewing of aversive stimuli reflects individual differences in state negative affect. Mériaux K, Wartenburger I, Kazzner P, Prehn K, Villringer A, van der Meer E, Heekeren HR, 2007. (Submitted) .....	18
III	A neural network reflecting individual differences in cognitive processing of emotions during perceptual decision making. Mériaux K, Wartenburger I, Kazzner P, Prehn K, Lammers CH, van der Meer E, Villringer A, Heekeren HR, 2006. Neuroimage 33(3): 1016-27. ....	46
	SUPPLEMENTS .....	47
	PUBLICATIONS .....	48
	STATEMENT OF AUTHORSHIP.....	50

## GLOSSAR

ACC	anterior cingulate cortex
ANS	autonomous nervous system
BOLD	blood-oxygen-level dependent
dACC	dorsal anterior cingulate cortex
dIPFC	dorsolateral prefrontal cortex
fMRI	functional magnetic resonance imaging
PANAS	Positive and Negative Affect Schedule
PFC	prefrontal cortex
PPI	psychophysiological interaction analysis
SCL	skin conductance level
SNA	state negative affect
STAI	State-Trait Anxiety Inventory
TAS	Toronto Alexithymia Scale
vIPFC	ventrolateral prefrontal cortex

# 1 INTRODUCTION

Emotions represent a fundamental aspect of human experience and consciousness and have a significant impact on health and psychological well-being. They embody the hedonic tone of an event for the individual and motivate goal-oriented behavior by prompting adaptive actions.

By initiating approach- or withdrawal-related behavior emotions keep an organism's homeostatic equilibrium (Damasio, 1994; Panksepp et al., 1997; Damasio, 1999). As a genetically coded automatism they involve changes at the physiological level (e.g. secretion of hormones, changes in muscle tension), at the expressive-motor level (e.g. changes in mimic and body posture) and changes at the level of subjective experience. Subjectively experienced emotional states can be characterized by the dimensions valence and arousal<sup>1</sup> (Wundt, 1924; for a review see Feldman-Barrett & Russell, 1999). Valence represents the hedonic tone of an emotion (i.e., pleasure - displeasure), whereas activation or arousal refers to the energy level of the emotion (i.e., sleep - arousal). However, it is still a matter of debate which dimension has a greater influence on information processing.

Recent approaches in cognitive psychology, namely multi-level theories of emotions, conceptualize emotions as a result of both controlled cognitive appraisal and automatic, reflex-like processes that provide the organism with quick physiological and behavioral responses appropriate to the situation (Leventhal, 1980; Leventhal & Scherer, 1987; Power & Dalgleish, 1999; Teasdale, 1999; Smith & Kirby, 2000; Philippot & Schaefer, 2001; Philippot et al., 2004). However, these theories have barely been tested on neurobiological grounds (but see Schaefer et al., 2003). Moreover, when investigating emotional processing one has to bear in mind that there is considerable variability in the nature and strength of emotional responses among individuals. For this reason, the precise nature of behavioral and neural mechanisms of emotion processing

---

<sup>1</sup> A third dimension of emotional experience defined by Wundt is *activation* which is characterized by the poles tension vs. relief.

may only be revealed when such interindividual variability is considered (Davidson & Irwin, 1999; Davidson, 2003a; Hamann & Canli, 2004; Canli et al., 2004; Dalgleish, 2004; Thompson-Schill et al., 2005; Fitzgerald et al., 2006).

Hence, the present work aims at elucidating behavioral and neurobiological correlates of how individual differences in affectivity or cognitive processing of emotions modulate automatic and controlled emotion processes as characterized by multi-level theories. Considering how automatic and controlled processes affect human emotional well-being and social behavior it is valuable to elucidate its behavioral and neural basis.

## 1.1 Cognitive Theories of Emotion

Early cognitive theories of emotion (Schachter & Singer, 1962; Lazarus, 1966) defended the notion that no emotion can arise without a cognitive appraisal process that evaluates the significance of a stimulus for the organism. More recent multi-level theories of emotion, however, suggest that emotions may be generated by various ways using different processes (Leventhal, 1980; Leventhal & Scherer, 1987; Power & Dalgleish, 1999; Teasdale, 1999; Smith & Kirby, 2000; Philippot & Schaefer, 2001; Philippot et al., 2004). They propose that emotions may not only be generated by cognitive appraisal but also by automatic, reflex-like processes. The need for such a 'second route' (Power & Dalgleish, 1999) to emotion is based on evidence that emotions have an innate and genetically anchored component that works independently of controlled appraisal processes. For instance, the biological preparedness that renders humans more vulnerable to develop phobias towards spiders or snakes than to cars or footballs supports the notion that biologically anchored mechanisms mediate (aversive) emotional experience (Seligman, 1971). Similarly, the fact that basic emotions have universal mimic expressions argues for an innate component of emotion generation (Ekman, 1992).

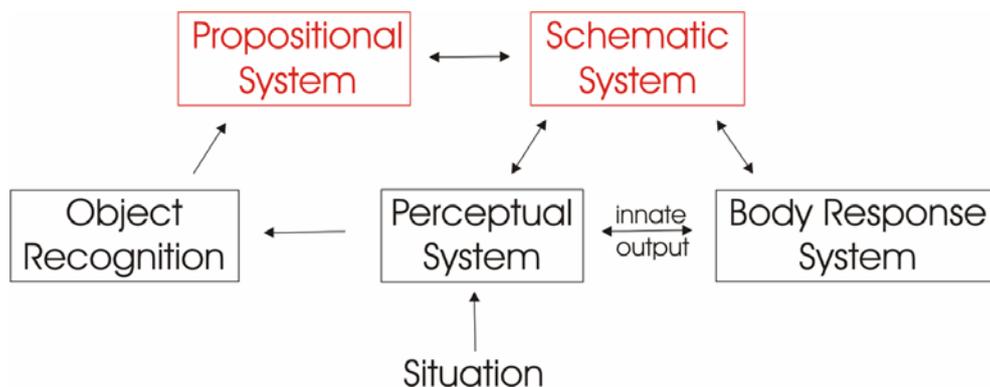
Within multi-level theories, the different processes by which emotions can be generated are typically integrated in a hierarchical processing system that consists of different levels of varying degrees of abstraction. Most theories specify processes of emotion generation, but do neglect processes of emotion regulation that maintain, accentuate, or attenuate an emotional response. However, as they constitute an essential part of emotion processing, a complete account of emotion should consider emotion regulatory mechanisms. In this regard, the dual memory model of emotion by Philippot et al. (2001, 2004) is the most comprehensive multi-level model of emotion as it integrates a process model of emotion with processes of emotion regulation.

The following chapter gives detailed insight into this multi-level model of emotion.

### 1.1.1 The Dual Memory Model of Emotion

The model distinguishes between type of memory activated, so-called *structure*, and the type of *processes* operating at these levels.

At the *structural* level, two types of emotional memory systems are proposed: the schematic system and the propositional system (Philippot & Schaefer, 2001; Philippot et al., 2004). These two types represent a distinction common to all multi-level models of emotions: the schematic system refers to an automatic and implicit memory that conveys the emotional meaning of a situation to an individual, the propositional systems pertains to declarative conceptual knowledge about emotions. They receive their input from different systems and in turn feed into different output systems (see Figure 1 for the schematic and the propositional system as well as other structures defined by the dual memory model of emotion).



**Figure 1: Architecture of the Dual Memory Model of Emotion.** In the perceptual system the raw sensory input is analyzed to extract basic perceptual features in a modality-dependent manner. Perceptual systems represent innate structures and have an innate output to the body response system thereby automatically triggering autonomic and behavioral body responses. The schematic system refers to an implicit memory that conveys immediate emotional meaning of a situation for a given individual. Perceptual features are fed into the object recognition system which allows for the construction of discrete mental representation, the concepts that are the building blocks of the propositional system. The propositional system consists of declarative knowledge about emotion. In contrast to the schematic system, the propositional system is specific and has “truth validity”, that is, can be declared true or false (adapted from Philippot et al., 2004).

The schematic system is based on schemata. A schema is an implicit memory that integrates sensory, perceptual, and semantic information of a given category of emotional experiences, on the one hand, and their relation to the activation of specific body response systems, on the other

hand. The authors suggest that a schema may be conceptualized as the records of an individual's emotional classical conditioning. Repeated activation of perceptual features and their innate connections to body response systems (see Figure 1) become integrated in an abstract representation to form a schema. The schema is not directly available to consciousness and information can only enter consciousness by direct experience. However, the content of a schema can be inferred by the feelings and body responses induced upon activation of a schema. Put briefly, the schema represents the core of emotional activation and provides the organism with wholly prepared, immediate response modes to situations in the environment.

In contrast, the propositional system consists of declarative knowledge about emotion. Knowledge at the propositional level is accessible to consciousness and can be activated willfully. Consequently, information can enter this cognitive structure through conversation, reading and so forth. It constitutes the basis for conscious identification of emotion, for verbal communication about emotion, and for willful coping in emotional situations.

As outlined above, different *processes* operate on these levels and they differ with regard to automaticity and with regard to consciousness. Processes at the schematic level are by definition automatic and unconscious, that is, they are effortless, fast and difficult to stop or regulate; they consume minimal attentional or processing capacity and utilize low levels of cognitive processing with minimal analysis. Once a schema is activated this leads to activation of the related body responses. This activation is bi-directional, meaning that activation of specific body responses may also activate a related schema. That is, activation of a body state can feed back positively in the activation of a schema. At the neurological level this may occur 1) centrally, by direct association between the schema and the body response system; and 2) peripherally, via the production of actual body responses that feed into the schema via the perceptual system.

At the propositional level both automatic (i.e., priming effects) *and* conscious or controlled processes occur. Controlled processes are strategic, intentional, voluntary and effortful, they

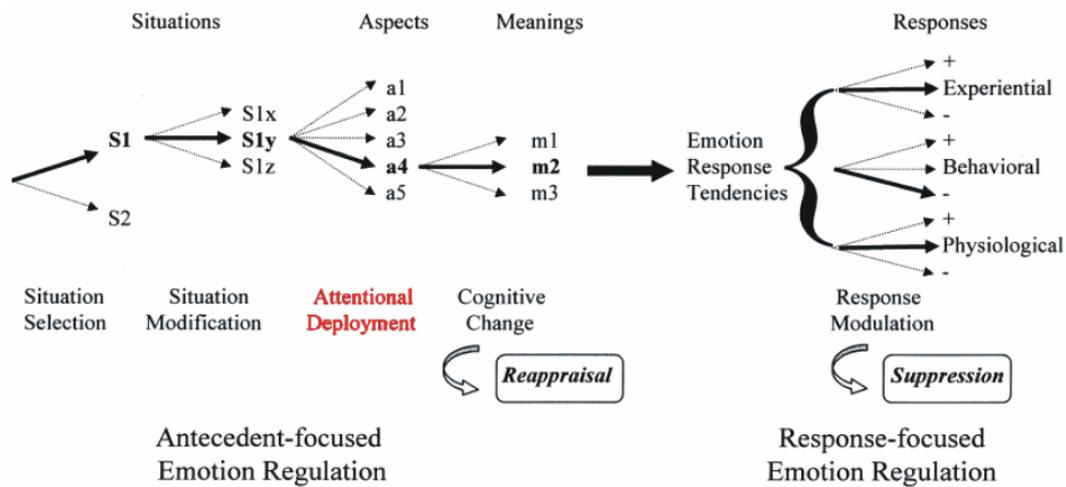
consume attentional and processing resources and use higher levels of cognitive processing, such as semantic analysis (Logan, 1988; McNally, 1995; Sternberg, 1996). Controlled processes activate information stored at the propositional level such as knowledge on emotional states, and allow their transmission into working memory. Once the knowledge is represented in working memory it allows us to deliberately identify and talk about emotions (Philippot et al., 2002).

Multi-level theories of emotion have barely been tested on neurobiological grounds. Using positron emission tomography, Schaefer et al. (2003) investigated the neural correlates of the schematic and propositional emotion processing modes. Subjects performed a mental imagery task to induce emotional experiences of different qualities (i.e., happiness, anger, affection, sadness and neutral) while simultaneously repeating sentences that encouraged emotional processing according to the schematic or propositional mode. For the schematic mode, metaphoric sentences reflected a holistic, spontaneous way of appraising the situation (e.g. 'Everything collapses around me', thought to reflect 'hot' processing of emotions). For the propositional mode, explicit, analytical questions about specific elements of the scenario were used ('Is this situation important for me?', thought to reflect 'cold' processing of emotions) (Schaefer et al., 2003). Schematic processing was associated with increased activity in the ventromedial prefrontal cortex, whereas propositional processing was associated with activation of the anterolateral prefrontal cortex involved in explicit and voluntary processing of emotions.

However, a potential shortcoming of this study is the triggering of the schematic processing mode. First, it differed from the propositional processing in that schematic sentences were statements, whereas the propositional ones were questions adding a systematic confound to the study. Second, and more importantly, processing at the schematic level is automatic by definition. However, repeating preconceived sentences implies effortful cognitive processing which is a characteristic of the propositional processing mode.

As has been outlined before, most multi-level theories of emotion characterize processes of emotion generation but do neglect processes of emotion regulation, although they constitute an essential part of emotion processing. In this regard, the dual memory model of emotion by Philippot et al. (2001, 2004) is exceptional as it integrates a process model of emotion with processes of emotion regulation.

A comprehensive model of emotion regulation has been developed by Gross (Gross, 1998a; Gross, 1998b; Gross, 2001; Gross, 2002). He defines emotion regulation as processes by which we influence which emotions we have, when we have them, and how we experience and express them (Gross, 1998a). In his process model of emotion regulation strategies are distinguished with regard to the time of their occurrence (Gross, 2001). Antecedent-focused emotion regulation strategies occur before the emotion response tendencies have become fully activated, whereas response-focused strategies occur once an emotion response tendency has already been activated (see Figure 2).



**Figure 2: A Process Model of Emotion Regulation.** Gross' model illustrates how different strategies may occur along the time line of the unfolding emotional response. According to this model, emotion may be regulated at five points in the emotion generative process: a) selection of the situation, b) modification of the situation, c) deployment of attention, d) change of cognitions, and e) modulation of experiential, behavioral, or physiological responses (adapted from Gross, 2002).

The cognitive emotion regulation strategies formulated within the dual memory model of emotion tie up to what Gross defines as *attentional deployment* (see Figure 2). They represent attentional top-down processes that modulate the (bottom-up) emotional activation that rests within a schema. Thus, emotion regulation becomes a question of regulating the activation of the schema and its related body responses. This can be achieved by re-direction of attention away from or elaboration of emotional information<sup>2</sup>. The automatic activation of a schema by emotional stimuli may be overridden by a willful attentional focus on elements that are incongruent with the schema. However, these processes may not be as straightforward as they first appear. Automatic activation operates quickly and requires few resources whereas the voluntary processes of re-directing one's attention are relatively slower and require more cognitive resources as they involve much inhibition. Consequently, a conflict may arise between the two response modes.

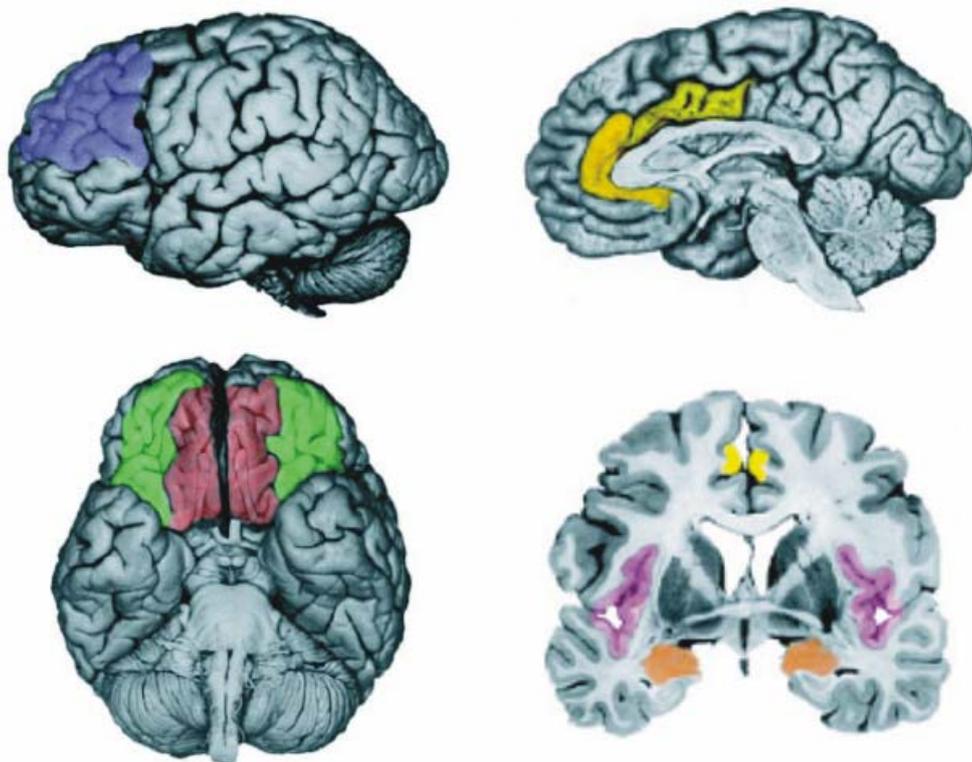
<sup>2</sup> A third mean to regulate activation of a schema is by regulation of the peripheral feedback, e.g. facial muscle manipulation.

An alternative to the re-direction of attention towards elements that are not associated with the schema would be to focus willfully on the emotional content by elaborating it. The authors propose that willful elaboration uses executive processes that have an inhibitory action on the activated schema and thereby regulate emotional activation.

However, to date little is known about how these processes operate at the neural level. Schaefer et al. (2003) investigated the neural correlates of the propositional and schematic processing mode using positron emission tomography but did not distinguish between the two cognitive regulation strategies they specify within their framework. Moreover, implementation of schematic processing is critical. The present work goes beyond the study by Schaefer et al. (2003) by testing behavioral as well as neural correlates of the hypothesized processing modes. The schematic processing mode is realized by a passive viewing paradigm to allow for the automatic activation of the schema without inhibition by controlled processes. The propositional processing mode is achieved by task instructions that engage either re-direction of attention from or willful elaboration of emotional information. Individual differences measures were taken into account to investigate their influence on the behavioral and neural correlates of the schematic and propositional processing modes.

## 1.2 Neuroanatomy of Emotion

Recently, there has been a convergence in lesions and neuroimaging data in the identification of neural circuits underlying emotions in the brain that goes beyond the view that emotions are represented exclusively subcortical (Davidson, 2003b). Rather, emotions consist of differentiated components, that is, physiological arousal, behavioral expression, subjective feeling, as well as regulatory mechanisms that are instantiated in a distributed network of subcortical *and* cortical brain regions. The brain regions implicated in emotion processing comprise the dorsolateral, ventromedial, and orbitofrontal prefrontal cortices, as well as the anterior cingulate cortices, the amygdalae and the insular cortices (see Figure 3; Damasio et al., 2000; for reviews see Davidson & Irwin, 1999; Dolan, 2002).



**Figure 3: Brain Regions Implicated in Emotional Experience.** Upper left, lateral view: dorsolateral prefrontal cortex (blue). Upper right, medial view: anterior cingulate cortex (yellow). Lower left, inferior view: bilateral orbitofrontal (green) and ventromedial cortices (red). Lower right, coronal view: bilateral anterior cingulate cortices (yellow), insular cortices (pink) and amygdalae (orange) (adapted from Davidson et al., 2000).

### 1.2.1 The Prefrontal Cortex

The prefrontal cortex is a brain region critically involved in affect processing and its subdivisions underlie different functions in emotion processing. As outlined above, the schematic and propositional processing modes of emotions as hypothesized by the dual memory model of emotion (Philippot et al., 2004) are associated with changes in activity in the ventromedial and anterolateral prefrontal cortex, respectively (Schaefer et al., 2003). Similarly, Baumgartner et al. reported that processing of emotional pictures activates the ‘cognitive part’ of the prefrontal cortex, namely the dorsolateral prefrontal cortex, whereas a combined stimulation of emotional pictures with emotional music rather recruits brain regions that are associated with intense emotional experience, such as the amygdala, the insula, and the ventromedial prefrontal cortex (Baumgartner et al., 2006b). Moreover, the different dimensions of emotion, valence and intensity, are differentially correlated with activity in the ventromedial and dorsolateral prefrontal cortex and with activity in the ventrolateral and dorsomedial prefrontal cortex, respectively (Grimm et al., 2006). This indicates segregated neural representation of different emotion dimensions in different prefrontal cortical regions.

### 1.2.2 The Anterior Cingulate Cortex

Papez noted that tumors pressing on the anterior cingulate cortex produced ‘loss of spontaneity in emotion, thought and activity’ (Papez, 1937). Building on Papez work McLean proposed that the cingulate cortex elaborates on the emotional experience by transmitting it to higher order cognitive brain areas, such as the prefrontal cortex (McLean, 1949). Interestingly, recent neuroimaging studies indeed related activation of the anterior cingulate cortex to the conscious experience of emotion (Lane et al., 1998). Of particular importance for the present work is McLean’s suggestion that a discommunication between the limbic system and neocortical areas due to impaired function of the cingulate cortex represents the neurobiological basis for the psychological construct of alexithymia, which involves difficulties in identifying and describing

one's own emotions (McLean, 1949; Sifneos, 1973; see chapter 1.3.3. and 4.3. for detailed information on alexithymia and its behavioral and neural correlates).

The anterior cingulate cortex has also been related to regulatory functions. For instance, it has been implicated in the intentional modulation of bodily arousal suggesting that this structure integrates cognitive states with bodily responses (Critchley et al., 2001). Moreover, it has been associated with the regulation of higher cognitive processes, such as monitoring of errors and conflict and with the implementation of adaptive behavioral responses by recruiting, for instance, the prefrontal cortex (Bush et al., 2000; Botvinick et al., 2004; Kerns et al., 2004; Ullsperger et al., 2004).

Most importantly for the present study, the anterior cingulate cortex together with the prefrontal cortex has been associated with the cognitive regulation of emotion (Posner & Rothbart, 1998). Functional imaging studies in that domain focused either on attentional deployment or on cognitive change or reappraisal (Hariri et al., 2000; Beauregard et al., 2001; Ochsner et al., 2002; Hariri et al., 2003; Levesque et al., 2003; Ochsner et al., 2004; for a review see Ochsner & Gross, 2005), however, the focus of the present work is attentional deployment. Attentional deployment either refers to selective attention to non-emotional aspects of stimuli (implicit processing) or conscious interpretation and elaboration of the emotional content (explicit processing). Implicit processing of emotional stimuli as compared to explicit processing is associated with increased responses in emotion processing regions, such as the amygdala or insular cortex (Liberzon et al., 2000; Critchley et al., 2000), whereas limiting attention to emotional stimuli by implementing a cognitive task as compared to passive viewing conditions activates prefrontal regions (Lange et al., 2003) and simultaneously decreased activation in limbic regions (Taylor et al., 2003). More specifically, when subjects judged emotional compared to perceptual characteristics of stimuli, that is, elaborated on emotional content, a reciprocal relationship between prefrontal and limbic regions was found (Hariri et al., 2000; Hariri et al., 2003). This implies that explicit processing of emotions, such as elaborating or labeling emotions, recruits neocortical regions, such as the

prefrontal and the anterior cingulate cortex, that presumably exert a regulatory effect on emotional responses mediated by limbic regions.

However, there is considerable variability in the ability to cognitively elaborate on and regulate emotions that need to be taken into account when investigating the neural correlates of emotion regulatory strategies. To date, only one study has investigated how individual differences in trait rumination (i.e., the tendency to focus on negative aspects of one's self or one's life) modulate the neural systems supporting cognitive regulation of emotion (Ray et al., 2005), but none has investigated the effects of a general impairment of cognitively processing emotions in a healthy sample during cognitive regulation of emotion. However, see chapter 1.3.3. for the current literature about the effects of alexithymia on neural correlates of emotion processing in *clinical* samples.

### 1.2.3 The Amygdala

The amygdala is a key emotion-processing region and is activated during exposure to aversive stimuli from multiple sensory modalities. The amygdala is engaged in the automatic processing of negatively valenced faces (schematic processing mode; Morris et al., 1998; Whalen et al., 1998), but also plays a significant role during conscious evaluation of emotional faces, even when subjects are engaged in making other than emotional judgments, e.g. gender judgments (propositional processing mode; Critchley et al., 2000; Gorno-Tempini et al., 2001; Vuilleumier et al., 2001; Pessoa et al., 2002). Thus it is clear that one need not attend to the emotional valence of faces in order to observe amygdala activation, but it remains unclear to what extent the amygdala responses is modulated by different task demands. While some studies report on greater activity during explicit than implicit coding (Gur et al., 2002), others report greater activity during implicit relative to explicit conditions (Hariri et al., 2000; Critchley et al., 2000) or found no difference between explicit vs. implicit processing of facial emotions (Gorno-Tempini et al., 2001). Thus, activation of the amygdala may be task specific.

#### 1.2.4 The Insular Cortex

This structure is one of the key brain regions in a theoretical framework of emotion that primarily emphasizes the bodily experience or 'embodiment' of emotion. Within this framework emotions are perceived as a multi-tiered and evolutionary shaped mechanism aimed at maintaining the organism's homeostasis. Therefore, the insular cortex is richly interconnected with sensory, prefrontal, motor and limbic brain regions to execute adaptive actions between the organism and its environment, that is, facial and other bodily expressions via the musculo-skeletal system, and changes in the internal visceral milieu (Cechetto & Chen, 1990; Augustine, 1996; Craig, 2003; Critchley et al., 2004). The insula is also associated with the processing of taste information and with the experience of the emotion of disgust (Phillips et al., 1997).

The current view is that the perception of feelings from the entire body represented in the insula constitutes the basis for an image of the physical self, which is a characteristic of human consciousness and self-awareness (Damasio, 1994; Damasio, 1999; Craig, 2002; Craig, 2003; Craig, 2004).

### 1.3 Individual Differences in Affectivity

One of the most salient features of emotion processing is the variability among individuals in how they experience and express emotions (Frijda, 1986; Ekman & Davidson, 1994; Scherer, 1999). For affect, individual differences in both quality and magnitude of the response are rather the rule than the exception. This variability has been termed *affective style* and refers to individual differences in temporary emotional states as well as to consistent individual differences in dispositional mood or stable personality traits (Davidson & Irwin, 1999; Davidson, 2004).

Conventional neuroimaging studies have relied on group analyses in identifying common regions of activation across subjects and treated variance between individuals as noise. However, using the information of such variation will aid in understanding how specific processes are realized in the brain. For instance, recent approaches in affective neuroscience demonstrate how individual differences in affectivity relate to differences at the structural (Gundel et al., 2004; Hadjikhani et al., 2006; Iidaka et al., 2006; Barros-Loscertales et al., 2006; Wright et al., 2007) and functional level (Davidson & Irwin, 1999; Canli et al., 2002; Etkin et al., 2004; Canli et al., 2004; Meriau et al., 2006, for reviews see Hamann & Canli, 2004; Thompson-Schill et al., 2005) by incorporating measures of individual differences into statistical functional magnetic resonance imaging (fMRI) analyses. Nevertheless, correlational approaches merely establish a relation between variables and do not implicate causal mechanisms.

For the most part, the present work is concerned with the processing of aversive stimuli. Therefore, individual differences in anxiety and negative affect were investigated because these individual differences measures may be especially related to altered processing of negative information. Furthermore, the present work investigates the neural correlates of cognitively processing emotional stimuli, referred to as propositional processing by Philippot et al. (2004). Because there is considerable variability with regard to how individuals process emotions,

individual differences in the ability to identify and describe emotional states in oneself and others were also assessed.

### 1.3.1 Anxiety

Individual differences in anxiety are associated with an attentional bias in the processing of threatening stimuli (Fox et al., 2005; Bar-Haim et al., 2005; Bar-Haim et al., 2007) and influence memory performance (Dobson & Markham, 1992; Hock & Egloff, 1998; Shackman et al., 2006). A useful tool to investigate the influence of anxiety on processing of emotional stimuli is the emotional stroop test, whereby subjects have to name the ink color of a presented emotional or neutral word while ignoring the word meaning (Williams et al., 1996). Typically, response times to name the ink color are longer when the word to be ignored is emotional compared to when it is neutral. This is explained by increased allocation of attentional resources towards the emotionally salient information due to automatic bottom-up processes and has been termed emotional interference effect (Pratto & John, 1991; Williams et al., 1997). The emotional interference effect is more robust and pronounced in clinical populations suffering from anxiety disorders (Williams et al., 1996). The interference effect of emotional stimuli in healthy individuals is less marked, but also moderated by individual differences in state and trait anxiety (Richards et al., 1992; Teasdale & Barnard, 1993; Egloff & Hock, 2001). The effect of trait anxiety has been more thoroughly investigated than the effect of state anxiety (Bar-Haim et al., 2007). Broadbent and Broadbent suggest that the two factors interact with state anxiety having a much greater impact in individuals with high trait anxiety than in those with low trait anxiety (Broadbent & Broadbent, 1988). Others suggest that both trait anxiety (irrespective of state anxiety) and state anxiety (irrespective of trait anxiety) are sufficient to produce an attentional bias (Mogg et al., 1990). However, the exact relationship of trait and state anxiety and their effects on emotional interference remain unclear.

### 1.3.2 Negative Affect

Negative affect is a common factor of both anxiety and depression (Clark & Watson, 1991). As with anxiety negative affect can be differentiated into trait and state negative affect. Whereas *trait* negative affect represents a stable personality trait reflecting a general tendency to react with a downbeat attitude to challenging events in the environment, *state* negative affect is a rather short-lived and acute emotional response associated with intense bodily reactions. Consequently, the neural representation of trait and state negative affect may differ. At the neural level individual differences in *trait* negative affect have been associated with increased cerebral blood flow during resting state in the bilateral ventromedial prefrontal cortex (Zald et al., 2002) and in the amygdala (Abercrombie et al., 1998). Moreover, individual differences in trait negative affect are associated with increased amygdala activity during maintenance of a negative emotional state (Schaefer et al., 2002). However, so far it remains unclear how individual differences in *state* negative affect are instantiated at the neural level during the passive perception of emotional stimuli. As outlined above, negative affect is a common factor of both anxiety and sadness. It has recently been proposed that the insula plays a key role in anxiety proneness (Paulus & Stein, 2006). Accordingly, anxiety-prone healthy subjects show greater responses in the bilateral insulae during anticipation of aversive pictures compared to non-anxious subjects (Simmons et al., 2006). Sadness, the other major constituent of negative affect, also modulates insular activity. Transient sadness induced by autobiographical memory scripts of past sad events in healthy female subjects activates the left insula, amongst other regions (Liotti et al., 2000). Similarly, in females, transient sadness is associated with increased activation in the left insula and left amygdala (Levesque et al., 2003). Two PET studies also report on insular activation during self-induced sadness (George et al., 1995; Mayberg et al., 1999). Moreover, individual differences in sadness correlate positively with activity in the right insula and the right temporal pole (Eugene et al., 2003). To summarize, there is ample evidence that state negative affect as a common factor of both anxiety and sadness may modulate insular activity.

### 1.3.3 Impairment in the Cognitive Processing of Emotions (Alexithymia)

Cognitive processing of emotions refers to the ability to identify and verbalize one's emotions. This ability represents a continuous personality dimension with individuals having pronounced difficulties in this domain are said to suffer from alexithymia (Sifneos, 1973). Alexithymia is considered to be a disorder of affect regulation (Taylor et al., 1997). There is evidence that the ability to communicate one's own emotional state strongly relates to the ability to process external verbal or non-verbal emotional markers (Taylor, 2000). For example, individuals with higher levels of alexithymia are less accurate in identifying facial expressions of emotions than individuals with lower levels of alexithymia (Parker et al., 1993; Mann et al., 1994). Other studies using verbal and non-verbal emotional stimulus material, such as sentences, facial expressions, or emotional scenes, found impaired affect recognition in high-alexithymic compared to low-alexithymic subjects (Lane et al., 1996; Lane et al., 2000). For the underlying neural network McLean postulated a discommunication between the limbic system and neocortical areas (McLean, 1949). In this model, the limbic system is concerned with visceral and emotional functions, while the neocortex is involved in the more abstract and complex representation of emotions. Lane et al. found that conscious perception of emotion is associated with increased activity of the anterior cingulate cortex in healthy subjects and concluded that alexithymia may result from insufficient participation of this region in the neural circuitry processing emotional information (Lane et al., 1997; Lane et al., 1998). Functional activation studies relying on changes in blood flow (Berthoz et al., 2002; Huber et al., 2002; Kano et al., 2003) or electrophysiological signals (Aftanas et al., 2003) reported functional alterations of the anterior cingulate cortex in alexithymic subjects. Moreover, structural studies described anatomical alterations (Gundel et al., 2004) of the anterior cingulate cortex in alexithymic subjects. Thus, there is ample support for the hypothesis that *impaired* ability to identify and communicate one's emotional state may result from a discommunication between the limbic system and the neocortex due to malfunction of the anterior cingulate cortex.

## 2 OPEN QUESTIONS AND HYPOTHESES

As pointed out before, a complete account of emotion should make reference to the different levels of analysis, that is, bridge the gap between psychological models of emotion and how emotions are processed at the level of brain structures and systems and, furthermore, how these give rise to individual differences.

According to the dual memory model, emotion processing can be differentiated with regard to the *processes* applied to the emotional stimuli, that is, the schematic and propositional processing mode (Philippot & Schaefer, 2001; Philippot et al., 2004). The schematic mode is characterized by automatic and effortless processes, whereas the propositional mode is characterized by voluntary and resource-consuming processes.

At the behavioral level the schematic and propositional processing mode is best tested using the emotional stroop task (Williams et al., 1996). Here, presentation of emotional words triggers schematic processing, whereas propositional processing is triggered by top-down cognitive strategies to re-direct one's attention to non-emotional characteristics of the stimuli, that is, the ink color of the words.

For the investigation of the schematic processing mode at the neural level, a passive viewing paradigm was chosen. It was assumed that the automatic schematic processing mode, or initial emotional response, is triggered by mere presentation of emotional stimuli (International Affective Picture System, IAPS, Lang et al., 1999), and may develop more naturally without any top down cognitive processes interfering. In a second neuroimaging study, the propositional processing mode is triggered using different task instructions that engage different cognitive regulation strategies (attentional re-direction or emotional elaboration). Here, the automatic activation of an emotional schema through the presentation of facial expression (Pictures of Facial Affect, Ekman & Friesen, 1976) is overridden by top-down influences.

However, special focus of the present work is how the schematic and propositional processing modes are modulated by individual differences in emotional processing. Thus, individual differences in anxiety and state negative affect were assessed as well as individual differences in the ability to cognitively process emotions.

The present thesis addresses the following questions:

1. How are the behavioral correlates of schematic and the propositional emotion processing modes modulated by individual differences in anxiety? Is emotional processing modulated by state or trait anxiety or an interaction of both? How do the emotional dimensions of valence and arousal influence emotional processing?
2. How are the neural correlates of the schematic processing mode of emotions as triggered by passive viewing of aversive pictures modulated by individual differences in *state* negative affect?
3. How are the neural correlates of the propositional processing mode as triggered by cognitive regulation strategies (attentional re-direction and emotional elaboration) modulated by individual differences in cognitive processing of emotions?

### *Hypotheses*

- I. The activation of emotional schemata is automatic and operates very quickly. During the processing of emotional compared to neutral stimuli the fast and automatic activation of the schematic processing system interrupts the slower and controlled top-down cognitive processes representing the propositional processing mode (e.g. naming of ink-color of words). Hence, ink color naming of emotional as compared to neutral words results in longer response times. When controlling for arousal the emotional interference is independent of

valence. Within the dual memory model of emotion it is assumed that anxiety lowers the perceptual threshold for perceptual features congruent with the schema. Hence, it is hypothesized that individual differences in either state or trait anxiety or an interaction of both further increase emotional interference for negative stimuli.

II. Passive viewing of emotional stimuli automatically activates emotional schemata. Such automated processing of emotional information is consistent with the schematic processing mode, which may be modulated by individual differences in affectivity. For instance, anxious individuals show an attentional bias for threat-related stimuli (Christianson, 1992). This bias is observed without conscious perception of threat-relevant information (Mogg & Bradley, 1999) and thus would be the consequence of automatic processes (Philippot & Schaefer, 2001; Philippot et al., 2004). This indicates that the schematic processing mode may be modulated by the individual's emotional state. Emotional states are by definition rather short, but intense episodes of synchronized responses of the body response system (Scherer, 2000). These autonomic and expressive body responses feed back into the perceptual system via a feedback loop and re-activate the relevant schema. Thus, individuals with high state negative affect would show an attentional bias towards schema-congruent aversive information. The output of the body response system would feed back via the perceptual system into the re-activation of the schema thereby enhancing its activation level. The feedback of physiological body responses is represented in the insula. Hence, neurobiological theories have associated the insula with interoception to provide a neural basis for a 'basic feeling state' or 'sentient self'. It is hypothesized that individual differences in state negative affect would modulate schematic processing as to enhance activation of the schema and related body responses. The association of individual differences in state negative affect with schematic processing during passive viewing of aversive pictures would be represented in the insular cortex, the cortical site for representation of body responses and 'sentient self'.

I. Aversive emotional stimuli automatically activate a related schema and associated body responses, which together represent the emotional response of an individual. In the second neuroimaging experiment the schematic processing mode is triggered by the presentation of aversive emotional faces. To trigger a propositional processing mode, subjects were presented with task instructions that engaged top-down cognitive processes, that is, re-direction of attention or willful elaboration of facial expressions. These processes can be subsumed under emotion regulatory strategies. Controlled emotion regulatory strategies imply executive processing that inhibit the activation of the schema and thereby reduce emotional experience. The main focus of this experiment was on how individual differences in the cognitive processing of emotions modulate the propositional processing mode. That is, individual differences in cognitive processing of emotions are hypothesized to modulate the neural correlates of re-direction of attention or willful elaboration of facial expressions. Impaired ability to cognitively process emotions (alexithymia) has been associated with changes in activity of the anterior cingulate cortex (see chapter 1.3.3.). Hence, it is hypothesized that individual differences in the ability to cognitively process emotions in a healthy sample modulate activity in the anterior cingulate cortex during both re-direction of attention from and willful elaboration of emotional stimuli. Furthermore, following McLean's theoretical model (1949) for the underlying neural network of alexithymia, it is hypothesized that the ability to cognitively process emotions relies on the functional integration of brain regions associated with emotional and cognitive processing. This functional integration of specialized brain regions is best understood in terms of effective connectivity. Hence, it is predicted that individual differences in the ability to cognitively process emotions is reflected in differential effective connectivity of the anterior cingulate cortex with the prefrontal cortex and the limbic system, respectively.

## 3 METHODS

### 3.1 Psychophysics

At the behavioral level reaction time data and error rates were measured to assess information processing speed and task difficulty. In a behavioral study individual valence and arousal ratings were obtained for emotional stimuli to assess emotional meaning of stimuli to participants. Behavioral data from a memory and recognition surprise test were collected as a manipulation check.

### 3.2 Psychometrics

Psychometrics is the field concerned with the differences between individuals or group of individuals. To assess individual differences in emotional states and in personality standardized and validated questionnaires were administered. Individual differences in emotional states were measured using the Positive And Negative Affect Schedule (PANAS, Watson et al., 1988; Krohne et al., 1996) and State-Trait Anxiety Inventory (STAI, Laux et al., 1981; Spielberger, 1983). Individual differences in cognitive processing of emotions were investigated using the Toronto Alexithymia Scale-26 (TAS, Bagby et al., 1994a; Bagby et al., 1994b; Kupfer et al., 2001).

#### 3.2.1 The Positive and Negative Affect Schedule

This questionnaire serves a global assessment of subjective emotional experience. The Positive and Negative Affect Schedule consists of 20 adjectives of positive and negative mood states, respectively. To assess state affect subjects rate their *current* affective state on the basis of these adjectives using a 5-point rating scale, whereas rating of the same adjectives with regard to the subject's *general* experience assesses trait aspects of affectivity. High positive affect reflects enthusiasm, activity and alertness, whereas low positive affect reflects lethargy and sadness. High

negative affect indicates petulance, nervousness, and anxiety, whereas low negative affect reflects quietude and stability. Higher scores are indicative of increased (state or trait) positive or negative affect.

### 3.2.2 The State-Trait Anxiety Inventory

The State-Trait Anxiety Inventory is a self-report questionnaire, which includes separate measures of state and trait anxiety. State anxiety reflects a ‘transitory emotional state or condition of the human organism that is characterized by subjective, consciously perceived feelings of tension and apprehension, and heightened autonomic nervous system activity.’ State anxiety may fluctuate over time and can vary in intensity. In contrast, trait anxiety denotes ‘relatively stable individual differences in anxiety proneness’ and refers to a general tendency to respond with anxiety to perceived threats in the environment (Spielberger, 1983). Higher scores indicate increased levels of state or trait anxiety.

### 3.2.3 The Toronto Alexithymia Scale-26

This self-report rating scale assesses a) difficulty identifying feelings and distinguishing between feelings and the bodily sensations of emotional arousal; b) difficulty communicating feelings; and c) externally oriented thinking. For the German version of the TAS-26 questionnaire a cut-off point of  $\geq 54$  has been suggested (Kupfer et al., 2001), however, in addition to identifying a clinical category, the TAS is also thought to measure a continuum of alexithymia in the general population (Bagby et al., 1994b). Higher scores on each of these sub-scales are indicative of poor ability to cognitively process emotions.

### **3.3 Psychophysiology**

#### **3.3.1 Principles and Technique**

Skin conductance activity is a valid and sensible marker of emotional arousal and an objective index of emotional behavior (Boucsein, 1992). It exclusively reflects activity of the sympathetic axis of the autonomic nervous system. Eccrine sweat glands are the major contributors to skin conductance activity (Boucsein, 1992). While their primary function is thermoregulation, they are also responsive to emotional stimuli. Because eccrine sweat glands are most densely situated on the palmar and plantar surfaces, emotion-evoked sweating is usually most evident in these areas. Assessment of skin conductance activity within the electromagnetically hostile MRI may cause distortion or noise in the data collected. In the present experiments, MRI compatible devices were used to reduce electromagnetic interference to a minimum (SC5, Psylab, Contact Precisions Instruments, Boston, USA). A double-shielded cable protected the analog signal from scanner-related artifacts. The analog signal was transferred out of the scanner room using a low pass filter (Minicircuits; Model BLP-1.9) at the scanner penetration panel to remove scanner-related high frequency noise.

### **3.4 Functional Magnetic Resonance Imaging**

FMRI is a non-invasive technique to visualize changes in blood oxygenation in the human brain. Regional changes in brain activation can be mapped with a spatial resolution of 2-3 mm and a temporal resolution of a few seconds.

#### **3.4.1 Principles and Technique**

The hemodynamic-metabolic approach is based on the fact that neuronal activity is coupled to energy metabolism (Sokoloff, 1989). Active neurons consume oxygen, which leads to an increase in deoxygenated blood (deoxyhemoglobin). This is immediately followed by an increase in

regional cerebral blood flow, which over-compensates the increased oxygen demand. This overcompensation leads to an increase in oxygenation and a decrease in local deoxyhemoglobin concentration. Due to the paramagnetic properties of deoxyhemoglobin (Pauling & Coryell, 1936) and its relative change in concentration, the fMRI signal intensity increases. The blood oxygen level dependent contrast, termed BOLD by Ogawa (Ogawa et al., 1990) is a complex function of cerebral blood flow, blood volume and oxygen consumption and represents an indirect measurement of neuronal activity.

The BOLD contrast was used to image the activated human brain for the first time in 1991 and first results using the BOLD contrast for imaging brain function were published in 1992 (Ogawa et al., 1992; Kwong et al., 1992; Bandettini et al., 1992; Frahm et al., 1992). However, to date, the exact relationship between the measured fMRI signal and the underlying neural activity is still a matter of debate. To date it is accepted, that

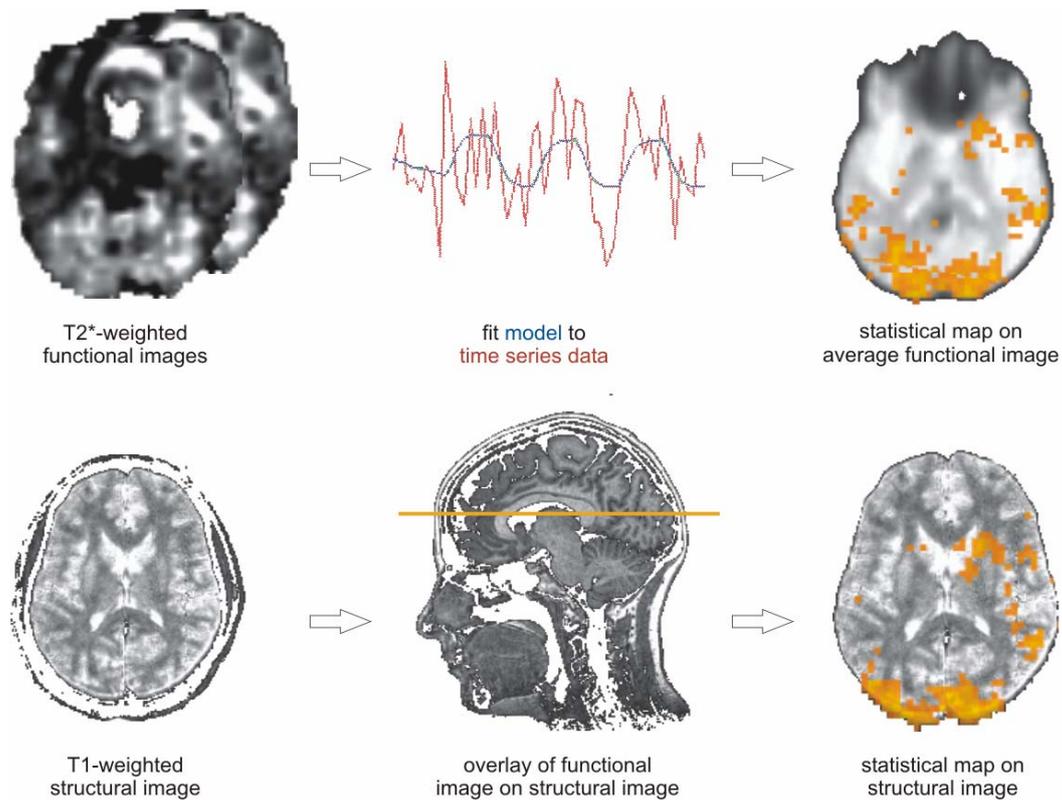
the BOLD contrast directly and monotonically reflects neural activity (Logothetis et al., 2001) specifically, the BOLD contrast correlates highly with single unit spiking activity as well as local field potentials (Mukamel et al., 2005)

negative BOLD responses are associated with a reduction in neuronal activity and/or hemodynamic changes independent of local changes in neuronal activity (Shmuel et al., 2002)

### 3.4.2 Data Acquisition and Analysis

For the acquisition of structural and functional images the different relaxation times  $T_1$  and  $T_2^*$  of different tissues in the head are exploited.  $T_1$ - and  $T_2^*$ -weighted images are achieved by altering two fundamental sequence-timing parameters: the repeat time between subsequent radio frequency excitation pulses (TR), and the time to echo following the excitation pulse (TE). A high-resolution anatomical image (up to  $1 \text{ mm}^3$ ) with good gray-white matter discrimination is typically acquired using a gradient echo sequence (e.g. 3D-FLASH). The BOLD contrast used for functional images exploits the fact that  $T_2^*$ -relaxation time of brain tissue with reduced

deoxyhemoglobin concentration is enhanced and the signal strength increased. Rapid acquisition of multi-slice whole brain volumes with echo planar imaging allows for fine temporal mapping of the dynamics of the BOLD signal change (see Figure 4 for schematic presentation of fMRI analysis).



**Figure 4: FMRI Analysis.** The data is analysed based on general linear modelling (GLM), known as multiple regression. First row: A general linear model consisting of a number of predictor variables denoting the experimental conditions (model) is fitted to individual fMRI time series data from T2\*-weighted functional images. A weighted sum of these predictor variables that produces the closest match to the actual data time series is computed and individually fit for every voxel. This gives a unique set of weights (beta coefficients) for each voxel which are converted to a Z statistics and thresholded. The statistical map is then registered to an average functional image. Second row: To increase spatial resolution an high resolution structural image is acquired to which the functional image is registered. When single subject analyses are fed into a higher-level group analysis the average high-resolution image from all subjects is registered to a standard brain (MNI). The transformation parameters used are then applied for the registration of the group's statistic maps to take them into standard space (not shown).

## 4 EXPERIMENTS

### 4.1 The influence of word valence, word arousal, and individual differences in anxiety on emotional interference

*“Emotional Stroop Test: Effect of Word Arousal and Subject Anxiety on Emotional Interference”.*  
Dresler T, Mériaux K, Heekeren HR, van der Meer E, 2007. (Submitted)

#### *Introduction and Purpose*

The schematic processing mode is triggered by mere presentation of emotional stimuli using the emotional stroop test. The propositional processing mode is triggered by the voluntary processing strategy of naming the ink color and is consistent with the emotion regulatory strategy of re-directing one’s attention to non-emotional characteristics of a stimuli or situation. Consequently, a conflict arises between the two processing modes: bottom-up activation of schematic processing interferes with top-down propositional processing. The voluntary propositional processing mode requires increased cognitive resources to inhibit powerful and automatic bottom-up processes. This conflict is mirrored in longer response times (in naming the ink color) when the word to be ignored is emotional compared to when it is neutral (McKenna & Sharma, 1995; Sharma & McKenna, 2001; Koven et al., 2003).

It has been a matter of date whether emotional interference is influenced by valence or arousal. Pratto and John (1991) found that negative words lead to longer color naming latencies than positive words. The authors argued that negative stimuli attract more attentional resources relative to positive stimuli as they are of higher saliency for the individual (Pratto & John, 1991). Evidence for an interference effect of positive words is scarce (Pratto & John, 1991; Martin et al., 1991; Dalgleish, 1995) but has led to the notion that emotional interference may be rather explained by arousal and not by valence (Anderson, 2005; Schimmack, 2005).

As has been pointed out before (see chapter 1.3.1.) the emotional Stroop interference effect of emotional stimuli in healthy individuals is further modulated by individual differences in anxiety (Richards et al., 1992; Teasdale & Barnard, 1993; Egloff & Hock, 2001). However, it remains unclear whether *state* or *trait* anxiety or an interaction modulates the emotional interference effect (Martin et al., 1991; Egloff & Hock, 2001; Bar-Haim et al., 2007).

The present study investigates the effects of word valence and arousal, and of individual differences in anxiety on emotional interference in a healthy sample. The emotional Stroop test is employed while controlling for confounding factors, such as word arousal and individual differences in trait and state anxiety. Subsequent to the experiment, subjects were presented with a surprise memory task where they had to recall the displayed words. It was hypothesized that the emotional interference effect is mediated by arousal and not valence as long as arousal level of positive and negative stimuli is kept constant. Similarly, it was predicted that emotional words are better remembered than neutral words. It was furthermore hypothesized that trait or state anxiety or an interaction increase emotional interference of negative words.

### *Results and Discussion*

Consistent with the hypothesis (Nr. I, p. 20/21) analyses of response times indicated an emotional interference effect for emotional words, independent of word valence. Furthermore, interference in color naming was associated with better recall of the emotional as compared to neutral words. A regression analysis revealed that not attention but arousal of words predicted better memory performance.

The results support the ‘emotionality hypothesis’, which postulates that both negative and positive stimuli cause interference (Martin et al., 1991; Schimmack, 2005). Consequently, activation of an emotional schema does not primarily depend on the stimulus’ valence, but on the arousal associated with it. The influence of arousal over valence has also been demonstrated for memory enhancement for emotional words (Kensinger & Corkin, 2003). Emotionally arousing

(pleasant and unpleasant) words had a greater modulating influence on the 'attentional blink' during rapid serial word presentation as compared to emotional words that were rated low in terms of arousal indicating that arousal is a crucial parameter in mediating emotional processing (Keil & Ihssen, 2004). More specifically, a study investigating electroencephalographic event-related brain-potentials during reading of emotional words showed that emotion-related enhancement of cortical activity along the dominant processing pathway is due to arousal, rather than valence of the stimuli (Kissler et al., 2007).

Individual differences in state anxiety were associated with emotional interference, that is, subjects with higher state anxiety showed increased response times when naming the ink color of emotional as compared to neutral words. This is only partially consistent with the hypothesis as an effect of trait anxiety or interactive effects of state and trait anxiety were also expected. However, the results are in line with a study reporting that state and not trait anxiety modulated components of event-related potentials related to attentional processes (Mercado et al., 2006). The absence of an effect of trait anxiety may be also due to the overall low trait anxiety level in the healthy sample investigated. It was predicted that emotional interference is increased by individual difference in anxiety for negative words only. However, inconsistent with the hypothesis, emotional interference was increased by individual differences for both negative and positive words. How can this finding be explained? According to the dual memory model of Philippot et al. (2001, 2004) anxiety lowers the perceptual threshold for perceptual characteristics of stimuli that are congruent with the schema, that is, for negative or anxiogenic stimuli features. Alternatively, it has been postulated that anxiety generally lowers the perceptual threshold for socially relevant signals or cues, independent of their valence (Bradley et al., 1999; Rossignol et al., 2005; Bar-Haim et al., 2007). The present findings support the latter notion.

To conclude, the findings indicate that arousal and not valence of emotional stimuli determines emotional interference. Moreover, individual differences in state anxiety enhance emotional

interference for emotional words regardless of valence indicating an attentional bias in state anxious individual for positive as well as neutral words.

## 4.2 The influence of individual differences in state negative affect on neural correlates of passive viewing of aversive stimuli

*“Insular activity during passive viewing of aversive stimuli reflects individual differences in state negative affect”*. Mériaux K, Wartenburger I, Prehn K, Kazzer P, Villringer A, van der Meer E, Heekeren HR, 2007. (Submitted)

### *Introduction and Purpose*

The dual memory model of emotion postulates that perceptual processing of negative stimuli activates a related emotional schema that triggers autonomic and behavioral body responses related to the schema. The model further assumes that, at the neural level, the linkage between the schema and its related body responses feed back positively via the perceptual system resulting in re-activation of the schema. Furthermore, the individual’s emotional state is known to bias attention towards aspects of stimuli or situations that are emotionally relevant or congruent with the already activated schema thereby further enhancing activation of the schema (Christianson, 1992). In other words, the attentional bias in individuals with increased negative affect to schema-congruent aversive aspects might feedback in continuous processing of these aspects, and might bias the evaluation of the situation toward the already activated emotion (McNally, 1995). Indeed, such feedback loops among the activation of a fear schema, the production of bodily responses, and their positive feedback on the schema have been documented in clinical samples (Ehlers et al., 1988; Kenardy et al., 1990). As outlined before, the insula is the neural site for the representation of physiological feedback and as a neural basis for a ‘basic feeling state (such as negative affect) and the ‘sentient self’ (Craig, 2002; Craig, 2003).

23 female subjects were monitored using fMRI while passively viewing negative emotional stimuli. Individual differences in state negative affect were assessed using the PANAS. To control for changes in autonomic arousal associated with the processing of negative emotional material skin conductance level was assessed simultaneously. Skin conductance level reflects a general

arousal level in contrast to rapid, transient skin conductance responses that occur to novel or otherwise salient stimuli and reflect complex attentional processes (Dawson et al., 2000).

### *Results and Discussion*

Skin conductance level increased in response to aversive relative to neutral pictures. This is in line with other studies reporting increased skin conductance activity in response to aversive relative to neutral stimuli (Greenwald et al., 1998; Amrhein et al., 2004; Baumgartner et al., 2006a). There was no association between skin conductance level and state negative affect in either condition. This is contrary to the hypothesis predicting that increased state negative affect is associated with enhanced activation of the schema and increased output of the body response system (Nr. II, p. 21). Supposedly, the failure to demonstrate an association between state negative affect and body responses relates to the scale used to measure state negative affect, since there was little range in state negative affect scores. However, consistent with the hypothesis (Nr. II, p. 21), individual differences in state negative affect were associated with changes in activity in the insula during passive viewing of aversive relative to neutral stimuli.

The present findings go well together with the results of a recent meta-analysis that found negative emotions to activate the left mid insula at coordinates corresponding accurately to the location of insular activity found in the present study (Wager et al., 2003). Another meta-analysis by Wager & Feldmann-Barrett on the functional specialization of the insula also revealed a stronger bias towards *left* mid insular activation for withdrawal-related emotions (Wager & Barrett, 2004). Similarly, individual differences in state anxiety correlate with activity in the left mid insula, again, with coordinates of peak activation that correspond to the coordinates of peak activation of left mid insula in the present study (Chua et al., 1999). Taken together, these findings support our interpretation of a valence-dependent modulation of left middle insular activity.

How can the finding of covariation of left insular activity with individual differences in state negative affect be interpreted? The insula has been implicated in the representation of autonomic arousal or more generally in interoception. The physiological feedback of the whole body is integrated in the insula, which makes this structure an autonomic and homeostatic center (Augustine, 1996; Craig, 2002). Hence, increased activity of the insula in individuals with high state negative affect may represent increased output of the body response system, that is, autonomic arousal. However, individuals with high state negative affect as compared to individuals with low state negative affect did not show increased autonomic arousal in response to aversive relative to neutral stimuli.

So what then is it that is represented in the insula? Insular activity may reflect representation of visceral changes other than sympathetically induced changes in skin conductance level, that is, representation of parasympathetically induced changes that occur in coordinated opponent interaction with sympathetic changes. For instance, stimulation of the left insula results in parasympathetic effects (bradycardia and decreases in blood pressure; Oppenheimer et al., 1992). Likewise, Craig proposed a forebrain emotional asymmetry whereby the left forebrain is associated predominantly with parasympathetic activity, and the right forebrain is associated with sympathetic activity (Craig, 2005). In the present study no measures of parasympathetic activity, such as deceleration of heart rate were taken. Therefore, it cannot be ruled out the possibility that the finding of covariation of left insular activity with individual differences in state negative affect may be driven by associated changes in parasympathetic activity.

Autonomic arousal is only one dimension characterizing emotional experience. Emotional experience may also be defined by valence indicating pleasure-displeasure, or hedonic tone (Wundt, 1924; Lang et al., 1993; Feldman-Barrett & Russell, 1999). Hence, increased activity of the insula in individuals with high state negative affect as compared to individuals with low state negative affect may reflect increased processing of hedonic information of the emotional stimuli. Studies specifically investigating the neural correlates of valence showed that reports of valence

of emotional pictures is associated with left insular activity, that is, insular activity increases with reported negative valence (Anders et al., 2004). However, in the present study, converging behavioral evidence such as individuals' ratings of the valence dimension of presented stimuli would have provided stronger evidence for the engagement of the insula in valence-dependent processing of emotion.

The dual memory model of emotion assumes that the emotional state of an individual may lower the perceptual threshold for stimuli characteristics that are congruent with the already activated schema. This is clearly evident in anxious subjects that show an attentional bias towards negative information (Mathews & MacLeod, 1985; MacLeod et al., 1986; Mogg et al., 1993; Mercado et al., 2006). This attentional bias is particularly high in conditions of high *state* anxiety (Mercado et al., 2006). Similarly, in the study reported here, individuals with high *state* negative affect may show an attentional bias towards schema-congruent aversive aspects that might feedback in continuous processing of these aspects, and biasing the evaluation of the situation toward the already activated emotion (McNally, 1995).

In conclusion, greater recruitment of the insula in response to aversive relative to neutral stimuli in individuals with high state negative affect may represent increased processing of the hedonic dimension of salient aversive stimuli.

### **4.3 The influence of individual differences in cognitive processing of emotions on neural correlates of perceptual decision-making on emotional stimuli**

*“A neural network reflecting individual differences in cognitive processing of emotions during perceptual decision-making” Mériaux K, Wartenburger I, Kaźmier P, Prehn K, Lammers CH, van der Meer E, Villringer A, Heekeren HR, 2006. Neuroimage 33(3), 1016-27.*

#### *Introduction and Purpose*

The dual memory model of emotion by Philippot provides an extensive and complex theoretical framework that integrates cognitive strategies of emotion regulation into a process model of emotion (Philippot & Schaefer, 2001; Philippot et al., 2004). The main focus of this experiment was to investigate how individual differences in the ability to cognitively process or regulate emotions modulate neural correlates of emotion regulatory strategies.

The dual memory model of emotion assumes that schematic processing of emotional stimuli as well related body responses are triggered automatically through presentation of emotional stimuli (Philippot & Schaefer, 2001; Philippot et al., 2004). The authors further postulate that these automatic processes may be over-ridden by an effortful propositional processing mode that may involve either re-direction of attention to non-emotional characteristics of the emotional stimulus or by elaboration of the emotional content of the stimulus. However, these processes may not be as straightforward as it first appears. Voluntary re-direction of attention requires increased cognitive resources as it involves inhibition of the activation of the schema and hence a conflict occurs between automatic schematic processing and the voluntary propositional processing. An alternative is to focus willingly on the emotional characteristics of the stimulus and to elaborate or label them. Such willful elaboration implies executive processing known to inhibit the activated schema and therefore regulates emotional experience. As individuals differ with regard to how they regulate or elaborate emotions these individual differences have to be taken into account when investigating neural correlates of emotion regulatory strategies.

Using fMRI, we investigated the neural correlates of different emotion regulation strategies in 23 healthy female subjects which differed in their ability to cognitively process emotions as assessed using the TAS-26 self-report questionnaire. We employed a perceptual decision making paradigm during which subjects had to either re-direct their attention away from the emotional content of a stimulus (i.e., making gender decisions on aversive facial expressions) or to elaborate on the emotional content of the same stimulus (i.e., making emotion decisions on facial expressions). There is behavioral evidence that individuals with impaired ability to cognitively process emotions have an affect recognition deficit and are specifically less accurate in identifying emotional expressions (Parker et al., 1993; Mann et al., 1994; Lane et al., 1996; Lane et al., 2000). To identify brain regions associated with individual differences in the ability to cognitively process emotions TAS scores were used as a covariate in the fMRI analysis. TAS scores were correlated with activity in the dorsal anterior cingulate cortex during gender decisions, that is, individuals with impaired ability to cognitively process emotions showed increased activation of the dorsal anterior cingulate cortex during gender decisions. To investigate whether individual differences in the ability to cognitively process emotions depend on differences in the functional integration of emotional and cognitive brain regions, task-dependent changes in effective connectivity of the dorsal anterior cingulate cortex were investigated using a psychophysiological interaction analysis (Friston et al., 1997). A psychophysiological interaction analysis accounts for the brain's connectional structure and network functioning by exploring the functional interaction of a chosen region (here, the dorsal anterior cingulate cortex) across the whole brain and models the contextual modulation of this connectivity (Stephan, 2004).

## *Results and Discussion*

Response times between the two experimental conditions differed with faster response times during gender decisions compared to emotion decisions. Error rates did not differ between the two experimental conditions.

At the neural level individual differences in the ability to cognitively process emotions were associated with increased activity of the dorsal anterior cingulate cortex during re-direction of attention (gender decision). This is partly consistent with our hypothesis (Nr. III, p. 22) predicting that individual differences in the ability to cognitively process emotions covary with activity in the anterior cingulate cortex during *both* emotion regulatory strategies. Because neither response times nor error rates correlated with TAS score, the covariation of TAS scores with activation of the dorsal anterior cingulate cortex cannot be attributed to behavioral effects. Analyses of effective connectivity of the dorsal anterior cingulate cortex with regard to individual differences in cognitive processing of emotions revealed differences in the coupling of the dorsal anterior cingulate cortex with limbic and prefrontal regions, respectively, in subjects with high vs. low ability to cognitively process emotions (median split).

Alteration of anterior cingulate cortex activity in alexithymic subjects in response to emotional stimuli has been reported in other neuroimaging studies (Berthoz et al., 2002; Huber et al., 2002; Kano et al., 2003). But how can the differential effect of individual differences in the ability to cognitively process emotions on emotion and gender decisions be explained? During gender decisions only the gender characteristics of the stimulus are task-relevant, however, the emotional content of the stimulus carried by the automatically activated schema has higher saliency and interferes with the propositional processing of re-directing the attention. A conflict occurs between automatic schematic processing and the voluntary propositional processing mode that is reflected in increased activity of the dorsal anterior cingulate cortex which has been associated with conflict monitoring and cognitive control. The data imply that individuals with difficulties in cognitive processing of emotions engage in greater cognitive control to warrant allocation of

attentional resources to task-relevant information, i.e. gender characteristics. Indeed, alexithymia has been associated with good cognitive control (Keltikangas-Jarvinen, 1987). In contrast, during emotion decisions the automatically activated schema carries the emotional information that corresponds with the content of the propositional processing mode (elaboration of emotional information) and therefore no conflict occurs.

Consistent with the hypothesis (Nr. III, p. 22), the psychophysiological interaction analysis revealed task-dependent changes in effective connectivity of the dorsal anterior cingulate cortex with prefrontal and limbic areas, respectively. Most importantly, the dorsal anterior cingulate cortex was coupled with the right ventrolateral prefrontal cortex during emotion but not during gender decisions. Likewise, activity in the right ventrolateral prefrontal cortex was increased during affect labeling as compared to gender labeling suggesting that this regions plays a critical role when putting emotions into words (Lieberman et al., 2007).

Connectivity measures were modulated by individual differences in the ability to cognitively process emotions. Individuals with impaired ability to cognitively process emotions show decreased connectivity of the dorsal anterior cingulate cortex with prefrontal areas, especially with the right ventrolateral prefrontal cortex during both emotion and gender decisions. Activity in the ventrolateral prefrontal cortex has been associated with evaluative judgments (Cunningham et al., 2003) and is sensitive to individual differences in how subjects typically try to reflectively control their responses towards emotionally laden social concepts (Cunningham et al., 2004). Thus, decreased connectivity of the dorsal anterior cingulate cortex with the right ventrolateral prefrontal cortex may implicate reduced reflective processes, which may give rise to difficulties in cognitively processing emotions.

In contrast, connectivity of the dorsal anterior cingulate cortex with the left amygdala was increased in individuals with impaired ability to cognitively process emotions. The amygdala plays a significant role during conscious evaluation of emotional faces (Critchley et al., 2000; Gorno-Tempini et al., 2001; Vuilleumier et al., 2001; Pessoa et al., 2002). For instance, intact amygdala

activation is necessary for enhanced activation in visual sensory cortex during processing of fearful faces, indicating that increased activation of the visual sensory areas results from emotional evaluation of the stimuli by the amygdala (Vuilleumier et al., 2004; Adolphs, 2004). This suggests a more general role for the amygdala in directing attention to perceptual characteristics needed for accurate evaluation of emotional faces (Anderson & Phelps, 2002; Vuilleumier et al., 2004; Adolphs, 2004; Vuilleumier, 2005; Adolphs et al., 2005). Increased effective connectivity between the dorsal anterior cingulate cortex and the left amygdala in individuals with impaired ability to cognitively process emotions may reflect increased affective influence on the dorsal anterior cingulate cortex to enhance information processing by guiding attention to salient emotional characteristics.

In conclusion, neural correlates of re-directing attention to non-emotional characteristics of emotional stimuli, but *not* elaboration of the same stimuli were modulated by individual differences in the ability to cognitively process emotions. Moreover, the ability to cognitively process emotions relies on the functional integration of brain regions associated with emotional and cognitive processing. These data support a theoretical model postulating that impaired ability to cognitively process emotions is reflected by a discommunication between prefrontal and limbic regions (McLean, 1949).

## 5 DISCUSSION AND CONCLUSION

Whereas the investigation of the neural correlates of dimensions of emotions such as valence has received much interest, the study of different processing modes is relatively underexplored (Schaefer et al., 2003; Kalisch et al., 2006). What is more, there is considerable variability among the experience and expression of emotions (Hamann & Canli, 2004). Studies investigating the neural correlates of emotion processing have only recently begun to take these individual differences into account.

The present work aimed at bringing together these two aspects of emotion processing and investigated how individual differences in affectivity and in the cognitive processing of emotions modulated the behavioral and neural correlates of the schematic and propositional processing mode as defined by the dual memory model of emotion (Philippot & Schaefer, 2001; Philippot et al., 2004).

The neural correlates of the schematic and propositional processing mode have been investigated before in a study using positron emission tomography (Schaefer et al., 2003). Subjects performed an emotional mental imagery task while mentally repeating sentences that were assumed to trigger schematic and propositional processing of emotions. The results supported the hypothesized distinction between the two processing modes: schematic processing was associated with increased activity in the ventromedial prefrontal cortex, while propositional processing was associated with activity in the anterolateral prefrontal cortex. Similarly, an fMRI study investigated the neural correlates of so-called high- and low-level appraisal mechanisms that closely correspond to the processing modes defined by Philippot et al. (Kalisch et al., 2006). Low-level appraisal (of aversive emotions) was triggered by anticipation of impending pain, whereas varying cognitive load through a concurrent, unrelated memory task indirectly modulated high-level appraisal of emotion. High-level appraisal was related to activity in the

dorsal medial prefrontal cortex/anterior cingulate cortex, whereas in the study by Schaefer et al. (2003) corresponding propositional processing was associated with activity in the anterolateral prefrontal cortex. The conflicting findings may be explained by the different paradigms used and point towards a key difficulty in the identification of the neural correlates of emotional processing modes. The triggering of the different processes, particularly the schematic processing mode is not straightforward and its operationalization, if feasible at all, may not clearly distinguish between processing modes. For instance, although schematic processing is often seen as implicit and automatic it does contain stored sensory-type representations and therefore draws on working memory resources (Scherer, 2001). No cognitive task triggered propositional processing of emotional stimuli, however, propositional processing can also occur automatically. For instance, some propositions can be activated at an unconscious level and influence subsequent processing of emotional information (Philippot et al., 2004). Moreover, it has been suggested that emotion regulatory strategies may be invoked voluntarily as well as automatically as soon as an emotional response is elicited (Jackson et al., 2003; Goldsmith & Davidson, 2004). In the respective experiment in the present work, subjects were able to freely associate on the contents of the emotional stimuli, which may implicate both the activation of propositional processes as well as voluntary or automatically evoked emotion regulation strategies. Subliminal presentation of stimuli would clearly circumvent the overlap of controlled and automatic processes (LeDoux, 1996; Ohman, 2005), however such an experimental manipulation would not represent naturalistic processing.

Therefore, in the present work schematic processing of emotional information was triggered using a passive viewing paradigm to allow the emotional response to develop as naturally as possible without top-down interference through propositional processing. Consistent with the hypothesis, individuals with high state negative affect showed increased activity in the left insula during passive viewing of aversive relative to neutral stimuli. However, inconsistent with the

hypothesis state negative affect was not associated with increased autonomic arousal. This renders the explanation of insular activity as reflecting increased autonomic arousal rather unlikely. Therefore it should rather be interpreted as reflecting increased representation of valence or hedonic tone of the emotional experience. In individuals with high state negative affect activation of the left insula may represent increased salience or value of aversive stimuli by establishing a link between the sensory information of the stimuli with a representation of how the stimulus affects the individual's experiential feeling state.

The core of emotional activation rests within the schema. Hence, regulation of emotion becomes a question of modulating the activation of the schema. The dual memory model of emotion postulates that schema activation can be regulated by re-direction of attention or elaboration of emotional information, emotion regulatory strategies that require controlled processing at the propositional level (Philippot et al., 2004).

At the behavioral level color naming of emotional words as compared to neutral words resulted in prolonged response times referred to as emotional interference. This effect was independent of valence, but was mainly driven by arousal of stimuli. Emotional interference indicates a conflict between the automatic processing of the emotional information at the schematic level and the controlled processing of ink color naming at the propositional level. In other words, the re-direction of attention from the salient emotional content of the word to non-emotional aspects is associated with increased cognitive effort as reflected by prolonged response times.

Emotional interference, again independent of valence, was modulated by individual differences in state anxiety, that is, individuals with increases state anxiety showed increased emotional interference. Anxiety is assumed to lower the perceptual threshold for stimuli characteristics associated with the anxiogenic schemata resulting in an attentional bias for schema-relevant stimuli (Philippot et al., 2004). However, the findings of the present study speak against this notion, as emotional interference in high anxious subjects was independent of valence. Rather, it

seems that anxiety generally affects the perceptual threshold for arousing stimuli, not only for schema-relevant, that is, negative stimuli.

Alternatively, it may be that increased emotional interference in anxious subjects is not mediated by lowered perceptual thresholds but by difficulties in willfully disengaging attention from emotional stimuli (Koster et al., 2004). In other words, subjects with increased state anxiety may have to expend more cognitive effort to voluntarily execute propositional mechanisms to re-direct attention to stimuli characteristics such as ink color. A reduced ability to exert top-down attentional control on emotional processing has been stated for anxiety (Derryberry & Reed, 2002). Likewise, high state-anxious individuals or individuals with high negative affect exhibit greater difficulties in disengaging attention from emotional stimuli (Compton, 2000; Fox et al., 2001) or show an reduced ability to inhibit the processing of emotional information (Fox, 1994; Yiend & Mathews, 2001; Fox et al., 2005; Koster et al., 2006).

At the neural level the propositional processing mode was triggered by asking the subjects to either re-direct their attention or to elaborate emotional information, note that both are strategies of emotion regulation. Impaired ability to cognitively process emotions is considered to be a disorder of emotion regulation. In the respective experiment of the present study it was therefore predicted that individual differences in cognitive processing of emotions would covary with regional brain activity during *both* re-direction of attention or elaboration of facial expression. However, contrary to the expectations individual differences in cognitive processing of emotions only covaried with dorsal cingulate cortex activity during re-direction of attention. This region has been implicated in conflict monitoring (Carter et al., 1998; van Veen & Carter, 2002) and signals a need to intensify or re-direct attention or control (Botvinick et al., 2004). In the present experiment a conflict occurred between the bottom-up processing at the schematic level (salient emotional faces) and the top-down processing at the propositional level (gender decision). The findings suggest that individuals with impaired ability to cognitively process emotions engage in

greater cognitive control to warrant allocation of attentional resources to task-relevant information, i.e. gender characteristics. Indeed, alexithymia has been associated with good cognitive control (Keltikangas-Jarvinen, 1987).

In contrast, during elaboration of emotional information individual differences in cognitively processing emotions did not covary with activity in the dorsal anterior cingulate cortex. This is because the perceptual information processed at the schematic level (emotional characteristics) corresponded to the perceptual information processed at the propositional level and thus no conflict occurs.

The findings both at the behavioral and at the neural level indicate that emotion regulatory strategies are differentially modulated by individual differences in state anxiety and in the cognitive processing of emotions. Re-direction of attention is associated with increased cognitive effort both in state anxious individuals and in individuals with difficulties in cognitive processing of emotions. In contrast, elaboration of emotional information appears not to be associated with increased cognitive effort. However, this has only been established at the neural level. At the behavioral level, it would be interesting to investigate the effect of emotional elaboration on response times during an emotional stroop task, that is, to ask the subjects to label emotional words in terms of valence (positive vs. negative). Shortened response times during emotional elaboration as compared to color labeling would represent a facilitation effect, devoid of conflict. The findings point towards a qualitative difference in the effectiveness of emotion regulatory strategies. Findings at the neural level indicate that re-direction of attention as compared to elaboration of emotional information may represent a less effective emotion regulatory strategy in individuals with difficulties to cognitively process emotions.

Indeed, experimental and individual difference studies found various strategies to be differently effective (Gross, 1998b; Jackson et al., 2000). At the neural level, cognitive distraction during anticipation of emotional states effectively down-regulates aversive emotion processing but is not

equally effective during actual emotion processing (Erk et al., 2006). This indicates that emotion regulatory strategies may be differentially effective at different time points of the unfolding emotional response.

Future research will have to address the methodological issues raised so far. Emotional processes consist of automatic and controlled processes that operate in isolation or simultaneously depending on the level of processing, the time line of the emotional response and the experimental condition. Thus, one has to carefully think about how to trigger schematic and propositional processing to be able to clearly differentiate them, if this is possible at all. For instance, with regard to controlled processes it should be noted that levels of abstractness and complexity of propositional processing of emotions (e.g. affect labeling vs. reappraisal, denial, suppression) may have different consequences on behavioral outcomes and brain activations (Gross, 1998b; Gross, 2002; Ochsner et al., 2002; Ochsner & Gross, 2005; Lieberman et al., 2007).

Research on the effectiveness of different emotion regulatory strategies and its behavioral and neural correlates should directly compare various regulation strategies (e.g., elaboration of emotion, reappraisal, re-direction of attention). Combining psychophysiological and neuroimaging methods with individual differences measures in emotion regulation may certainly yield valuable information on emotion regulation and its subcomponents.

Moreover, for a complete account of emotion processing the inclusion of positive emotional stimuli should be considered as there is evidence showing that positive and negative emotions may be processed differently with regard to hemisphere (right vs. left) (for reviews see Davidson, 1993; Davidson & Irwin, 1999) and gray matter (cortical vs. subcortical) (Paradiso et al., 1999). Also, emotion regulation processes appear to depend on different neural circuits when regulating positive or negative emotions (Kim & Hamann, 2007; Erk et al., 2007).

As the emotional experience is characterized by changes at i) the physiological level, ii) the expressive-motor level, and iii) the level of subjective experience, controlling for variables such as

autonomic arousal, motor-response tendencies and individual differences is essential not to relate brain activations to idiosyncratic demands of the experimental design employed but rather to the emotional state induced (Barrett & Wager, 2006). For instance, individual differences in affectivity such as positive affect, extraversion/neuroticism (Canli et al., 2002; Canli et al., 2004; Eisenberger et al., 2005), or in the cognitive processing of emotions (e.g., reappraisal mechanisms, repression/sensitization and rumination; Siegle et al., 2002; Ray et al., 2005; Rauch et al., 2007) as well as individual differences in self-relevance or salience of emotional stimuli may differentially affect behavioral and neural correlates of emotion processing and should be carefully distinguished and systematically investigated. With regard to individual differences a gender balanced approach is indispensable as gender differences in the processing of emotions have been shown at the behavioral, psychophysiological and neural level (George et al., 1996; Killgore & Yurgelun-Todd, 2001; Bradley et al., 2001; Piefke et al., 2005, for a review see Cahill, 2006).

In conclusion, the present work identified the behavioral and neural correlates of the schematic and propositional processing mode and how these are modulated by individual differences in affectivity and in the cognitive processing of emotions. The approach to test hypotheses derived from psychological frameworks of emotions with neuroscientific methods is a promising approach to improve our understanding of human emotional experience.

## REFERENCES

- Abercrombie, HC, Schaefer, SM, Larson, CL, Oakes, TR, Lindgren, KA, Holden, JE, Perlman, SB, Turski, PA, Krahn, DD, Benca, RM, Davidson, RJ (1998). Metabolic rate in the right amygdala predicts negative affect in depressed patients. *Neuroreport* 9, 3301-3307.
- Adolphs, R (2004). Emotional vision. *Nat. Neurosci.* 7, 1167-1168.
- Adolphs, R, Gosselin, F, Buchanan, TW, Tranel, D, Schyns, P, Damasio, AR (2005). A mechanism for impaired fear recognition after amygdala damage. *Nature* 433, 68-72.
- Aftanas, LI, Varlamov, AA, Reva, NV, Pavlov, SV (2003). Disruption of early event-related theta synchronization of human EEG in alexithymics viewing affective pictures. *Neurosci. Lett.* 340, 57-60.
- Amrhein, C, Muhlberger, A, Pauli, P, Wiedemann, G (2004). Modulation of event-related brain potentials during affective picture processing: a complement to startle reflex and skin conductance response? *Int. J. Psychophysiology* 54, 231-240.
- Anders, S, Lotze, M, Erb, M, Grodd, W, Birbaumer, N (2004). Brain activity underlying emotional valence and arousal: A response-related fMRI study. *Hum Brain Mapp* 23, 200-209.
- Anderson, AK (2005). Affective influences on the attentional dynamics supporting awareness. *J Exp Psychol Gen* 134, 258-281.
- Anderson, AK, Phelps, EA (2002). Is the human amygdala critical for the subjective experience of emotion? Evidence of intact dispositional affect in patients with amygdala lesions. *J. Cogn Neurosci.* 14, 709-720.
- Augustine, JR (1996). Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Res. Brain Res. Rev.* 22, 229-244.
- Bagby, RM, Taylor, GJ, Parker, JD (1994a). The Twenty-item Toronto Alexithymia Scale--II. Convergent, discriminant, and concurrent validity. *J. Psychosom. Res.* 38, 33-40.
- Bagby, R, Parker, J, Taylor, G (1994b). The twenty-item Toronto Alexithymia Scale--I. Item selection and cross-validation of the factor structure. *J. Psychosom. Res.* 38, 23-32.
- Bandettini, PA, Wong, EC, Hinks, RS, Tikofsky, RS, Hyde, JS (1992). Time course EPI of human brain function during task activation. *Magn Reson. Med.* 25, 390-397.
- Bar-Haim, Y, Lamy, D, Glickman, S (2005). Attentional bias in anxiety: a behavioral and ERP study. *Brain Cogn* 59, 11-22.
- Bar-Haim, Y, Lamy, D, Pergamin, L, Bakermans-Kranenburg, MJ, van IJzendoorn, MH (2007). Threat-related attentional bias in anxious and nonanxious individuals: a meta-analytic study. *Psychol Bull.* 133, 1-24.
- Barrett, LF, Wager, TD (2006). The structure of emotion - Evidence from neuroimaging studies. *Curr Dir Psychol Sci* 15, 79-83.
- Barros-Loscertales, A, Meseguer, V, Sanjuan, A, Belloch, V, Parcet, MA, Torrubia, R, Avila, C (2006). Behavioral Inhibition System activity is associated with increased amygdala and

- hippocampal gray matter volume: A voxel-based morphometry study. *Neuroimage* 33, 1011-1015.
- Baumgartner, T, Esslen, M, Jancke, L (2006a). From emotion perception to emotion experience: Emotions evoked by pictures and classical music. *Int J Psychophysiology* 60, 34-43.
- Baumgartner, T, Lutz, K, Schmidt, CF, Jancke, L (2006b). The emotional power of music: How music enhances the feeling of affective pictures. *Brain Res* 1075, 151-164.
- Beauregard, M, Levesque, J, Bourgouin, P (2001). Neural correlates of conscious self-regulation of emotion. *J. Neurosci.* 21, RC165.
- Berthoz, S, Artiges, E, Van De Moortele, PF, Poline, JB, Rouquette, S, Consoli, SM, Martinot, JL (2002). Effect of impaired recognition and expression of emotions on frontocingulate cortices: an fMRI study of men with alexithymia. *Am. J. Psychiatry* 159, 961-967.
- Botvinick, MM, Cohen, JD, Carter, CS (2004). Conflict monitoring and anterior cingulate cortex: an update. *Trends Cogn Sci.* 8, 539-546.
- Boucsein, W (1992). *Electrodermal Activity*. New York: Plenum Press.
- Bradley, BP, Mogg, K, White, J, Groom, C, de, BJ (1999). Attentional bias for emotional faces in generalized anxiety disorder. *Br. J Clin. Psychol* 38 (*Pt 3*), 267-278.
- Bradley, MM, Codispoti, M, Sabatinelli, D, Lang, PJ (2001). Emotion and motivation II: sex differences in picture processing. *Emotion* 1, 300-319.
- Broadbent, D, Broadbent, M (1988). Anxiety and attentional bias: State and Trait. *Cogn Emot* 2, 165-183.
- Bush, G, Luu, P, Posner, MI (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends Cogn Sci.* 4, 215-222.
- Cahill, L (2006). Why sex matters for neuroscience. *Nat. Rev. Neurosci.* 7, 477-484.
- Canli, T, Amin, Z, Haas, B, Omura, K, Constable, RT (2004). A double dissociation between mood states and personality traits in the anterior cingulate. *Behav. Neurosci.* 118, 897-904.
- Canli, T, Sivers, H, Whitfield, SL, Gotlib, IH, Gabrieli, JD (2002). Amygdala response to happy faces as a function of extraversion. *Science* 296, 2191.
- Carter, CS, Braver, TS, Barch, DM, Botvinick, MM, Noll, D, Cohen, JD (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science* 280, 747-749.
- Cechetto, DF, Chen, SJ (1990). Subcortical sites mediating sympathetic responses from insular cortex in rats. *Am. J. Physiol* 258, R245-R255.
- Christianson, SA (1992). Emotional-Stress and Eyewitness Memory - A Critical-Review. *Psychol. Bull.* 112, 284-309.
- Chua, P, Krams, M, Toni, I, Passingham, R, Dolan, R (1999). A functional anatomy of anticipatory anxiety. *Neuroimage* 9, 563-571.
- Clark, LA, Watson, D (1991). Tripartite model of anxiety and depression: psychometric evidence and taxonomic implications. *J. Abnorm. Psychol.* 100, 316-336.
- Compton, RJ (2000). Ability to disengage attention predicts negative affect. *Cogn Emot* 14, 401-415.

- Craig, AD (2002). How do you feel? Interoception: the sense of the physiological condition of the body. *Nat. Rev. Neurosci.* 3, 655-666.
- Craig, AD (2003). Interoception: the sense of the physiological condition of the body. *Curr. Opin. Neurobiol.* 13, 500-505.
- Craig, AD (2004). Human feelings: why are some more aware than others? *Trends Cogn Sci.* 8, 239-241.
- Craig, AD (2005). Forebrain emotional asymmetry: a neuroanatomical basis? *Trends Cogn Sci.* 9, 566-571.
- Critchley, H, Daly, E, Phillips, M, Brammer, M, Bullmore, E, Williams, S, Van, AT, Robertson, D, David, A, Murphy, D (2000). Explicit and implicit neural mechanisms for processing of social information from facial expressions: a functional magnetic resonance imaging study. *Hum. Brain Mapp.* 9, 93-105.
- Critchley, HD, Melmed, RN, Featherstone, E, Mathias, CJ, Dolan, RJ (2001). Brain activity during biofeedback relaxation - A functional neuroimaging investigation. *Brain* 124, 1003-1012.
- Critchley, HD, Wiens, S, Rotshtein, P, Ohman, A, Dolan, RJ (2004). Neural systems supporting interoceptive awareness. *Nat. Neurosci.* 7, 189-195.
- Cunningham, WA, Johnson, MK, Gatenby, JC, Gore, JC, Banaji, MR (2003). Neural components of social evaluation. *J. Pers. Soc. Psychol.* 85, 639-649.
- Cunningham, WA, Raye, CL, Johnson, MK (2004). Implicit and explicit evaluation: fMRI correlates of valence, emotional intensity, and control in the processing of attitudes. *J. Cogn Neurosci.* 16, 1717-1729.
- Dalgleish, T (1995). Performance on the Emotional Stroop Task in Groups of Anxious, Expert, and Control Subjects - A Comparison of Computer and Card Presentation Formats. *Cogn. Emot.* 9, 341-362.
- Dalgleish, T (2004). The emotional brain. *Nat. Rev. Neurosci.* 5, 583-589.
- Damasio, AR (1994). *Descartes' error: emotion, reason and the human brain.* Gosset/Putnam Books, New York.
- Damasio, AR (1999). *The Feeling of What Happens: Body and Emotion in the Making of Consciousness.* Harcourt Brace, New York.
- Damasio, AR, Grabowski, TJ, Bechara, A, Damasio, H, Ponto, LL, Parvizi, J, Hichwa, RD (2000). Subcortical and cortical brain activity during the feeling of self-generated emotions. *Nat. Neurosci.* 3, 1049-1056.
- Davidson, RJ (2004). Well-being and affective style: neural substrates and biobehavioural correlates. *Philos. Trans. R. Soc. Lond B Biol. Sci.* 359, 1395-1411.
- Davidson, RJ (1993). Cerebral asymmetry and emotion: conceptual and methodological conundrums. *Cogn. Emot.* 7, 115-138.
- Davidson, RJ (2003a). Affective neuroscience and psychophysiology: toward a synthesis. *Psychophysiology* 40, 655-665.
- Davidson, RJ (2003b). Seven sins in the study of emotion: Correctives from affective neuroscience. *Brain Cogn.* 52, 129-132.

- Davidson, RJ, Irwin, W (1999). The functional neuroanatomy of emotion and affective style. *Trends Cogn Sci.* 3, 11-21.
- Dawson, ME, Schell, AM, Filion, DL (2000). The electrodermal system. In: Cacioppo, JT, Tassinary, LG, Berntson, GG (Eds.), *Handbook of Psychophysiology*. Cambridge University Press, Cambridge, pp. 200-223.
- Derryberry, D, Reed, MA (2002). Anxiety-related attentional biases and their regulation by attentional control. *J. Abnorm. Psychol.* 111, 225-236.
- Dobson, M, Markham, R (1992). Individual differences in anxiety level and eyewitness memory. *J Gen Psychol* 119, 343-350.
- Dolan, RJ (2002). Emotion, cognition, and behavior. *Science* 298, 1191-1194.
- Egloff, B, Hock, M (2001). Interactive effects of state anxiety and trait anxiety on emotional Stroop interference. *Pers. Individ. Diff.* 31, 875-882.
- Ehlers, A, Margraf, J, Roth, WT (1988). Selective information processing, interoception, and panic attacks. In: Hand, I, Wittchen, HV (Eds.), *Panic and Phobia2. Treatment and variables affecting course and outcome*. Springer Verlag, Berlin.
- Eisenberger, NI, Lieberman, MD, Satpute, AB (2005). Personality from a controlled processing perspective: an fMRI study of neuroticism, extraversion, and self-consciousness. *Cogn Affect. Behav. Neurosci.* 5, 169-181.
- Ekman, P (1992). An Argument for Basic Emotions. *Cogn. Emot.* 6, 169-200.
- Ekman, P, Davidson, RJ (1994). *The Nature of Emotions: Fundamental Questions*. Oxford University Press, New York.
- Ekman, P, Friesen, WV (1976). *Pictures of Facial Affect*. Consulting Psychologists Press, Palo Alto.
- Erk, S, Abler, B, Walter, H (2006). Cognitive modulation of emotion anticipation. *Eur. J Neurosci.* 24, 1227-1236.
- Erk, S, Kleczar, A, Walter, H (2007). Valence-specific regulation effects in a working memory task with emotional context. *Neuroimage* 37(2), 623-32.
- Etkin, A, Klemenhagen, KC, Dudman, JT, Rogan, MT, Hen, R, Kandel, ER, Hirsch, J (2004). Individual differences in trait anxiety predict the response of the basolateral amygdala to unconsciously processed fearful faces. *Neuron* 44, 1043-1055.
- Eugene, F, Levesque, J, Mensour, B, Leroux, JM, Beaudoin, G, Bourgouin, P, Beauregard, M (2003). The impact of individual differences on the neural circuitry underlying sadness. *Neuroimage.* 19, 354-364.
- Feldman-Barrett, L, Russell, JA (1999). The structure of current affect: controversies and emerging consensus. *Curr. Dir. Psychol. Sci.* 8, 10-14.
- Fitzgerald, DA, Angstadt, M, Jelsone, LM, Nathan, PJ, Phan, KL (2006). Beyond threat: amygdala reactivity across multiple expressions of facial affect. *Neuroimage* 30, 1441-1448.
- Fox, E (1994). Attentional Bias in Anxiety - A Defective Inhibition Hypothesis. *Cogn. Emot.* 8, 165-195.

- Fox, E, Russo, R, Bowles, R, Dutton, K (2001). Do threatening stimuli draw or hold visual attention in subclinical anxiety? *J. Exp. Psychol. Gen.* 130, 681-700.
- Fox, E, Russo, R, Georgiou, GA (2005). Anxiety modulates the degree of attentive resources required to process emotional faces. *Cogn Affect. Behav. Neurosci.* 5, 396-404.
- Frahm, J, Bruhn, H, Merboldt, KD, Hanicke, W (1992). Dynamic Mr Imaging of Human Brain Oxygenation During Rest and Photic-Stimulation. *J. Magn. Res. Imag.* 2, 501-505.
- Frijda, NH (1986). *The emotions*. Cambridge University Press, Cambridge, UK.
- Friston, KJ, Buechel, C, Fink, GR, Morris, J, Rolls, E, Dolan, RJ (1997). Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage.* 6, 218-229.
- George, MS, Ketter, TA, Parekh, PI, Herscovitch, P, Post, RM (1996). Gender differences in regional cerebral blood flow during transient self-induced sadness or happiness. *Biol. Psychiatry* 40, 859-871.
- George, MS, Ketter, TA, Parekh, PI, Horwitz, B, Herscovitch, P, Post, RM (1995). Brain Activity During Transient Sadness and Happiness in Healthy Women. *Am. J. Psychiatry* 152, 341-351.
- Goldsmith, HH, Davidson, RJ (2004). Disambiguating the components of emotion regulation. *Child Dev.* 75, 361-365.
- Gorno-Tempini, ML, Pradelli, S, Serafini, M, Pagnoni, G, Baraldi, P, Porro, C, Nicoletti, R, Umita, C, Nichelli, P (2001). Explicit and incidental facial expression processing: an fMRI study. *Neuroimage.* 14, 465-473.
- Greenwald, M, Cook, E, Lang, P (1998). Affective judgment and physiological response: dimensional covariation in the evaluation of pictorial stimuli. *J. Psychophysiology* 3, 51-64.
- Grimm, S, Schmidt, CF, Bermpohl, F, Heinzl, A, Dahlem, Y, Wyss, M, Hell, D, Boesiger, P, Boeker, H, Northoff, G (2006). Segregated neural representation of distinct emotion dimensions in the prefrontal cortex - an fMRI study. *Neuroimage* 30, 325-340.
- Gross, JJ (2001). Emotion regulation in adulthood: Timing is everything. *Curr. Dir. Psychol. Sci.* 10, 214-219.
- Gross, JJ (1998a). The Emerging Field of Emotion Regulation: An Integrative Review. *Rev. Gen. Psychol.* 2, 271-299.
- Gross, JJ (1998b). Antecedent- and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. *J. Pers. Soc. Psychol.* 74, 224-237.
- Gross, JJ (2002). Emotion regulation: affective, cognitive, and social consequences. *Psychophysiology* 39, 281-291.
- Gundel, H, Lopez-Sala, A, Ceballos-Baumann, AO, Deus, J, Cardoner, N, Marten-Mittag, B, Soriano-Mas, C, Pujol, J (2004). Alexithymia correlates with the size of the right anterior cingulate. *Psychosom. Med.* 66, 132-140.
- Gur, RC, Schroeder, L, Turner, T, McGrath, C, Chan, RM, Turetsky, BI, Alsop, D, Maldjian, J, Gur, RE (2002). Brain activation during facial emotion processing. *Neuroimage.* 16, 651-662.

- Hadjikhani, N, Joseph, RM, Snyder, J, Tager-Flusberg, H (2006). Anatomical differences in the mirror neuron system and social cognition network in autism. *Cereb. Cortex* 16, 1276-1282.
- Hamann, S, Canli, T (2004). Individual differences in emotion processing. *Curr. Opin. Neurobiol.* 14, 233-238.
- Hariri, AR, Bookheimer, SY, Mazziotta, JC (2000). Modulating emotional responses: effects of a neocortical network on the limbic system. *Neuroreport* 11, 43-48.
- Hariri, AR, Mattay, VS, Tessitore, A, Fera, F, Weinberger, DR (2003). Neocortical modulation of the amygdala response to fearful stimuli. *Biol. Psychiatry* 53, 494-501.
- Hock, M, Egloff, B (1998). [Interindividual differences in priming and memory effects of threatening stimuli: effect of cognitive avoidance and vigilant anxiety coping]. *Z. Exp Psychol* 45, 149-166.
- Huber, M, Herholz, K, Habedank, B, Thiel, A, Muller-Kupfers, M, Ebel, H, Subic-Wrana, C, Kohle, K, Heiss, WD (2002). [Different patterns of regional brain activation during emotional stimulation in alexithymics in comparison with normal controls]. *Psychother. Psychosom. Med. Psychol.* 52, 469-478.
- Iidaka, T, Matsumoto, A, Ozaki, N, Suzuki, T, Iwata, N, Yamamoto, Y, Okada, T, Sadato, N (2006). Volume of left amygdala subregion predicted temperamental trait of harm avoidance in female young subjects. A voxel-based morphometry study. *Brain Res.* 1125, 85-93.
- Jackson, DC, Malmstadt, JR, Larson, CL, Davidson, RJ (2000). Suppression and enhancement of emotional responses to unpleasant pictures. *Psychophysiology* 37, 515-522.
- Jackson, DC, Mueller, CJ, Dolski, I, Dalton, KM, Nitschke, JB, Urry, HL, Rosenkranz, MA, Ryff, CD, Singer, BH, Davidson, RJ (2003). Now you feel it, now you don't: frontal brain electrical asymmetry and individual differences in emotion regulation. *Psychol. Sci.* 14, 612-617.
- Kalisch, R, Wiech, K, Critchley, HD, Dolan, RJ (2006). Levels of appraisal: A medial prefrontal role in high-level appraisal of emotional material. *Neuroimage* 30, 1458-1466.
- Kano, M, Fukudo, S, Gyoba, J, Kamachi, M, Tagawa, M, Mochizuki, H, Itoh, M, Hongo, M, Yanai, K (2003). Specific brain processing of facial expressions in people with alexithymia: an H2 15O-PET study. *Brain* 126, 1474-1484.
- Keil, A, Ihssen, N (2004). Identification facilitation for emotionally arousing verbs during the attentional blink. *Emotion* 4, 23-35.
- Keltikangas-Jarvinen, L (1987). Concept of alexithymia. II. The consistency of alexithymia. *Psychother. Psychosom.* 47, 113-120.
- Kenardy, J, Oei, TPS, Evans, L (1990). Hyperventilation and Panic Attacks. *Aust. N. Z. J. Psychiatry* 24, 261-267.
- Kensinger, EA, Corkin, S (2003). Memory enhancement for emotional words: are emotional words more vividly remembered than neutral words? *Mem. Cognit.* 31, 1169-1180.
- Kerns, JG, Cohen, JD, MacDonald, AW, III, Cho, RY, Stenger, VA, Carter, CS (2004). Anterior cingulate conflict monitoring and adjustments in control. *Science* 303, 1023-1026.

- Killgore, WD, Yurgelun-Todd, DA (2001). Sex differences in amygdala activation during the perception of facial affect. *Neuroreport* 12, 2543-2547.
- Kim, SH, Hamann, S (2007). Neural correlates of positive and negative emotion regulation. *J Cogn Neurosci.* 19, 776-798.
- Kissler, J, Herbert, C, Peyk, P, Junghofer, M (2007). Buzzwords: early cortical responses to emotional words during reading. *Psychol Sci.* 18, 475-480.
- Koster, EHW, Crombez, G, Verschuere, B, Damme, S, Wiersema, JR (2006). Components of attentional bias to threat in high trait anxiety: Facilitated engagement, impaired disengagement, and attentional avoidance. *Behav. Res. Ther.* 44, 1757-1771.
- Koster, EHW, Crombez, G, Verschuere, B, De Houwer, J (2004). Selective attention to threat in the dot probe paradigm: differentiating vigilance and difficulty to disengage. *Behav. Res. Ther.* 42, 1183-1192.
- Koven, NS, Heller, W, Banich, MT, Miller, GA (2003). Relationships of distinct affective dimensions to performance on an emotional stroop task. *Cogn. Ther. Res.* 27, 671-680.
- Krohne, HW, Egloff, B, Kohlmann, C-W, Tausch, A (1996). Untersuchung mit einer deutschen Version der "Positive and Negative Affect Schedule" (PANAS). *Diagnostica* 42, 139-156.
- Kupfer, J, Brosig, B, Brähler, E (2001). Toronto-Alexithymie-Skala-26 (TAS-26). Hogrefe Testverlag, Göttingen.
- Kwong, KK, Belliveau, JW, Chesler, DA, Goldberg, IE, Weisskoff, RM, Poncelet, BP, Kennedy, DN, Hoppel, BE, Cohen, MS, Turner, R, . (1992). Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc. Natl. Acad. Sci. U. S. A* 89, 5675-5679.
- Lane, RD, Ahern, GL, Schwartz, GE, Kaszniak, AW (1997). Is alexithymia the emotional equivalent of blindsight? *Biol. Psychiatry* 42, 834-844.
- Lane, RD, Reiman, EM, Axelrod, B, Yun, LS, Holmes, A, Schwartz, GE (1998). Neural correlates of levels of emotional awareness. Evidence of an interaction between emotion and attention in the anterior cingulate cortex. *J. Cogn Neurosci.* 10, 525-535.
- Lane, RD, Sechrest, L, Reidel, R, Weldon, V, Kaszniak, A, Schwartz, GE (1996). Impaired verbal and nonverbal emotion recognition in alexithymia. *Psychosom. Med.* 58, 203-210.
- Lane, RD, Sechrest, L, Riedel, R, Shapiro, DE, Kaszniak, AW (2000). Pervasive emotion recognition deficit common to alexithymia and the repressive coping style. *Psychosom. Med.* 62, 492-501.
- Lang, PJ, Bradley, MM, Cuthbert, BN (1999). The International Affective Picture System (IAPS): Technical Manual and Affective Ratings. Gainesville, FL: NIMH Center for the Study of Emotion and Attention. University of Florida.
- Lang, PJ, Greenwald, MK, Bradley, MM, Hamm, AO (1993). Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology* 30, 261-273.
- Lange, K, Williams, LM, Young, AW, Bullmore, ET, Brammer, MJ, Williams, SC, Gray, JA, Phillips, ML (2003). Task instructions modulate neural responses to fearful facial expressions. *Biol. Psychiatry* 53, 226-232.

- Laux, L, Glanzmann, P, Schaffner, P, Spielberger, CD (1981). State-Trait-Angstinventar (STAI). Beltz Testgesellschaft, Weinheim.
- Lazarus, RS (1966). Psychological stress and the coping process. McGraw-Hill, New York.
- LeDoux, JE (1996). The Emotional Brain: The Mysterious Underpinnings of Emotional Life. Simon and Schuster, New York.
- Leventhal, H (1980). Toward a comprehensive theory of emotion. In: L.Berkowitz (Ed.), Advances in experimental and social psychology. Academic Press, New York.
- Leventhal, H, Scherer, K (1987). The Relationship of Emotion to Cognition: A Functional Approach to a Semantic Controversy. Cogn. Emot. 1, 3-28.
- Levesque, J, Eugene, F, Joannette, Y, Paquette, V, Mensour, B, Beaudoin, G, Leroux, JM, Bourgouin, P, Beauregard, M (2003). Neural circuitry underlying voluntary suppression of sadness. Biol. Psychiatry 53, 502-510.
- Liberzon, I, Taylor, SF, Fig, LM, Decker, LR, Koeppe, RA, Minoshima, S (2000). Limbic activation and psychophysiological responses to aversive visual stimuli. Interaction with cognitive task. Neuropsychopharmacology 23, 508-516.
- Lieberman, MD, Eisenberger, NI, Crockett, MJ, Tom, SM, Pfeifer, JH, Way, BM (2007). Putting feelings into words - Affect labeling disrupts amygdala activity in response to affective stimuli. Psychol. Sci. 18, 421-428.
- Liotti, M, Mayberg, HS, Brannan, SK, McGinnis, S, Jerabek, P, Fox, PT (2000). Differential limbic--cortical correlates of sadness and anxiety in healthy subjects: implications for affective disorders. Biol. Psychiatry 48, 30-42.
- Logan, GD (1988). Toward an instance theory of automatization. Psychol. Rev. 95, 492-527.
- Logothetis, NK, Pauls, J, Augath, M, Trinath, T, Oeltermann, A (2001). Neurophysiological investigation of the basis of the fMRI signal. Nature 412, 150-157.
- MacLeod, C, Mathews, A, Tata, P (1986). Attentional bias in emotional disorders. J Abnorm. Psychol 95, 15-20.
- Mann, LS, Wise, TN, Trinidad, A, Kohanski, R (1994). Alexithymia, affect recognition, and the five-factor model of personality in normal subjects. Psychol Rep. 74, 563-567.
- Martin, M, Williams, RM, Clark, DM (1991). Does Anxiety Lead to Selective Processing of Threat-Related Information. Behav. Res. Ther. 29, 147-160.
- Mathews, A, MacLeod, C (1985). Selective Processing of Threat Cues in Anxiety-States. Behav. Res. Ther. 23, 563-569.
- Mayberg, HS, Liotti, M, Brannan, SK, McGinnis, S, Mahurin, RK, Jerabek, PA, Silva, JA, Tekell, JL, Martin, CC, Lancaster, JL, Fox, PT (1999). Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. Am. J. Psychiatry 156, 675-682.
- McKenna, FP, Sharma, D (1995). Intrusive cognitions: an investigation of the emotional Stroop task. J. Exp. Psychol.: Learn. Mem. Cogn. 21, 1595-1607.
- McLean, PD (1949). Psychosomatic Disease and the "Visceral Brain": recent developments bearing on the Papez theory of emotion. Psychosom. Med. 1, 338-53.

- McNally, RJ (1995). Automaticity and the anxiety disorders. *Behav. Res. Ther.* 33, 747-754.
- Mercado, F, Carretie, L, Tapia, M, Gomez-Jarabo, G (2006). The influence of emotional context on attention in anxious subjects: neurophysiological correlates. *J. Anx. Dis.* 20, 72-84.
- Meriau, K, Wartenburger, I, Kazzner, P, Prehn, K, Lammers, CH, van der, ME, Villringer, A, Heekeren, HR (2006). A neural network reflecting individual differences in cognitive processing of emotions during perceptual decision making. *Neuroimage* 33, 1016-1027.
- Mogg, K, Bradley, BP (1999). Orienting of attention to threatening facial expressions presented under conditions of restricted awareness. *Cogn. Emot.* 13, 713-740.
- Mogg, K, Bradley, BP, Williams, R, Mathews, A (1993). Subliminal Processing of Emotional Information in Anxiety and Depression. *J. Abnorm. Psychol.* 102, 304-311.
- Mogg, K, Mathews, A, Bird, C, Macgregormorris, R (1990). Effects of Stress and Anxiety on the Processing of Threat Stimuli. *J. Pers. Soc. Psychol.* 59, 1230-1237.
- Morris, JS, Ohman, A, Dolan, RJ (1998). Conscious and unconscious emotional learning in the human amygdala. *Nature* 393, 467-470.
- Mukamel, R, Gelbard, H, Arieli, A, Hasson, U, Fried, I, Malach, R (2005). Coupling between neuronal firing, field potentials, and fMRI in human auditory cortex. *Science* 309, 951-954.
- Ochsner, KN, Bunge, SA, Gross, JJ, Gabrieli, JD (2002). Rethinking feelings: an fMRI study of the cognitive regulation of emotion. *J. Cogn Neurosci.* 14, 1215-1229.
- Ochsner, KN, Gross, JJ (2005). The cognitive control of emotion. *Trends Cogn Sci.* 9, 242-249.
- Ochsner, KN, Ray, RD, Cooper, JC, Robertson, ER, Chopra, S, Gabrieli, JD, Gross, JJ (2004). For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage.* 23, 483-499.
- Ogawa, S, Lee, TM, Kay, AR, Tank, DW (1990). Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc. Natl. Acad. Sci. U. S. A* 87, 9868-9872.
- Ogawa, S, Tank, DW, Menon, R, Ellermann, JM, Kim, SG, Merkle, H, Ugurbil, K (1992). Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. *Proc. Natl. Acad. Sci. U. S. A* 89, 5951-5955.
- Ohman, A (2005). The role of the amygdala in human fear: Automatic detection of threat. *Psychoneuroendocrinology* 30, 953-958.
- Oppenheimer, SM, Gelb, A, Girvin, JP, Hachinski, VC (1992). Cardiovascular effects of human insular cortex stimulation. *Neurology* 42, 1727-1732.
- Panksepp, J, Nelson, E, Bekkedal, M (1997). Brain systems for the mediation of social separation-distress and social-reward - Evolutionary antecedents and neuropeptide intermediaries. *Integr. Neurobiol. Affil.* 807, 78-100.
- Papez, JW (1937). A proposed mechanism of emotion. *Arch Neurol Psychiatry* 38, 725-743.
- Paradiso, S, Johnson, DL, Andreasen, NC, O'Leary, DS, Watkins, GL, Ponto, LLB, Hichwa, RD (1999). Cerebral blood flow changes associated with attribution of emotional valence to pleasant, unpleasant, and neutral visual stimuli in a PET study of normal subjects. *Am. J. Psychiatry* 156, 1618-1629.

- Parker, JD, Taylor, GJ, Bagby, RM (1993). Alexithymia and the recognition of facial expressions of emotion. *Psychother. Psychosom.* 59, 197-202.
- Pauling, L, Coryell, CD (1936). The Magnetic Properties and Structure of Hemoglobin, Oxyhemoglobin and Carbonmonoxyhemoglobin. *Proc. Natl. Acad. Sci. U. S. A* 22, 210-216.
- Paulus, MP, Stein, MB (2006). An insular view of anxiety. *Biol. Psychiatry* 60, 383-387.
- Pessoa, L, McKenna, M, Gutierrez, E, Ungerleider, LG (2002). Neural processing of emotional faces requires attention. *Proc. Natl. Acad. Sci. U. S. A* 99, 11458-11463.
- Philippot, P, Baeyens, C, Douilliez, C, Francart, B (2004). Cognitive Regulation of Emotion: Application to Clinical Disorders. In: Philippot, P, Feldman, RS (Eds.), *The regulation of emotion*. Lawrence Erlbaum, Mahwah, N.J., pp. 71-97.
- Philippot, P, Burgos, AI, Verhasselt, S, Baeyens, C (2002). Specifying emotional information: Modulation of emotional intensity via executive processes. In: Fernandez-Dols, JM (Ed.), *Proceedings of XIIth conference of the International Society for Research on Emotion*. ISRE, Cuenca, Spain, pp. 34-35.
- Philippot, P, Schaefer, A (2001). Emotion and memory. In: Mayne, TJ, Bonnano, GA (Eds.), *Emotion: Current Issues and Future Directions*. Guilford Press, New York, NY, pp. 82-122.
- Phillips, ML, Young, AW, Senior, C, Brammer, M, Andrew, C, Calder, AJ, Bullmore, ET, Perrett, DI, Rowland, D, Williams, SC, Gray, JA, David, AS (1997). A specific neural substrate for perceiving facial expressions of disgust. *Nature* 389, 495-498.
- Piefke, M, Weiss, PH, Markowitsch, HJ, Fink, GR (2005). Gender differences in the functional neuroanatomy of emotional episodic autobiographical memory. *Hum. Brain Mapp.* 24, 313-324.
- Posner, MI, Rothbart, MK (1998). Attention, self-regulation and consciousness. *Philos. Trans. R. Soc. Lond., B, Biol. Sci.* 353, 1915-1927.
- Power, MJ, Dalgleish, T (1999). Two routes to emotion: Some implication of multi-level theories of emotion for therapeutic practice. *Behav. Cogn. Psychother.* 27, 129-141.
- Pratto, F, John, OP (1991). Automatic Vigilance - the Attention-Grabbing Power of Negative Social Information. *J. Pers. Soc. Psychol.* 61, 380-391.
- Rauch, AV, Ohrmann, P, Bauer, J, Kugel, H, Engelien, A, Arolt, V, Heindel, W, Suslow, T (2007). Cognitive Coping Style Modulates Neural Responses to Emotional Faces in Healthy Humans: A 3-T fMRI Study. *Cereb. Cortex* Jan 11.
- Ray, RD, Ochsner, KN, Cooper, JC, Robertson, ER, Gabrieli, JDE, Gross, JJ (2005). Individual differences in trait rumination and the neural systems supporting cognitive reappraisal. *Cogn. Aff. Behav. Neurosci.* 5, 156-168.
- Richards, A, French, CC, Johnson, W, Napastek, J, Williams, J (1992). Effects of Mood Manipulation and Anxiety on Performance of An Emotional Stroop Task. *Br. J. Psychol.* 83, 479-491.
- Rossignol, M, Philippot, P, Douilliez, C, Crommelinck, M, Campanella, S (2005). The perception of fearful and happy facial expression is modulated by anxiety: an event-related potential study. *Neurosci. Lett.* 377, 115-120.

- Schachter, S, Singer, J (1962). Cognitive, social, and physiological determinants of emotional state. *Psychol Rev.* 69, 379-399.
- Schaefer, A, Collette, F, Philippot, P, van der, LM, Laureys, S, Delfiore, G, Degueldre, C, Maquet, P, Luxen, A, Salmon, E (2003). Neural correlates of "hot" and "cold" emotional processing: a multilevel approach to the functional anatomy of emotion. *Neuroimage.* 18, 938-949.
- Schaefer, SM, Jackson, DC, Davidson, RJ, Aguirre, GK, Kimberg, DY, Thompson-Schill, SL (2002). Modulation of amygdalar activity by the conscious regulation of negative emotion. *J. Cogn Neurosci.* 14, 913-921.
- Scherer, KR (2001). Appraisal considered as a process of multilevel sequential checking. In: Scherer, KR, Schorr, A, Johnstone, T (Eds.), *Appraisal Processes in Emotion: Theory, Methods, Research.* Oxford University Press, New York, pp. 92-120.
- Scherer, KR (1999). Appraisal Theory. In: Dalglish, T, Power, M (Eds.), *Handbook of emotion and cognition.* Wiley, Chichester, England, pp. 637-663.
- Scherer, K (2000). Psychological models of emotions. In: J Borod (Ed.), *The Neuropsychology of Emotion.* Oxford University Press, New York, pp. 137-162.
- Schimmack, U (2005). Attentional interference effects of emotional pictures: Threat, negativity, or arousal? *Emotion* 5, 55-66.
- Seligman, ME (1971). Phobias and Preparedness. *Behav. Ther.* 2, 307-320.
- Shackman, AJ, Sarinopoulos, I, Maxwell, JS, Pizzagalli, DA, Lavric, A, Davidson, RJ (2006). Anxiety selectively disrupts visuospatial working memory. *Emotion* 6, 40-61.
- Sharma, D, McKenna, FP (2001). The role of time pressure on the emotional Stroop task. *Br. J. Psychol.* 92, 471-481.
- Shmuel, A, Yacoub, E, Pfeuffer, J, Van de Moortele, PF, Adriany, G, Hu, X, Ugurbil, K (2002). Sustained negative BOLD, blood flow and oxygen consumption response and its coupling to the positive response in the human brain. *Neuron* 36, 1195-1210.
- Siegle, GJ, Steinhauser, SR, Thase, ME, Stenger, VA, Carter, CS (2002). Can't shake that feeling: Assessment of sustained event-related fMRI amygdala activity in response to emotional information in depressed individuals. *Biol. Psychiatry* 51, 693-707.
- Sifneos, PE (1973). The prevalence of 'alexithymic' characteristics in psychosomatic patients. *Psychother. Psychosom.* 22, 255-262.
- Simmons, A, Strigo, I, Matthews, SC, Paulus, MP, Stein, MB (2006). Anticipation of aversive visual stimuli is associated with increased insula activation in anxiety-prone subjects. *Biol. Psychiatry* 60, 402-409.
- Smith, CA, Kirby, LD (2000). Consequences requires antecedents: towards a process model of emotion elicitation. In: J.D.Forgas (Ed.), *Feeling and thinking: the role of affect in social cognition.* Cambridge University Press, New York, pp. 83-106.
- Sokoloff, L (1989). Circulation and energy metabolism of the brain. In: Siegel, G, Agranoff, B, Albers, R, Molinoff, P (Eds.), *Basic neurochemistry:molecular, cellular, and medical aspects.* Raven, New York, pp. 565-590.

- Spielberger, CD. Manual for the State-Trait Anxiety Inventory (STAI). (1983). Palo Alto, CA: Consulting Psychologists Press.
- Stephan, KE (2004). On the role of general system theory for functional neuroimaging. *J. Anat.* 205, 443-470.
- Sternberg, RJ (1996). *Cognitive psychology*. Harcourt Brace College Publishers, Fort Worth.
- Taylor, GJ (2000). Recent developments in alexithymia theory and research. *Can. J Psychiatry* 45, 134-142.
- Taylor, GJ, Bagby, RM, Parker, JDA (1997). *Disorders of Affect Regulation: Alexithymia in Medical and Psychiatric Illness*. Cambridge University Press, Cambridge.
- Taylor, SF, Phan, KL, Decker, LR, Liberzon, I (2003). Subjective rating of emotionally salient stimuli modulates neural activity. *Neuroimage*. 18, 650-659.
- Teasdale, JD (1999). Multi-level Theories of Cognition-Emotion Relations. In: Dalglish, T, Power, M (Eds.), *Handbook of Cognition and Emotion*. John Wiley and sons, Chichester, pp. 665-681.
- Teasdale, JD, Barnard, PJ (1993). *Affect, Cognition, and change: re-modelling depressive thought*. Erlbaum, Hove, UK.
- Thompson-Schill, SL, Braver, TS, Jonides, J (2005). Individual differences. *Cogn Affect. Behav. Neurosci.* 5, 115-116.
- Ullsperger, M, Volz, KG, von Cramon, DY (2004). A common neural system signaling the need for behavioral changes. *Trends Cogn Sci.* 8, 445-446.
- van Veen, V, Carter, CS (2002). The timing of action-monitoring processes in the anterior cingulate cortex. *J. Cogn Neurosci.* 14, 593-602.
- Vuilleumier, P (2005). Cognitive science: staring fear in the face. *Nature* 433, 22-23.
- Vuilleumier, P, Armony, JL, Driver, J, Dolan, RJ (2001). Effects of attention and emotion on face processing in the human brain: An event-related fMRI study. *Neuron* 30, 829-841.
- Vuilleumier, P, Richardson, MP, Armony, JL, Driver, J, Dolan, RJ (2004). Distant influences of amygdala lesion on visual cortical activation during emotional face processing. *Nat. Neurosci.* 7, 1271-1278.
- Wager, TD, Barrett, LF (2004). From affect to control: Functional specialization of the insula in motivation and regulation. Published online at *PsycExtra*.
- Wager, TD, Phan, KL, Liberzon, I, Taylor, SF (2003). Valence, gender, and lateralization of functional brain anatomy in emotion: a meta-analysis of findings from neuroimaging. *Neuroimage*. 19, 513-531.
- Watson, D, Clark, LA, Tellegen, A (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *J. Pers. Soc. Psychol.* 54, 1063-1070.
- Whalen, PJ, Rauch, SL, Etcoff, NL, McInerney, SC, Lee, MB, Jenike, MA (1998). Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. *J. Neurosci.* 18, 411-418.
- Williams, JMG, Mathews, A, MacLeod, C (1996). The emotional stroop task and psychopathology. *Psychol. Bull.* 120, 3-24.

- Williams, JMG, Watts, FN, MacLeod, C, Mathews, A (1997). *Cognitive Psychology and Emotional Disorders*. Wiley, New York.
- Wright, CI, Feczko, E, Dickerson, B, Williams, D (2007). Neuroanatomical correlates of personality in the elderly. *Neuroimage* 35, 263-272.
- Wundt, W (1924). *An introduction to psychology*. Allen & Unwin, London.
- Yiend, J, Mathews, A (2001). Anxiety and attention to threatening pictures. *Q J Exp Psychol A* 54, 665-681.
- Zald, DH, Mattson, DL, Pardo, JV (2002). Brain activity in ventromedial prefrontal cortex correlates with individual differences in negative affect. *Proc. Natl. Acad. Sci. U. S. A* 99, 2450-2454.

## RESEARCH ARTICLES

- I Emotional Stroop Test: Effect of Word Arousal and Subject Anxiety on Emotional Interference. Dresler T, Mériaux K, Heekeren HR, van der Meer E, 2007. (Submitted)

# Emotional Stroop Test: Effect of Word Arousal and Subject Anxiety on Emotional Interference

Thomas Dresler<sup>1,2</sup>, Katja Mériau<sup>1,2,3</sup>, Hauke R. Heekeren<sup>1,3</sup>, Elke van der Meer<sup>2</sup>

<sup>1</sup>Berlin NeuroImaging Center, Neuroscience Research Center & Department of Neurology, Charité University Medicine Berlin, Campus Mitte, Berlin, Germany, <sup>2</sup>Department of Psychology, Humboldt University, Berlin, Germany, <sup>3</sup>Max – Planck – Institute for Human Development, Berlin, Germany

Corresponding author: Thomas Dresler  
Berlin NeuroImaging Center, Department of Neurology  
Charité University Medicine Berlin, Campus Mitte  
Charitéplatz 1, 10117 Berlin, Germany

Phone: ++ 49-30-450560169

Fax: ++ 49-30-450560925

Email: [thomas.dresler@charite.de](mailto:thomas.dresler@charite.de)

**Short Title:** Influences on emotional Stroop interference

## **Abstract**

Inconsistent findings regarding the emotional Stroop effect in healthy subjects may be explained by confounding effects of stimulus valence and arousal, and individual differences in anxiety. Here, we examined reaction time data in a healthy sample using the emotional Stroop task while carefully matching arousal level of emotional words. Independent of valence, emotional words elicited emotional interference, indicating that arousal determines emotional interference. Furthermore, independent of valence, emotional words were better recalled and recognized than neutral words. With regard to individual differences in anxiety we found that state anxiety was associated with emotional interference, that is, subjects with high state anxiety showed greater interference than subjects with low state anxiety. There was no influence of trait anxiety. These findings indicate that the emotional Stroop interference effect is mediated by word arousal and not word valence. Furthermore, subjects' state anxiety influences emotional interference of highly arousing words by biasing attentional resources.

## Introduction

Emotional processes have an essential influence on cognitive processes (e.g., Oatley & Jenkins, 1996). One experimental procedure to investigate interference effects of emotional material on cognitive processing is the emotional Stroop test (e.g., Williams, Mathews & MacLeod, 1996), a modified version of the classical Stroop Test (Stroop, 1935). Here, subjects have to name the ink colour of emotional and neutral words as fast and accurately as possible, while at the same time ignoring the meaning of the word. A slowing of naming the ink colour of emotional words compared to naming the ink colour of neutral words has been labeled the emotional Stroop interference effect. Longer colour-naming latencies for emotional relative to neutral words are proposed to indicate allocation of attentional resources towards the emotionally salient information (Williams, Watts, MacLeod & Mathews, 1997). Such an attentional bias for emotional stimuli was also shown with pictures (Schimmack, 2005) and other tasks used in attention research, e.g. the dot probe task and the spatial cueing task (see Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg & van IJzendoorn, 2007).

However, there is some inconsistency in the literature on which parameter determines interference of emotional material. For instance, it is not clear whether the interference effect depends on *valence* or *arousal* of emotional material (Schimmack, 2005).

With regard to valence, Pratto and John (1991) found that negative words led to longer colour-naming latencies than positive words. The authors argued that negative stimuli attract more attentional resources relative to positive stimuli (Pratto & John, 1991) and thereby interfere with cognitive processes. This so-called attentional negativity bias has been confirmed by a number of studies using the emotional Stroop test (e.g., McKenna & Sharma, 1995; Sharma & McKenna, 2001). However, there is less consistent evidence for an interference effect of positive words (Dalglish, 1995; Martin, Williams & Clark, 1991; Pratto & John, 1991). A study by Pratto (1994) revealed that also highly arousing positive words elicited emotional interference. Similarly,

Schimmack (2005) reported that interference elicited by emotional pictures could only be explained by arousal level and not by valence. A study by Anderson (2005) using the attentional blink paradigm also indicates that arousal may be of greater importance in determining interference than valence of emotional stimuli. For instance, subjects tend to focus longer on arousing pictures than on less arousing ones, independently of their valence (Lang, Greenwald, Bradley & Hamm, 1993).

To summarize, there is evidence, that arousal of emotional stimuli is of greater importance than valence in determining interference effects of emotional stimuli.

However, when investigating the effects of valence and arousal on emotional interference, one has to control for the confounding factor of (inherently) higher arousal levels of negative stimuli (Compton, Banich, Mohanty, Milham, Herrington, Miller, Scalf, Webb & Heller, 2003; Martin et al., 1991). A study by Compton et al. (2003) controlling arousal level of positive and negative word stimuli showed that highly arousing stimuli elicited greater interference than stimuli with low arousal, however, the effect was more pronounced for negative words. To further elucidate whether the emotional Stroop interference effect in healthy subjects is mediated by valence or arousal, we used negative and positive words that were comparable in arousal level in an emotional Stroop experiment.

Furthermore, individual differences in affectivity, such as trait or state anxiety may also account for inconsistent findings concerning the emotional interference effect in healthy subjects. Interestingly, the emotional Stroop interference effect is more robust and pronounced in clinical populations suffering from anxiety disorders compared to healthy subjects (Sharma & McKenna, 2001, Williams et al., 1996). However, there is evidence that anxiety may also be an important factor in moderating the emotional interference effect in healthy subjects (Bar-Haim et al., 2007; Egloff & Hock, 2001; Richards, French, Johnson, Naparstek & Williams, 1992). Anxiety can be differentiated in trait and state anxiety whereas *trait* anxiety reflects a more general and relatively stable tendency to respond with anxiety, while *state* anxiety represents a more transitory and

temporary condition of anxiety that can differ between situations (Laux, Glanzmann & Spielberger, 1981). With regard to trait anxiety, Richards et al. (1992) showed that healthy subjects with a high *trait* anxiety displayed a higher emotional interference effect than subjects with low trait anxiety. Similar findings were obtained by Dawkins & Furnham (1989), Dalglish (1995) and others (see Williams et al., 1996 for a review), whereas Martin et al. (1991) and Egloff and Hock (2001) did not find an effect of trait anxiety. Only few studies examined the influence of subjects' *state* anxiety. They report an association of state anxiety with emotional interference similar to that found for trait anxiety (Bar-Haim et al., 2007). A study investigating the interactive effects of both trait and state anxiety did not find a direct effect of trait or state anxiety on the emotional interference effect in a healthy sample, but reported a significant interaction between trait and state anxiety on emotional interference such that high state anxiety potentiates interference in high trait anxious subjects but reduces it in low anxious subjects (Egloff & Hock, 2001).

The present study aimed at further elucidating whether the emotional interference may be explained by word valence or word arousal. Furthermore, we investigated the influence of individual differences in anxiety on emotional interference in a healthy sample. We therefore conducted an experimental study using the emotional Stroop test controlling for potentially confounding factors, such as word arousal and individual differences in trait and state anxiety.

We hypothesize that the emotional interference effect is mediated by arousal and not valence, that is, colour-naming latencies for negative and positive words will not differ when controlling for word arousal. Furthermore, we predict an influence of trait and state anxiety on emotional interference.

## Methods

### Subjects

Fifty university students (30 female, 20 male, age:  $25.2 \pm 3.3$  years (mean  $\pm$  standard deviation, SD) participated in the study. All subjects were enrolled at university or had already graduated. Female and male subjects did not differ with regard to age (female:  $25.4 \pm 3.3$ ; male:  $24.9 \pm 3.4$ ;  $t(48) = 0.604$ ,  $p = 0.549$ ). Individual differences in state and trait anxiety were assessed using the German version of the State-Trait Anxiety Inventory (STAI, Laux et al., 1981). Female and male subjects did not differ with regard to trait (female:  $37.4 \pm 6.2$ ; male:  $37.0 \pm 5.1$ ,  $t(48) = 1.421$ ,  $p = 0.126$ ) or state anxiety (female:  $33.9 \pm 7.4$ ; male:  $33.1 \pm 4.9$ ,  $t(48) = 0.404$ ,  $p = 0.688$ ). Based on self-reports forty-six subjects were right-handed, four female subjects were left-handed and one female ambidextrous.

### Stimulus Material

In a pilot study ( $n = 47$ ; age:  $27.0 \pm 7.6$  years) 300 selected nouns were rated with regard to valence and arousal using seven point rating scales. Out of these 300 nouns 20 negative words (e.g., *burglary*, *victim*; valence:  $-2.21 \pm 0.38$ ; arousal:  $4.26 \pm 0.12$ ), 20 positive words (e.g., *humour*, *party*; valence:  $1.81 \pm 0.58$ ; arousal:  $4.27 \pm 0.34$ ) and 20 neutral words (e.g., *oats*, *coil*; valence:  $0.12 \pm 0.25$ ; arousal:  $1.66 \pm 0.35$ ) were chosen for the emotional Stroop test. Positive and negative words did not differ with regard to arousal (Bonferroni corrected t-tests:  $t(38) = 0.105$ ,  $p = 1.0$ ), however, they were more arousing than neutral words (negative vs. neutral:  $t(38) = 31.068$ ,  $p < .001$ ; positive vs. neutral:  $t(38) = 23.795$ ,  $p < .001$ ). Negative, positive, and neutral words were comparable for number of letters ( $F(2, 57) = 1.139$ ,  $MSE = 2.648$ ,  $p = 0.327$ ), syllables ( $F(2, 57) = 0.064$ ,  $MSE = 0.262$ ,  $p = 0.938$ ) and frequency (The CELEX database,  $F(2, 57) = 0.058$ ,  $MSE = 2313.390$ ,  $p = 0.943$ ), respectively.

## Procedure

Emotional and neutral words in red, green, yellow, and blue colour were displayed separately on a black computer screen. Subjects were seated in a chair in approximately 70 cm distance to the screen. The luminance of colours of words was comparable ( $3 \text{ Candela/m}^2$ ) as measured with a luminance meter (Gossen company, type MAVOLUX digital). Subjects had to bimanually indicate the ink colour of the presented words using four keys of a standard computer keyboard (left hand: Z & X; right hand: . & <), while ignoring the meaning of the word. Words were presented on the screen until a response was given. Assignment of colours to keys was counterbalanced across subjects.

The experiment consisted of two runs, with each run containing four blocks of neutral, positive and negative words, respectively (in total twelve blocks). A block design was chosen, because it proved to be the best method to elicit emotional interference in healthy non-anxious subjects in comparison to a random and event-related stimulus presentation (Bar-Haim et al., 2007). Order of blocks was pseudo-randomised in an ABCBAC fashion (A = neutral, B = positive, C = negative) to avoid consecutive presentation of blocks of the same valence. Within each block ten words (trials) were presented. Order of trials was pseudo-randomised to avoid that consecutive trials elicited the same manual response. In total, subjects were exposed to 80 negative, 80 positive and 80 neutral words. Before each block a fixation cross was presented for 6 s, trials were separated by a fixation cross displayed for 1.5 s.

As a training phase, subjects performed the classical Stroop task prior to the experiment. The classical Stroop task consisted of two blocks: during the first block 60 congruent items (twelve practice trials, 48 test trials, e.g., the word “red” written in red colour), whereas during the second block 48 incongruent items (e.g., the word “red” written in blue colour) were displayed.

Subsequent to the emotional Stroop test, subjects were asked to recall and recognize the presented words in a surprise memory and recognition test (there was no instruction before the experiment to memorize the words). In the surprise memory test they were asked to write down

all the words they remembered. In the surprise recognition test, each of the 60 word stimuli from the experiment were presented with a distractor item and subjects had to indicate which one was originally presented in the experiment (e.g., *oats* vs. *boat*). Presentation of word pairs was pseudo-randomized, as was the screen position (top or bottom) of the target word. Distractor items were matched with target items in terms of valence and grammatical category (noun). Target and distractor items did not differ for number of letters ( $t(118) = .277, p = 0.782$ ), syllables ( $t(118) = .173, p = 0.782$ ) and frequency (The CELEX database,  $t(112) = 1.550, p = 0.124$ ).

## Results

### Reaction time data and error rates

Colour-naming errors (1.8%) and consecutive trials were eliminated from the data set. Individual reaction times of more than two standard deviations from a subject's mean were also excluded from further analysis (4.9%). Mean reaction times and error rates for negative, positive and neutral words, respectively are displayed in Table 1.

Insert Table 1

Reaction time data and error rate data were submitted to a repeated measure ANOVA. An alpha level of 0.05 was set throughout for all statistical tests. Reaction times were influenced by the experimental conditions ( $F(2, 98) = 7.074, MSE = 591.410, p = 0.001$ ). Emotional words elicited longer reaction times than neutral words ( $t(49) = 3.106, p = 0.003$ ). With regard to valence, post-hoc comparisons (Bonferroni corrected) revealed that reaction times for positive and negative words were significantly longer than for neutral words (positive:  $t(49) = 2.488, p = 0.049$ ; negative:  $t(49) = 3.431, p = 0.004$ ). Reaction times did not differ significantly between negative

and positive words ( $t(49) = 0.769, p = 1.0$ ). There was no effect of experimental conditions on error rates ( $F(2, 98) = 1.306, MSE = 1.690, p = 0.276$ ), that is, there was no speed-accuracy trade-off.

To investigate the magnitude of the emotional Stroop effect, we calculated an emotional interference score, defined as the difference between mean reaction times for neutral and negative words ( $RT_{\text{negative}} - RT_{\text{neutral}} = 14.25$  msec,  $SD = 40.49$ ) and for neutral and positive words ( $RT_{\text{positive}} - RT_{\text{neutral}} = 17.06$  msec,  $SD = 35.16$ ), respectively (see Table 1). The mean interference score for emotional words independent of valence was  $RT_{\text{emotional}} - RT_{\text{neutral}} = 15.65$  msec ( $SD = 35.63$ ). All interference scores were significantly different from zero ( $t(49) = 2.488, p = 0.016$ ;  $t(49) = 3.431, p = 0.001$ ;  $t(49) = 3.3106, p = 0.003$ ) and did not differ significantly from each other ( $p = 0.446$ ). We used Cohen's formula for dependent measures ( $d = M_1 - M_2 / SD_{\text{Difference}} * \sqrt{2}$ ) to calculate the effect sizes of interference scores (Cohen, 1988). The effect sizes were  $d = 0.49$  for negative vs. neutral,  $d = 0.68$  for positive vs. neutral and  $d = 0.61$  for emotional vs. neutral words and are comparable to those reported by Bar-Haim et al. (2007).

Reliability of emotional interference scores was tested using the split-half method. Interference scores from the first half of each run were correlated with the interference scores from the second half. Split-half reliability amounts to 0.76 (Spearman-Brown corrected), which is above the reliability scores for interference scores using a retest design with a one-week interval (Eide et al., 2002).

To summarize, reaction times did not differ between negative and positive words that were equal in arousal. However, reaction times for negative and positive words were both longer than for neutral words.

### **Individual differences in trait and state anxiety**

Individual differences in trait and state anxiety were assessed using the STAI (Laux et al., 1981). The mean trait anxiety score in our sample was 36.42 ( $SD = 5.83$ ), the mean state anxiety score

33.56 (SD = 6.53). Trait anxiety scores were normally distributed (Kolmogorov-Smirnov-Test = 0.659,  $p = 0.778$ ), however, state anxiety scores were not (Kolmogorov-Smirnov-Test = 1.373,  $p = 0.046$ ). Trait anxiety did not correlate with emotional interference (Pearson correlation  $r(50) = 0.24$ ,  $p = 0.089$ ). Conversely, state anxiety correlated with emotional interference (Spearman's rho  $\rho(50) = 0.41$ ,  $p = 0.003$ ).

To investigate effects of both trait and state anxiety on emotional interference we conducted a regression analysis with state and trait anxiety and its interaction term (after standardization) as continuous predictors of emotional interference. This regression model was significant ( $F(3, 46) = 3.643$ ,  $p = 0.019$ ,  $R^2 = 0.192$ ), and revealed a significant effect of state anxiety ( $\beta = 0.41$ ,  $p = 0.024$ ), but no effect of trait anxiety or the interaction term (both  $\beta < .05$ , *ns*).

To summarize, individual differences in state anxiety influenced emotional interference, however trait anxiety did not and there were no interactive effects of state and trait anxiety.

### **Memory data**

There was a significant effect of experimental conditions on free recall ( $F(2, 98) = 31.042$ ,  $MSE = 2.141$ ,  $p < 0.001$ ). Bonferroni corrected post-hoc t-tests revealed that negative ( $M = 3.44$ ,  $SD = 1.85$ ) and positive words ( $M = 3.88$ ,  $SD = 2.23$ ) were better recalled than neutral words ( $M = 1.70$ ,  $SD = 1.74$ ) (negative vs. neutral:  $t(49) = 6.127$ ,  $p < 0.001$ ; positive vs. neutral:  $t(49) = 6.888$ ,  $p < 0.001$ ). There was no difference between negative and positive words ( $t(49) = 1.596$ ,  $p = 0.351$ ).

Recognition of negative, positive and neutral words was above chance ( $t(49) > 24.000$ ,  $p < 0.001$ ).

There also was a significant effect of experimental conditions on recognition ( $F(2, 98) = 16.224$ ,  $MSE = 2.714$ ,  $p < 0.001$ ). Post-hoc t-tests revealed that negative ( $M = 17.50$ ,  $SD = 1.94$ ) and positive words ( $M = 17.06$ ,  $SD = 2.07$ ) were better recognized than neutral words ( $M = 15.70$ ,  $SD = 2.72$ ) (negative vs. neutral:  $t(49) = 4.950$ ,  $p < 0.001$ ; positive vs. neutral:  $t(49) = 4.131$ ,

$p < 0.001$ ). There was no difference between negative and positive words with regard to memory performance ( $t(49) = 1.509, p = 0.413$ ).

To control for the possibility of attention-mediated (instead of arousal-mediated) memory effects we conducted a regression analysis with a combined memory score for each word (sum of free recall and recognition score) as the to-be-predicted variable, and with words' mean reaction times and arousal scores as predictors (Lang et al. 1993). The regression model was significant ( $F(2, 57) = 8.827, p < 0.001, R^2 = 0.236$ ). However, only arousal scores predicted memory performance ( $\beta = 0.38, p = 0.002$ ) indicating that attention-mediating effects were irrelevant with regard to memory performance. There were no significant gender differences in the memory tasks.

## **Discussion**

In this experiment we investigated whether the emotional Stroop interference effect is determined by either word valence or word arousal. Furthermore, we investigated the influence of individual differences in anxiety on emotional interference.

Consistent with our hypothesis we found an emotional interference effect for emotional words, independent of word valence. The surprise memory and recognition test revealed that emotional words were better recalled and recognized as compared to neutral words and this effect was not mediated by attention, but by arousal. With regard to individual differences in anxiety, we found that state anxiety was associated with emotional interference, that is, emotional interference was increased in subjects with high state anxiety. Trait anxiety had no influence on emotional interference.

The results of the present study revealed a significant emotional interference effect for both negative and positive words, which were controlled for arousal. Ink colour-naming latencies did not differ between negative and positive words, thus, emotional interference occurred when word arousal was high, independent of word valence. Our results are in line with the findings by Compton et al. (2003) showing an arousal effect for negative and, albeit to a lesser degree, for positive words. Moreover, the effect sizes for the interference effects (about .50) in the present study are in line with the effect sizes reported in a recently published meta-analysis on emotional interference (Bar-Haim et al., 2007). This meta-analysis (including 172 studies) examined the conditions of threat-related attentional biases in anxious and non-anxious subjects under a variety of experimental conditions. They report a reliable attentional bias for different paradigms in anxious subjects. Interestingly, with regard to the emotional Stroop task they report that only blocked presentation of emotional words elicits emotional interference in non-clinical control subjects whereas mixed presentation did not. Similarly, in our study emotional interference occurred with a blocked presentation of emotional words of the same valence.

The emotional interference effect may be explained by the 'threat hypothesis', which postulates that only threatening (i.e., negative) material causes interference (Pratto & John, 1991; Martin et al., 1991; Schimmack, 2005). Alternatively, the 'emotionality hypothesis' postulates that emotional material, that is, both negative and positive stimuli cause interference (Martin et al., 1991; Schimmack, 2005). Here, emotionality is defined as an intensity aspect of emotion, that is, arousal (Martin et al., 1991). The interference effect may reflect increased allocation of attentional resources to emotional stimuli (Pratto & John, 1991). More specifically, it has been argued that an increase in arousal in response to a relevant emotional stimulus reflects the increase in processing capacity that facilitates further processing of a relevant stimulus. Thus, the interference effect reflects the reallocation of attentional resources to the emotional stimulus to allow for a more in-

depth processing of stimuli that may be of relevance for adaptive behaviour of an individual (Schimmack, 2005; Scherer, 2001, Pratto & John, 1991).

Individual differences in state anxiety were associated with the magnitude of the emotional interference effect, that is, subjects with higher state anxiety showed increased emotional interference. Anxiety is associated with an automatic allocation of attentional resources to threat-related stimuli (Williams et al., 1997) and thereby binds cognitive resources. Our findings indicate that state anxiety, as a stimulus limited and a temporally acute emotional state has an essential influence on emotional interference in healthy subjects. This is in accordance with other studies investigating the effect of state anxiety on emotional interference (for a review see Bar-Haim et al., 2007).

In contrast, individual differences in trait anxiety had no influence on the emotional interference effect in the present study. This is in line with the findings by Martin et al (1991) and by Egloff and Hock (2001) who did not report an effect of trait anxiety on emotional interference in a healthy sample (Egloff & Hock, 2001; Martin et al., 1991; but see Bar-Haim et al., 2007; Richards et al., 1992; Williams et al., 1996). The failure to demonstrate an association between trait anxiety and emotional interference may relate to the scale used to measure anxiety, since there was little range in trait anxiety scores in our sample (SD in t norm equivalent: 5.98) compared to the representative norm sample (Laux et al., 1981).

During the free recall and recognition memory tests, significantly more emotional words than neutral words were recalled and recognized. There was no difference in the number of recalled and recognized emotional words with regard to valence, which is in line with the reaction time data confirming an influence of arousal and not valence on processing of emotional information. An 'emotional memory enhancement effect' has been shown for a wide range of emotional material including pictures, words, and narrative tales (e.g., Hamann, 2001). Arousal level of

emotional words was higher than for neutral words, which may account for this memory enhancement effect. Indeed, arousing stimuli increase memory performance, that is, pictures that were rated as highly arousing are better remembered than less arousing pictures (Bradley, Greenwald, Petry & Lang, 1992). Alternatively, the memory effect may be explained by an attentional bias for emotional words in the emotional Stroop test, meaning that emotional words were better remembered and recognized because they were processed in more depth. However, the regression analysis revealed that only the arousal scores but not the different word reaction times were significant predictors of the combined memory score, indicating that memory performance is mediated by word arousal and not attention.

Further research on the interference effect of emotional material should consider subject characteristics (e.g. affectivity) and stimuli characteristics (e.g. arousal, dominance). For instance, it remains to be elucidated how individual differences in affectivity, such as negative or positive affect, depressive symptomatology and individual differences in coping styles (repression, sensitization) contribute to emotional interference effects (Bar-Haim et al., 2007). With regard to stimulus associated arousal, the additional assessment of psychophysiological changes (e.g., skin conductance, Lang et al., 1993) may aid to reveal the influence on arousal in cases where self-reported and objectively measured arousal dissociate as they do in repression (Asendorpf & Scherer, 1983).

## References

- Anderson, A.K. (2005). Affective influences on the attentional dynamics supporting awareness. *Journal of Experimental Psychology: General*, 134, 258–281.
- Asendorpf J.B. & Scherer K.R. (1983). The discrepant represser: Differentiation between low anxiety, high anxiety and repression of anxiety by autonomic-facial-verbal patterns of behavior. *Journal of Personality and Social Psychology*, 45, 1334-1346.
- Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M.J. & van IJzendoorn, M.H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: A meta-analytic study. *Psychological Bulletin*, 133, 1-24.
- Bradley, M.M., Greenwald, M.K., Petry, M.C. & Lang, P.J. (1992). Remembering pictures: pleasure and arousal in memory. *Journal of Experimental Psychology: Learning, Memory, & Cognition* 18, 379-390.
- Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences* (2nd ed.). Hillsdale, NJ: Erlbaum.
- Compton, R.J., Banich, M.T., Mohanty, A., Milham, M.P., Herrington, J., Miller, G.A., Scalf, P.E., Webb, A. & Heller, W. (2003). Paying attention to emotion: An fMRI investigation of cognitive and emotional stroop tasks. *Cognitive, Affective & Behavioral Neuroscience*, 3, 81-96.
- Dalgleish, T. (1995). Performance on the emotional Stroop task in groups of anxious, expert, and control subjects: a comparison of computer and card presentation formats. *Cognition & Emotion*, 9, 341-362.
- Dawkins, K. & Furnham, A. (1989). The colour naming of emotional words. *British Journal of Psychology*, 80, 383-389.
- Egloff, B. & Hock, M. (2001). Interactive effects of state anxiety and trait anxiety on emotional Stroop interference. *Personality and Individual Differences*, 31, 875-882.
- Eide, P., Kemp, A., Silberstein, R. B., Nathan, P. J., & Stough, C. (2002). Test-retest reliability of the emotional Stroop task: Examining the paradox of measurement change. *The Journal of Psychology*, 136, 514-520.
- Hamann, S. (2001). Cognitive and neural mechanisms of emotional memory. *Trends in Cognitive Sciences*, 5, 394-400.
- Lang, P.J., Greenwald, M.K., Bradley, M.M. & Hamm, A.O. (1993). Looking at pictures: Affective, facial, visceral, and behavioral reactions. *Psychophysiology* 30, 261–273.
- Laux, L., Glanzmann, P.S.P. & Spielberger, C.D. (1981). *Das State-Trait-Angstinventar (STAI)*. Weinheim: Beltz.
- Martin, M., Williams, R.M. & Clark, D.M. (1991). Does anxiety lead to selective processing of threat-related information? *Behaviour Research and Therapy*, 29, 147-160.
- McKenna, F. & Sharma, D. (1995). Intrusive cognitions: An investigation of the emotional Stroop task. *Journal of Experimental Psychology*, 21, 1595-1607.
- Oatley, K. & Jenkins, J.M. (1996). *Understanding Emotions*. Boston: Blackwell Publishers.

- Pratto, F. & John, O.P. (1991). Automatic Vigilance: The Attention-Grabbing Power of Negative Social Information. *Journal of Personality and Social Psychology*, 61, 380-391.
- Pratto, F. (1994). Consciousness and automatic evaluation. In P. M. Niedenthal & S. Kitayama (Eds.), *The heart's eye: Emotional influences in perception and attention* (pp. 115–143). San Diego, CA: Academic Press.
- Richards, A., French, C.C., Johnson, W., Naparstek, J. & Williams, J. (1992). Effects of mood manipulation and anxiety on performance of an emotional Stroop task. *British Journal of Psychology*, 83, 479-491.
- Scherer, K. R. (2001). Appraisal considered as a process of multilevel sequential checking. In K. R. Scherer, A. Schorr, & T. Johnstone (Eds.), *Appraisal Processes in Emotion* (pp. 92–120). Oxford, England: Oxford University Press.
- Schimmack, U. (2005). Attentional interference effects of emotional pictures: Threat, negativity, or arousal? *Emotion*, 5, 55-66.
- Sharma, D. & McKenna, F.P. (2001). The role of time pressure on the emotional Stroop task. *British Journal of Psychology*, 92 *Part 3*, 471-481.
- Stroop, J.R. (1935) Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, 18, 643–662
- Williams, J.M.G., Mathews, A. & MacLeod, C. (1996). The emotional Stroop task and psychopathology. *Psychological Bulletin*, 120, 3-24.
- Williams, J.M.G., Watts, F. N., MacLeod, C., & Mathews, A. (1997). *Cognitive Psychology and Emotional Disorders* (2nd ed.). New York: Wiley.

**Table 1. Reaction times (in milliseconds) and error rates for negative, positive and neutral word (N = 50).**

	<b>Negative</b>	<b>Positive</b>	<b>Neutral</b>
<b>Mean reaction times (<math>\pm</math> SD)</b>	733.59 ( $\pm$ 132.70)	736.41 ( $\pm$ 126.07)	719.35 ( $\pm$ 109.37)
<b>Mean error rates (<math>\pm</math> SD)</b>	1.68 ( $\pm$ 1.91)	1.26 ( $\pm$ 1.32)	1.48 ( $\pm$ 0.85)

SD = standard deviation

**II Insular activity during passive viewing of aversive stimuli reflects individual differences in state negative affect. Mériaux K, Wartenburger I, Kazzner P, Prehn K, Villringer A, van der Meer E, Heekeren HR, 2007. (Submitted)**

# Insular Activity during Passive Viewing of Aversive Stimuli Reflects Individual Differences in State Negative Affect

Mériaux Katja<sup>1,2,3</sup>, Wartenburger Isabell<sup>1</sup>, Kazzner Philipp<sup>1</sup>, Prehn Kristin<sup>1,2,3</sup>, Villringer Arno<sup>1</sup>, van der Meer Elke<sup>2</sup>, Heekeren Hauke R<sup>1,3,4</sup>

<sup>1</sup>Berlin NeuroImaging Center, Neuroscience Research Center & Dept. of Neurology, Charité University Medicine Berlin, Campus Mitte, Berlin, Germany, <sup>2</sup>Dept. of Psychology, Humboldt University, Berlin, Germany, <sup>3</sup>Max – Planck – Institute for Human Development, Berlin, Germany, <sup>4</sup>Max – Planck – Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Corresponding author: Katja Mériaux  
Berlin NeuroImaging Center, Dept. of Neurology  
Charité University Medicine Berlin, Campus Mitte  
Charitéplatz 1, 10117 Berlin, Germany

Phone: ++49-30-450560265

Fax: ++49-30-450560952

Email: [katja.meriau@charite.de](mailto:katja.meriau@charite.de)

**Running title:** negative affect & insular activity

## **Abstract**

### **Background**

People differ with regard to how they perceive, experience, and express negative affect. While *trait* negative affect reflects a stable, sustained personality trait, *state* negative affect represents a stimulus limited and temporally acute emotion. So far, little is known about the neural systems mediating the relationship between negative affect and acute emotion processing.

### **Methodology/Principal Findings**

To address this issue we investigated how individual differences in state negative affect are reflected in changes in blood oxygen level-dependent responses during passive viewing of emotional stimuli in a healthy female sample. To assess autonomic arousal we simultaneously recorded changes in skin conductance level. At the *psychophysiological* level we found increased skin conductance level in response to aversive relative to neutral pictures. However, there was no association of state negative affect with skin conductance level. At the *neural* level we found that high state negative affect was associated with increased left insular activity during passive viewing of aversive stimuli.

### **Conclusions/Significance**

The insula has been implicated in interoceptive processes and in the integration of sensory, visceral and affective information thus contributing to subjective emotional experience. Greater recruitment of the insula in response to aversive relative to neutral stimuli in subjects with high state negative affect may represent increased processing of salient aversive stimuli.

## Introduction

Perception, experience, and expression of emotions are subject to great interindividual variability. The identification of the neural correlates of these aspects of emotions may therefore crucially depend on the specific sample and their characteristics in emotion processing [1,2]. Accordingly, findings from neuroimaging studies concerning the neural correlates of emotions are often inconsistent. Relating individual differences in emotional reactivity or emotional experience to brain imaging data derived from group analyses will not only aid to clarify conflicting findings but may reveal the precise nature of neural mechanisms involved in emotion processing [3–7].

When individuals are asked to report on their emotional states, negative affect emerges as a higher order factor in factorial analyses and generally reflects subjective distress [8]. Negative affect can be differentiated into trait and state negative affect and is a common factor of both anxiety and depression [9]. *Trait* negative affect reflects a stable personality trait, that is, a negative emotional activation, which is sustained and not bound to discrete cues. In contrast, *state* negative affect is stimulus limited and a temporally acute emotion.

At the neural level individual differences in *trait* negative affect have been associated with increased cerebral blood flow during resting state in the bilateral ventromedial prefrontal cortex [10] and in the amygdala [11]. Greater increases in amygdala response during active maintenance of a negative mood are associated with subjects' self-reported trait negative affect [12]. Trait negative affect may be implemented by plastic changes of the brain, whereas a momentary change of mood (i.e., state negative affect) allowing for short-lived cognitive, behavioral, and physiological adaptation may be differentially represented. However, so far it remains unclear how individual differences in *state* negative affect are instantiated at the neural level.

As outlined above, feelings such as anxiety and sadness/depression can be subsumed under negative affect [9]. Several imaging studies have reported insular activation to be modulated by

negative affect. In healthy subjects, individual differences in *anxiety* modulate activity of the amygdala during unconscious processing of threat-related stimuli [13], as well as during conscious processing of fearful faces [14]. It has recently been proposed that the insula plays a key role in anxiety proneness [15]. For instance, anxiety-prone healthy subjects show greater responses in the bilateral insulae during anticipation of aversive pictures compared to non-anxious subjects [16].

*Sadness*, the other major constituent of negative affect, also modulates insular activity. Sadness induced by autobiographical memory scripts of past sad events in healthy female subjects activates the left insula, amongst other regions [17]. Moreover, individual differences in sadness correlate positively with activity in the right insula and the right temporal pole [1]. In females, transient sadness is associated with increased activation in the left insula and left amygdala [18]. Two PET studies also report on insular activation during self-induced sadness [19,20].

Altered insula functioning has also been shown in both patients with manifest anxiety disorders and clinical depression. For instance, patients with social phobia show increased insular activity during anticipation of a public speaking task as compared to healthy controls [21]. Another fMRI study reports increased activation in the right insula and right amygdala, amongst other regions, during down-regulation of sadness in patients with major depressive disorder [22]. Moreover, in these patients remission of a depressive episode after pharmacological treatment is characterized by metabolic decreases in the bilateral insulae and subgenual cingulate cortex [20,23].

In sum, both in healthy and clinical populations altered insula activation seems to play a crucial role in anxiety and sadness, that is, in negative affect. As outlined above, negative affect can be differentiated into state and trait negative affect. Therefore, the goal of the present study was to investigate how individual differences in *state* negative affect are represented at the neural level during exposition to aversive stimuli. To address this issue, we monitored blood oxygen level-dependent (BOLD) responses in a healthy female sample during passive viewing of aversive

stimuli. To investigate changes in autonomic arousal, we simultaneously measured skin conductance level. Individual differences in state negative affect were assessed using the Positive and Negative Affect Scale (PANAS) [24]. Based on the findings cited above, we hypothesized that individual differences in state negative affect correlate positively with activity in limbic and paralimbic regions, such as the insular cortex and the amygdala during exposition to aversive stimuli. At the psychophysiological level we found increased skin conductance level in response to aversive relative to neutral pictures. However, there was no association between skin conductance level and state negative affect, or difference in skin conductance level between subjects with high and low state negative affect, respectively. Furthermore, we found that individual differences in state negative affect were associated with activity in the left insula.

## **Methods**

### **Subjects**

Gender differences in emotion processing have been reported at the psychophysiological level. Women show greater reactivity in response to aversive stimuli compared to men [25] and they also show differential activation patterns at the neural level [26–28] (for a review see [29]). Therefore, only female subjects were included in the present study. 23 healthy female subjects without any history of neurological or psychiatric disorders participated in the experiment ( $27.1 \pm 4.7$  years, mean  $\pm$  SD). They were all right-handed as assessed by the Edinburgh Handedness Inventory [30]. The study was approved by the local ethics committee of the Charité University Medicine Berlin, and participants gave written informed consent prior to investigation.

## **Psychometric Assessment**

Before subjects went into the scanner we assessed individual differences in state and trait negative affect using the Positive and Negative Affect Scale (PANAS) [24]. The Negative Affect scale consists of ten adjectives of mood states (e.g., nervous, afraid or upset). To assess state negative affect subjects rated their *current* affective state on the basis of these adjectives using a 5-point rating scale.

## **Stimuli**

Neutral and aversive pictures were selected from the standardized International Affective Picture System (IAPS, [31]). Neutral stimuli consisted of pictures of household objects and scenes or abstract three-dimensional figures. Aversive pictures displayed threatening scenes, objects, animals or wounded people (65% of the aversive pictures were threat-related, sad and disgust pictures represented 35%). Hence, the two sets of stimuli were not matched with regard to human forms and figures. Mean normative ratings for pleasure, arousal, and dominance (taken from the technical manual of the IAPS) for selected neutral and aversive pictures, and results of t-test are provided in Table 1. The ratings differed significantly for neutral and aversive pictures [31].

Insert Table 1

Thirteen blocks of neutral pictures [A] and 12 blocks of aversive pictures [B] were presented in an ABA fashion. Within a block, four pictures of the same valence were presented. Each picture was shown only once, resulting in the presentation of 52 neutral and 48 aversive pictures. Each picture was displayed for 4.3 s resulting in a block duration of 17.5 s. The whole experiment lasted 7.5 min. To allow the future application in clinical populations, we kept the experiment as short as possible; therefore no rest periods (fixation periods) were included in the experiment.

Stimuli were displayed using the experimental control software Presentation (Neurobehavioral Systems Inc, Albany, CA). Subjects were instructed to pay attention to the pictures [32,33].

## **Data Acquisition**

*Psychophysiological data.* Autonomic arousal can be assessed by measuring skin conductance activity, which reflects activity within the sympathetic axis of the autonomic nervous system. Skin conductance activity is a sensitive index of emotion-related sympathetic activity; it is thus a specific measure of arousal during evaluation of emotional pictorial stimuli and closely corresponds to subjective arousal ratings [34,35]. In the scanner, skin conductance activity was continuously monitored using silver electrodes taped to the palmar surface of the left hand to investigate changes in autonomic arousal during the aversive and the neutral condition. A double-shielded cable protected the analog signal from scanner-related artifacts. The analog skin conductance signal was displayed online and recorded digitally using a skin conductance processing unit (SC5, Psylab, Contact Precisions Instruments, Boston, USA) outside the scanner room. Skin conductance activity was directly measured in conductance (micro-Siemens,  $\mu\text{S}$ ) and recorded at a sample rate of 600 Hz using Psylab software.

*fMRI data.* Whole brain MRI data were collected on a 1.5 T Siemens Vision (Erlangen, Germany). Axially oriented echoplanar scans were acquired using standard parameters (TE, 40 ms; TR, 2500 ms; flip angle, 90°; FOV, 256 mm; matrix, 64 x 64; voxel size, 4 x 4 x 4.6 mm; 26 slices). A sagittally oriented T1-weighted volume (TE, 5 ms; TR, 20 ms; flip angle, 30°; matrix, 256 x 256; voxel size, 1 x 1 x 1 mm) and a proton-density-weighted volume (TE, 15 ms; TR, 4350 ms; flip angle, 180°; matrix, 252 x 256; voxel size, 1 x 1 x 4.6 mm) were acquired for registration of the functional images.

## Data Analysis

*Psychophysiological data.* For 18 subjects skin conductance data were useable and analyzed with Matlab® 7.0.4. (The MathWorks, Inc., MA, USA). Skin conductance data were detrended, normalized using z-transformation ([36], p.155), and sampled down to 60 Hz. Data were averaged across experimental blocks, baseline corrected across the first 50 time points and averaged across subjects. Because we used short stimulus presentations (3.75 sec) in combination with a block design, phasic changes such as skin conductance responses could not be analyzed. Rather, we analyzed the data with regard to tonic changes. A skin conductance level (SCL) index ( $(SCL_{\text{aversive}} - SCL_{\text{neutral}}) / (SCL_{\text{aversive}} + SCL_{\text{neutral}})$ ) was computed as a proxy for autonomic arousal. The SCL index represents information with regard to the relative change across the conditions, whereas indices such as area under the curve or peak signal represent only condition specific values. The skin conductance level index was subjected to an analysis of variance (ANOVA) to investigate changes in autonomic arousal during the aversive and the neutral condition.

*FMRI data.* FMRI data were analyzed using a mixed effects approach within the framework of the general linear model as implemented in FSL (FMRIB's Software Library, <http://www.fmrib.ox.ac.uk/fsl>, [37]) and AFNI (<http://afni.nimh.nih.gov>, [10]). Slice-time and motion corrected volumes were spatially smoothed using a Gaussian kernel of FWHM 8 mm and high-pass filtered (sigma = 50.5 s). Time series were modeled using a box-car function convolved with a hemodynamic response function (gamma variate). Registration to high resolution and standard images was carried out using FLIRT [38,39]. Contrast images were computed for the main effect of task (aversive vs. neutral) and transformed, after spatial normalization, into standard MNI space [38]. Group effects were computed using the transformed contrast images in a mixed effects model treating subjects as random. In the higher-level analysis,  $Z$  (Gaussianized  $T$ ) statistic images were thresholded at  $Z > 3.09$ , corresponding to  $p < 0.001$ , uncorrected. We report those clusters that survived this threshold and had a size of at least 12

voxels. Demeaned state negative affect scores were used as a covariate to identify brain regions, in which fMRI signal changes in response to aversive pictures covaried with individual differences in state negative affect. We found significant covariation of demeaned state negative affect scores with activity in the left insula (see results section). To further explore the covariation of the left insula with state negative affect scores we used the cluster of activated insula voxels (peak voxel  $x = -40$ ,  $y = 0$ ,  $z = -4$ , cf. Table 2) in a region of interest (ROI) analysis. From the contrast images for the main effect of task (aversive vs. neutral) parameter estimates were extracted from this insula ROI and were correlated with individual state negative affect scores. Because of the positive skew of state negative affect scores we used a non-parametric measure of correlation, Spearman's rho.

Because we simultaneously acquired skin conductance level data we were interested in the neural network representing skin conductance changes. For each subject, we set up a new GLM analysis with individual SCL-time series to identify the SCL-related network.

Skin conductance level time series acquired during MR scanning were down-sampled to match the number of acquired volumes and were convolved with a hemodynamic response function (gamma variate). Slice-time and motion corrected volumes were spatially smoothed using a Gaussian kernel of FWHM 5 mm and high-pass filtered ( $\sigma = 50.5$  s). Group effects were computed using the transformed contrast images in a mixed effects model treating subjects as random. In the higher-level analysis,  $Z$  (Gaussianized  $T$ ) statistic images were thresholded at  $Z > 3.09$ , corresponding to  $p < 0.001$ , uncorrected. Again, we report only those clusters that survived this threshold and had a size of at least 12 voxels.

## Results

### Psychometric Assessment and Psychophysiological Data

The mean state negative affect score in our sample was  $11.7 \pm 1.7$  (mean  $\pm$  sd), which is similar to a previous report of negative affect in a healthy sample ( $11.78 \pm 2.33$ ; 118). State negative affect scores in our sample were not normally distributed (Kolmogorov-Smirnov-Z = 0.235,  $p = 0.002$ ) because of positive skew. This is consistent with normative data on the distribution of negative affect in a general adult population ( $N = 1,003$ ) [40]. Furthermore, state and trait negative affect scores were uncorrelated ( $r = 0.373$ ,  $p = 0.80$ ) in the present sample, thereby supporting the independence of state and trait negative affect.

Skin conductance level index did not correlate with state negative affect scores (for  $n = 18$ :  $11.9 \pm 1.7$ ) in either condition (aversive:  $r = 0.08$ ,  $p = 0.762$ ; neutral:  $r = 0.12$ ,  $p = 0.633$ ). This was confirmed by a more lenient approach where the group was median-split into two subgroups with high and low state negative affect, respectively. The two subgroups differed significantly with regard to state negative affect ( $t = -7.012$ ,  $p < 0.001$ ). However, with respect to SCL repeated measures ANOVA indicated a significant effect of condition ( $F = 8.977$ ;  $p = 0.005$ ), but no effect of group ( $F = 0.339$ ;  $p = 0.564$ ) or group by condition interaction ( $F = 0.120$ ;  $p = 0.731$ ).

### Functional MRI Data

#### *Main effects of condition*

A mixed effects group analysis ( $n = 23$ ,  $Z > 3.09$ ,  $p < 0.001$ , uncorrected) comparing the aversive to the neutral condition revealed activation in right frontal regions (BA 9/10), the bilateral amygdalae, the bilateral precuneus (BA 19), right parietal cortex (BA 7) and middle occipital gyrus (BA 37) (see Table 2).

*Covariation of BOLD responses with state negative affect scores during passive viewing of aversive relative to neutral pictures*

State negative affect scores covaried with changes in BOLD responses during the aversive condition relative to the neutral condition in the left insula (BA 13) (see Table 2 and Fig. 1, left panel). An ROI analysis of the left insula confirmed that state negative affect scores correlated positively with BOLD responses in this region during passive viewing of aversive stimuli (see Fig. 1, right panel). That is, subjects with high state negative affect showed an increased BOLD response in the left insula during the aversive relative to the neutral condition.

Insert Table 2 about here

Insert Fig. 1 about here

*Representation of changes in skin conductance level*

Representation of changes in skin conductance level was associated with predominantly right hemispheric activations in the inferior frontal gyrus (BA 10/47) extending into the anterior insula, the Precuneus (BA 39) and cuneus (BA 19) ( $n = 18$ ,  $Z > 3.09$ ,  $p < 0.001$ , uncorrected). In the left hemisphere representation of changes in skin conductance level was associated with activations in the middle frontal gyrus (BA 10), the caudate tail extending into thalamus with pulvinar and putamen (see Table 3 and Fig. 2). That is, increased autonomic arousal was associated with predominantly right lateralized activations in frontal, limbic, and parietal regions.

Insert Table 3 about here

Insert Fig. 2 about here

## Discussion

In the present study, we investigated how individual differences in state negative affect are represented at the neural level during exposure to aversive stimuli. At the psychophysiological level we found increased skin conductance level in response to aversive relative to neutral pictures. However, there was no association between skin conductance level and state negative affect, or difference in skin conductance level between subjects with high and low state negative affect, respectively. At the neural level we found that individual differences in state negative affect were associated with differences in left insular activity during passive viewing of aversive relative to neutral stimuli.

At the psychophysiological level we found a significantly increased skin conductance level in response to aversive relative to neutral pictures in the overall group. This is in line with other studies reporting on increased skin conductance activity in response to aversive relative to neutral pictures of the IAPS [41,42]. This association may also be mediated by increased arousal associated with aversive pictures as indicated by the normative ratings on valence and arousal of stimuli of the IAPS material set [34,35]. We did not find an association of state negative affect with psychophysiological measures as indicated by the ANOVA and the non-significant correlation between skin conductance level index and state negative affect scores. The missing association between these two measures might relate to the scale used to measure state negative affect, because there was little range in state negative affect scores ( $11.7 \pm 1.7$ ).

Consistent with previous findings on neural processing of aversive stimuli we found that passive viewing of aversive relative to neutral pictures activated the amygdala [43–46] as well as frontal [43,47], parietal [43,47] and occipital [43,44,46] regions.

In an additional analysis we found changes in skin conductance level to be correlated with activity in a set of brain regions comprising frontal regions extending into the anterior insula, the caudate

body and tail extending into the posterior insula and the thalamus, and parietal, temporal and occipital cortices. These results are in line with previous studies examining skin conductance related neural activity [48–50]. Bearing in mind that entire time series were included as regressors, neural representation may not only represent changes across conditions but also phasic changes to single stimuli [51]. Moreover, differences in habituation across the experiment may have influenced our findings. In this regard, it has been shown that reduced habituation of autonomic arousal across the experiment is associated with increased BOLD activation in females [52].

### **Individual differences in state negative affect**

In our sample of healthy female subjects increased state negative affect correlated positively with activity in the left insula during passive viewing of aversive relative to neutral pictures.

The insula has been implicated in the representation of visceral changes and more generally in the representation of interoceptive processes [53–57]. Interoception can be defined as the sense of the physiological condition of the entire body, comprising interoceptive sensations such as muscular and visceral sensations, vasomotor activity, hunger, thirst, air hunger, and somatosensory feelings, such as temperature, itch, pain and sensual touch (for reviews see [54,55]). According to Craig, the objective physiological condition of the entire body (physical self) is represented in the dorsal posterior insula. This representation provides the basis for a meta-representation of the state of the body in the middle and anterior insula that is associated with emotional self-awareness [1,58,59].

Thus, the literature suggests a strong involvement of the insula in the representation of visceral changes of the body that are associated with any emotional engagement. In the present study, insular activity was correlated with state negative affect. Hence, insular activity may reflect not only arousal or intensity associated with emotions, but also the representation of emotional aspects such as valence or hedonic tone. However, because we did not find an association

between autonomic arousal and state negative affect we argue for a valence-dependent modulation of insular activity.

Autonomic arousal is only one dimension characterizing emotional experience. Psychological theories have proposed that the affective space can be described as a space formed by two bipolar, but independent dimensions: arousal or activation indicating the intensity of the felt emotion, and valence, indicating pleasure or displeasure, or hedonic tone [35,60,61]. Indeed, at the neural level valence and arousal for odors and taste can be dissociated, with intensity of odors and taste represented in the amygdala and valence represented in the orbitofrontal cortex [62–64]. The covariation of left insular activity with individual differences in state negative affect found in our study may reflect the valence or hedonic tone of the affective experience. For instance, the bilateral anterior insula is activated during the anticipation of and exposure to aversive pictures [65,66]. Studies specifically investigating the neural correlates of valence showed that reports of valence of emotional pictures are associated with left insular activity, that is, insular activity increases with reported negative valence [67]. Beside the left insula, valence-dependent modulation of activity was also reported for the medial prefrontal cortex [68].

In the present study, activity in the left insula reflected individual differences in negative affect. A recent meta-analysis found that negative emotions/withdrawal activate the insula and the cerebellum [69]. A density analysis (i.e., calculating the density distribution of activation foci throughout the brain) showed a focal withdrawal-related density in the left mid insula ( $x = -40, y = -2, z = 3$ , in the MNI coordinate system; [69]); notably, these coordinates correspond nicely to the location of insular activity maximally covarying with individual differences in state negative affect ( $x = -40, y = 0, z = -4$ , MNI) reported in our study. The findings were confirmed by another meta-analysis by Wager & Feldmann-Barrett [70] on the functional specialization of the insula, which also revealed a stronger bias towards *left* insular

activation during emotion processing. Of special importance for the present study is that left (and right) *mid* insula activations were highly predictive of withdrawal-related emotions [70,71]. Most importantly, individual differences in state anxiety correlate with activity in the left mid insula (as well as left orbitofrontal, left inferior frontal gyrus, and left anterior cingulate), with coordinates of peak activation ( $x = -40, y = -6, z = -15$ , MNI) [72] that also correspond to the coordinates of peak activation of left mid insula covarying with state negative affect in the present study ( $x = -40, y = 0, z = -4$ , MNI). Taken together, these findings support our interpretation of a valence-dependent modulation of left middle insular activity.

What is the functional meaning of covariation of activity in the left insula with individual differences in state negative affect? The salience of an aversive context is especially strong in anxious subjects, as revealed by their attentional bias towards negative information [73–76]. This attentional bias is particularly high in conditions of high *state* anxiety [73]. Similarly, in the study reported here, the aversiveness of the stimuli might have been of special significance or value to subjects with high *state* negative affect. Because of the interconnectedness of the insula with the amygdala, the orbito- and prefrontal cortex, the insula is well positioned to integrate information about the salience (both appetitive and aversive) and relative value of a stimulus (depending on the homeostatic body state of an individual) and to predict how it might affect the body state [15]. With regard to our findings, increased insular activity in individuals with high state negative affect may thus reflect increased processing of salient aversive stimuli, resulting in altered interoceptive feedback processes that indicate a specific body reaction when exposed to aversive relative to neutral stimuli. This saliency may then be instantiated in a bodily sensation, such as changes in heart rate, blood pressure, respiration rate, gastrointestinal interoceptive processes [77–79], as well as muscle tension, temperature or vasomotor activity [54,55], which is reflected in increased activity in the insula.

With the goal in mind to use the present paradigm in clinical populations, we kept the experiment as short as possible. As a consequence, we did not include rest periods (fixation periods) in the experiment. The brevity of the experimental design comes at a cost: By contrasting the aversive relative to the neutral condition one cannot determine the relative influence of the two conditions on the correlation of BOLD responses with individual differences in state negative affect. Behavioral and fMRI studies have suggested that interpretation of neutral stimuli can be affected by *anxiety* level [80,81]. Nevertheless, there also is behavioral evidence that interpretation of neutral faces can vary depending on the presence of other primary expressions in the experimental context [82]. Accordingly, Somerville et al. argued that the observed amygdala response to neutral faces is not surprising given the fact, that in comparison with the positive faces shown, neutral faces represented the most negative stimuli in their paradigm [80]. In the present study neutral stimuli were presented in the context of *aversive* stimuli. Therefore, it is rather unlikely that correlations of BOLD responses with individual differences in state negative affect are dictated by differences in activations to *neutral* stimuli.

In conclusion, at the psychophysiological level we found increased skin conductance level in response to aversive relative to neutral pictures. However, there was no association between skin conductance level and state negative affect, or difference in skin conductance level between subjects with high and low state negative affect, respectively. At the neural level we found that individual differences in state negative affect were associated with differences in left insular activity during passive viewing of aversive relative to neutral stimuli. Because subjects with high and low state negative affect did not differ with regard to autonomic arousal, we cannot ascribe insular activity to the representation of autonomic arousal. This finding implicates that state negative affect is represented in the insular cortex in terms of hedonic tone.

## References

1. Eugene F, Levesque J, Mensour B, Leroux JM, Beaudoin G et al. (2003) The impact of individual differences on the neural circuitry underlying sadness. *Neuroimage* 19: 354-364.
2. Lundh LG, Simonsson-Sarnecki M (2001) Alexithymia, emotion, and somatic complaints. *J Pers* 69: 483-510.
3. Hornak J, Bramham J, Rolls ET, Morris RG, O'Doherty J et al. (2003) Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulate cortices. *Brain* 126: 1691-1712.
4. Thompson-Schill SL, Braver TS, Jonides J (2005) Individual differences. *Cogn Affect Behav Neurosci* 5: 115-116.
5. Canli T, Amin Z, Haas B, Omura K, Constable RT (2004) A double dissociation between mood states and personality traits in the anterior cingulate. *Behav Neurosci* 118: 897-904.
6. Hamann S, Canli T (2004) Individual differences in emotion processing. *Curr Opin Neurobiol* 14: 233-238.
7. Davidson RJ, Irwin W (1999) The functional neuroanatomy of emotion and affective style. *Trends Cogn Sci* 3: 11-21.
8. Watson D, Tellegen A (1985) Toward A Consensual Structure of Mood. *Psychological Bulletin* 98: 219-235.
9. Clark LA, Watson D (1991) Tripartite model of anxiety and depression: psychometric evidence and taxonomic implications. *J Abnorm Psychol* 100: 316-336.
10. Cox RW (1996) AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Comput Biomed Res* 29: 162-173.
11. Phan KL, Fitzgerald DA, Nathan PJ, Moore GJ, Uhde TW et al. (2005) Neural substrates for voluntary suppression of negative affect: a functional magnetic resonance imaging study. *Biol Psychiatry* 57: 210-219.
12. Schaefer SM, Jackson DC, Davidson RJ, Aguirre GK, Kimberg DY et al. (2002) Modulation of amygdalar activity by the conscious regulation of negative emotion. *J Cogn Neurosci* 14: 913-921.
13. Etkin A, Klemenhagen KC, Dudman JT, Rogan MT, Hen R et al. (2004) Individual differences in trait anxiety predict the response of the basolateral amygdala to unconsciously processed fearful faces. *Neuron* 44: 1043-1055.
14. Bishop S, Duncan J, Brett M, Lawrence AD (2004) Prefrontal cortical function and anxiety: controlling attention to threat-related stimuli. *Nat Neurosci* 7: 184-188.
15. Critchley HD, Daly EM, Bullmore ET, Williams SC, Van AT et al. (2000) The functional neuroanatomy of social behaviour: changes in cerebral blood flow when people with autistic disorder process facial expressions. *Brain* 123 (*Pt 11*): 2203-2212.

16. Simmons A, Strigo I, Matthews SC, Paulus MP, Stein MB (2006) Anticipation of aversive visual stimuli is associated with increased insula activation in anxiety-prone subjects. *Biol Psychiatry* 60: 402-409.
17. Lane RD, Reiman EM, Axelrod B, Yun LS, Holmes A et al. (1998) Neural correlates of levels of emotional awareness. Evidence of an interaction between emotion and attention in the anterior cingulate cortex. *J Cogn Neurosci* 10: 525-535.
18. Levesque J, Eugene F, Joanette Y, Paquette V, Mensour B et al. (2003) Neural circuitry underlying voluntary suppression of sadness. *Biol Psychiatry* 53: 502-510.
19. George MS, Ketter TA, Parekh PI, Horwitz B, Herscovitch P et al. (1995) Brain Activity During Transient Sadness and Happiness in Healthy Women. *Am J Psychiatry* 152: 341-351.
20. Mayberg HS, Liotti M, Brannan SK, McGinnis S, Mahurin RK et al. (1999) Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. *Am J Psychiatry* 156: 675-682.
21. Lorberbaum JP, Kose S, Johnson MR, Arana GW, Sullivan LK et al. (2004) Neural correlates of speech anticipatory anxiety in generalized social phobia. *Neuroreport* 15: 2701-2705.
22. Iancu I, Dannon PN, Poreh A, Lepkifker E, Grunhaus L (2001) Alexithymia and suicidality in panic disorder. *Compr Psychiatry* 42: 477-481.
23. Mayberg HS, Brannan SK, Tekell JL, Silva JA, Mahurin RK et al. (2000) Regional metabolic effects of fluoxetine in major depression: serial changes and relationship to clinical response. *Biol Psychiatry* 48: 830-843.
24. Krohne HW, Egloff B, Kohlmann C-W, Tausch A (1996) Untersuchung mit einer deutschen Version der "Positive and Negative Affect Schedule" (PANAS). *Diagnostica* 42: 139-156.
25. Bradley MM, Codispoti M, Sabatinelli D, Lang PJ (2001) Emotion and motivation II: sex differences in picture processing. *Emotion* 1: 300-319.
26. Piefke M, Weiss PH, Markowitsch HJ, Fink GR (2005) Gender differences in the functional neuroanatomy of emotional episodic autobiographical memory. *Hum Brain Mapp* 24: 313-324.
27. Killgore WD, Yurgelun-Todd DA (2001) Sex differences in amygdala activation during the perception of facial affect. *Neuroreport* 12: 2543-2547.
28. George MS, Ketter TA, Parekh PI, Herscovitch P, Post RM (1996) Gender differences in regional cerebral blood flow during transient self-induced sadness or happiness. *Biol Psychiatry* 40: 859-871.
29. Cahill L (2006) Why sex matters for neuroscience. *Nature Reviews Neuroscience* 7: 477-484.
30. Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9: 97-113.
31. Lang PJ, Bradley MM, Cuthbert BN (1999) The International Affective Picture System (IAPS): Technical Manual and Affective Ratings. In: Gainesville, FL: NIMH Center for the Study of Emotion and Attention, University of Florida.

32. Hutcherson CA, Goldin PR, Ochsner KN, Gabrieli JD, Barrett LF et al. (2005) Attention and emotion: Does rating emotion alter neural responses to amusing and sad films? *Neuroimage* 27: 656-668.
33. Schafer A, Schienle A, Vaitl D (2005) Stimulus type and design influence hemodynamic responses towards visual disgust and fear elicitors. *Int J Psychophysiology* 57: 53-59.
34. Lee TM, Liu HL, Hoosain R, Liao WT, Wu CT et al. (2002) Gender differences in neural correlates of recognition of happy and sad faces in humans assessed by functional magnetic resonance imaging. *Neurosci Lett* 333: 13-16.
35. Lang PJ, Greenwald MK, Bradley MM, Hamm AO (1993) Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology* 30: 261-273.
36. Pardo JV, Pardo PJ, Raichle ME (1993) Neural correlates of self-induced dysphoria. *Am J Psychiatry* 150: 713-719.
37. Smith SM, Jenkinson M, Woolrich MW, Beckmann CF, Behrens TE et al. (2004) Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage* 23 Suppl 1: S208-S219.
38. Jenkinson M, Bannister P, Brady M, Smith S (2002) Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage* 17: 825-841.
39. Jenkinson M, Smith S (2001) A global optimisation method for robust affine registration of brain images. *Med Image Anal* 5: 143-156.
40. Crawford JR, Henry JD (2004) The Positive and Negative Affect Schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. *Br J Clin Psychol* 43: 245-265.
41. Baumgartner T, Esslen M, Jancke L (2006) From emotion perception to emotion experience: Emotions evoked by pictures and classical music. *Int J Psychophysiology* 60: 34-43.
42. Amrhein C, Muhlberger A, Pauli P, Wiedemann G (2004) Modulation of event-related brain potentials during affective picture processing: a complement to startle reflex and skin conductance response? *Int J Psychophysiology* 54: 231-240.
43. Bermpohl F, Pascual-Leone A, Amedi A, Merabet LB, Fregni F et al. (2006) Dissociable networks for the expectancy and perception of emotional stimuli in the human brain. *Neuroimage* 30: 588-600.
44. Britton JC, Taylor SF, Sudheimer KD, Liberzon I (2006) Facial expressions and complex IAPS pictures: common and differential networks. *Neuroimage* 31: 906-919.
45. Hariri AR, Tessitore A, Mattay VS, Fera F, Weinberger DR (2002) The amygdala response to emotional stimuli: a comparison of faces and scenes. *Neuroimage* 17: 317-323.
46. Liberzon I, Taylor SF, Fig LM, Decker LR, Koeppe RA et al. (2000) Limbic activation and psychophysiologic responses to aversive visual stimuli. Interaction with cognitive task. *Neuropsychopharmacology* 23: 508-516.
47. Taylor SF, Phan KL, Decker LR, Liberzon I (2003) Subjective rating of emotionally salient stimuli modulates neural activity. *Neuroimage* 18: 650-659.

48. Critchley HD (2002) Electrodermal responses: What happens in the brain. *Neuroscientist* 8: 132-142.
49. Critchley H, Daly E, Phillips M, Brammer M, Bullmore E et al. (2000) Explicit and implicit neural mechanisms for processing of social information from facial expressions: a functional magnetic resonance imaging study. *Hum Brain Mapp* 9: 93-105.
50. Fredrikson M, Furmark T, Olsson MT, Fischer H, Andersson J et al. (1998) Functional neuroanatomical correlates of electrodermal activity: A positron emission tomographic study. *Psychophysiology* 35: 179-185.
51. Williams LM, Brown KJ, Das P, Boucsein W, Sokolov EN et al. (2004) The dynamics of cortico-amygdala and autonomic activity over the experimental time course of fear perception. *Cogn Brain Res* 21: 114-123.
52. Williams LM, Barton MJ, Kemp AH, Liddell BJ, Peduto A et al. (2005) Distinct amygdala-autonomic arousal profiles in response to fear signals in healthy males and females. *Neuroimage* 28: 618-626.
53. Critchley HD, Wiens S, Rotshtein P, Ohman A, Dolan RJ (2004) Neural systems supporting interoceptive awareness. *Nat Neurosci* 7: 189-195.
54. Craig AD (2003) Interoception: the sense of the physiological condition of the body. *Curr Opin Neurobiol* 13: 500-505.
55. Craig AD (2002) How do you feel? Interoception: the sense of the physiological condition of the body. *Nat Rev Neurosci* 3: 655-666.
56. Augustine JR (1996) Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Res Brain Res Rev* 22: 229-244.
57. Cechetto DF, Chen SJ (1990) Subcortical sites mediating sympathetic responses from insular cortex in rats. *Am J Physiol* 258: R245-R255.
58. Singer T, Seymour B, O'Doherty J, Kaube H, Dolan RJ et al. (2004) Empathy for pain involves the affective but not sensory components of pain. *Science* 303: 1157-1162.
59. Craig AD (2004) Human feelings: why are some more aware than others? *Trends Cogn Sci* 8: 239-241.
60. Feldman-Barrett L, Russell JA (1999) The structure of current affect: controversies and emerging consensus. *Curr Dir Psychol Sci* 8: 10-14.
61. Wundt W (1924) *An introduction to psychology*. London: Allen & Unwin.
62. Anderson AK, Sobel N (2003) Dissociating intensity from valence as sensory inputs to emotion. *Neuron* 39: 581-583.
63. Anderson AK, Christoff K, Stappen I, Panitz D, Ghahremani DG et al. (2003) Dissociated neural representations of intensity and valence in human olfaction. *Nat Neurosci* 6: 196-202.
64. Small DM, Gregory MD, Mak YE, Gitelman D, Mesulam MM et al. (2003) Dissociation of neural representation of intensity and affective valuation in human gustation. *Neuron* 39: 701-711.
65. Nitschke JB, Sarinopoulos I, Mackiewicz KL, Schaefer HS, Davidson RJ (2006) Functional neuroanatomy of aversion and its anticipation. *Neuroimage* 29: 106-116.

66. Schienle A, Schafer A, Stark R, Walter B, Vaitl D (2005) Gender differences in the processing of disgust- and fear-inducing pictures: an fMRI study. *Neuroreport* 16: 277-280.
67. Anders S, Lotze M, Erb M, Grodd W, Birbaumer N (2004) Brain activity underlying emotional valence and arousal: A response-related fMRI study. *Hum Brain Mapp* 23: 200-209.
68. Heinzl A, Bermpohl F, Niese R, Pfennig A, Pascual-Leone A et al. (2005) How do we modulate our emotions? Parametric fMRI reveals cortical midline structures as regions specifically involved in the processing of emotional valences. *Cogn Brain Res* 25: 348-358.
69. Wager TD, Phan KL, Liberzon I, Taylor SF (2003) Valence, gender, and lateralization of functional brain anatomy in emotion: a meta-analysis of findings from neuroimaging. *Neuroimage* 19: 513-531.
70. Wager TD, Barrett LF (2004) From affect to control: Functional specialization of the insula in motivation and regulation. Published online at *PsycExtra*
71. Barrett LF, Wager TD (2006) The structure of emotion - Evidence from neuroimaging studies. *Curr Dire Psychol Sci* 15: 79-83.
72. Chua P, Krams M, Toni I, Passingham R, Dolan R (1999) A functional anatomy of anticipatory anxiety. *Neuroimage* 9: 563-571.
73. Mercado F, Carretie L, Tapia M, Gomez-Jarabo G (2006) The influence of emotional context on attention in anxious subjects: neurophysiological correlates. *J Anx Dis* 20: 72-84.
74. Mogg K, Bradley BP, Williams R, Mathews A (1993) Subliminal Processing of Emotional Information in Anxiety and Depression. *J Abnorm Psychol* 102: 304-311.
75. MacLeod C, Mathews A, Tata P (1986) Attentional Bias in Emotional Disorders. *J Abnorm Psychol* 95: 15-20.
76. Mathews A, MacLeod C (1985) Selective Processing of Threat Cues in Anxiety-States. *Behav Res Ther* 23: 563-569.
77. Holzl R, Erasmus LP, Moltner A (1996) Detection, discrimination and sensation of visceral stimuli. *Biol Psychol* 42: 199-214.
78. Vaitl D (1996) Interoception. *Biol Psychol* 42: 1-27.
79. Steptoe A, Vogele C (1992) Individual differences in the perception of bodily sensations: the role of trait anxiety and coping style. *Behav Res Ther* 30: 597-607.
80. Ochsner KN, Ray RD, Cooper JC, Robertson ER, Chopra S et al. (2004) For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage* 23: 483-499.
81. Schaefer A, Collette F, Philippot P, van der LM, Laureys S et al. (2003) Neural correlates of "hot" and "cold" emotional processing: a multilevel approach to the functional anatomy of emotion. *Neuroimage* 18: 938-949.
82. Russell JA, Fehr B (1987) Relativity in the Perception of Emotion in Facial Expressions. *J Exp Psychol Gen* 116: 223-237.

**Fig. 1. Brain regions showing covariation of BOLD responses with state negative affect scores.** **Left panel:** State negative affect (SNA) scores covaried significantly with BOLD responses in the left insula during the aversive condition relative to the neutral condition. The figure shows activations from higher-level analysis thresholded at  $Z > 3.09$ , corresponding to  $p < 0.001$ , uncorrected, that were used as a mask for subsequent region of interest (ROI) analysis. **Right panel:** Covariation of state negative affect scores and BOLD responses in the left insula (ROI) during the aversive relative to the neutral condition ( $\rho$  = Spearman's rank correlation coefficient *rho*,  $p$  = p-value). Parameter estimates are displayed in 1/10,000 signal change.

**Fig. 2. Brain regions related to representation of skin conductance level independent of state negative affect.** Representation of skin conductance level activated regions predominantly in the right hemisphere, including the ventrolateral prefrontal cortex (VLPFC), the anterior and posterior insula (aIns/pIns), the middle temporal gyrus (MTG) (upper panels) as well as the thalamus (Th) with the putamen (Put), and insula (Ins) (lower panels). In the left hemisphere afferent representation of skin conductance level covaried with activation in the thalamus extending into the putamen (Put), and the pulvinar (Pul)(lower panels). Figure shows activations from higher-level analysis ( $n = 18$ ) thresholded at  $Z > 3.09$ , corresponding to  $p < 0.001$ , uncorrected.

**Table 1: Mean normative ratings for pleasure, arousal and dominance for neutral (N = 52) and aversive (N = 48) pictures**

	Neutral	Aversive	t, p
<b>Pleasure</b>	5.15 ( $\pm$ 0.66)	2.49 ( $\pm$ 0.86)	17.23, $p < 0.001$
<b>Arousal</b>	2.97 ( $\pm$ 0.59)	6.27 ( $\pm$ 0.81)	-23.06, $p < 0.001$
<b>Dominance</b>	5.95 ( $\pm$ 0.58)	3.43 ( $\pm$ 0.82)	17.58, $p < 0.001$

Mean ( $\pm$  standard deviations), t = t-value,  $p$  =  $p$ -value

**Table 2: Anatomical locations and coordinates of activations ( $p < 0.001$ , uncorr.,  $n = 23$ )\***

Anatomical region	Hemisphere	Brodmann Area	Z score	Cluster size	MNI (x, y, z)
Main effect: aversive vs. neutral					
Superior frontal gyrus	R	9	3.58	33	2, 58, 40
Medial frontal gyrus	L	10	3.39	28	-2, 62, 24
Amygdala	L		3.32	13	-16, -4, -14
Amygdala	R		3.89	98	16, -4, -16
Precuneus	L	19	3.6	15	-14, -92, 42
Precuneus	R	19	3.87	53	10, -88, 42
Superior parietal lobule	R	7	3.28	16	30, -56, 58
Middle occipital gyrus	R	37	6.39	15241	52, -74, 0
Covariation of BOLD responses with state negative affect scores during the aversive vs. neutral condition					
Insula	L	13	3.41	29	-40, 0, -4

**\* with cluster size  $\geq 12$  voxels**

**Table 3: Anatomical locations and coordinates of activations associated with skin conductance level during the aversive relative to the neutral condition controlling for state negative affect ( $p < 0.001$ , uncorr.,  $n = 18$ )**

Anatomical region	Hemisphere	Brodmann Area	Z score	Cluster size	MNI (x, y, z)
Middle frontal gyrus	R	10	3.96	181	50, 52, -4
Middle frontal gyrus	L	10	3.4	84	-36, 54, 2
Inferior frontal gyrus/ anterior insula	R	47	3.26	65	42, 18, -6
Inferior frontal gyrus	R	47	3.27	22	40, 24, -18
Thalamus/ Pulvinar	L		3.11	15	-12, -32, 2
Caudate Tail	L		3.88	2279	-34, -36, 2
Precuneus	R	39	4.24	2896	38, -70, 32
Cuneus	R	19	3.42	40	4, -92, 22

**\* with cluster size  $\geq 12$  voxels**

Figure 1

Insula

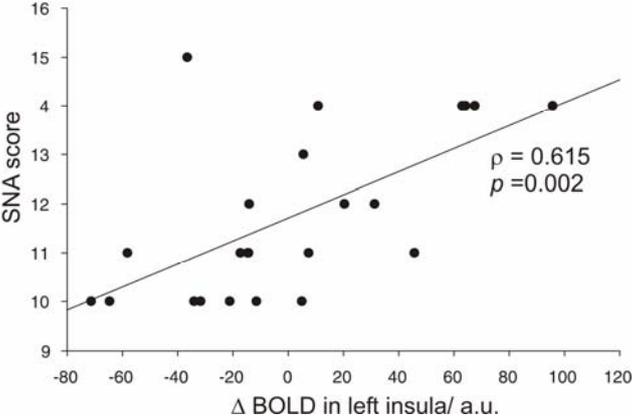
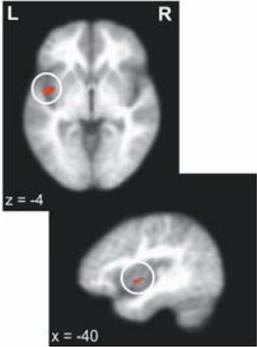
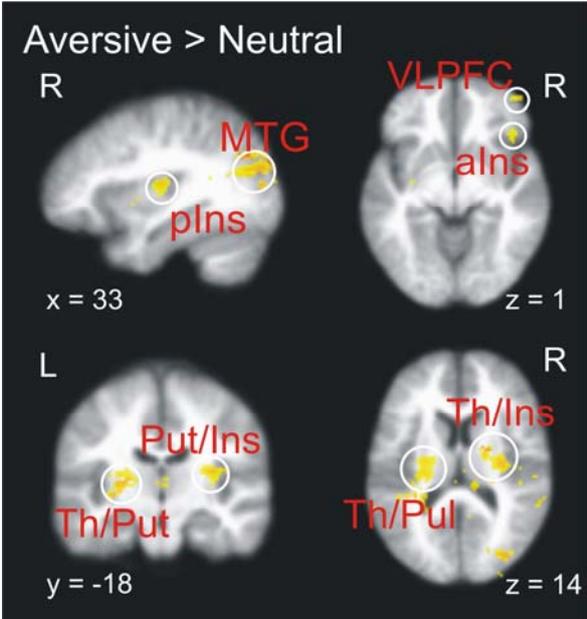


Figure 2



III A neural network reflecting individual differences in cognitive processing of emotions during perceptual decision making. Mériaux K, Wartenburger I, Kasper P, Prehn K, Lammers CH, van der Meer E, Villringer A, Heekeren HR, 2006. *Neuroimage* 33(3): 1016-27.

## SUPPLEMENTS

## **PUBLICATIONS**

### **Research Articles**

Mériaux K, Wartenburger I, Kazzner P, Prehn K, Villringer A, van der Meer E, Heekeren HR (2007). Insular activity reflects individual differences in negative affect. (Submitted)

Dresler T, Mériaux K, Heekeren HR, van der Meer, E (2007). Emotional Stroop Test: Effect of Word Arousal and Subject Anxiety on Emotional Interference. (Submitted)

Prehn K, Wartenburger I, Mériaux K, Scheibe C, Goodenough O, Villringer A, van der Meer E, Heekeren HR (2007). Moral judgment competence reflected in activity in right prefrontal cortex. (Submitted)

Mériaux K, Wartenburger I, Kazzner P, Prehn K, Lammers CH, van der Meer E, Villringer A, Heekeren HR (2006). A neural network reflecting individual differences in cognitive processing of emotions during perceptual decision making. *Neuroimage*, 33(3): 1016-27.

### **Abstracts**

Mériaux K, Wartenburger I, Kazzner P, Prehn K, Villringer A, van der Meer E, Heekeren HR (2006). Insular activity reflects individual differences in negative affect independent of autonomic arousal. *Neuroimage*, 31, Suppl.1, S70.

Prehn K, Wartenburger I, Mériaux K, Scheibe C, Goodenough OR, Villringer A, van der Meer E, Heekeren HR (2006). Influence of individual differences in moral judgment competence on neural correlates of normative judgments. *Neuroimage*, 31, Suppl.1, S84.

Mériaux K, Kazzler P, Wartenburger I, Prehn K, Lammers CH, Villringer A, Heekeren HR (2005). Neural correlates of individual differences in the ability to identify and communicate one's emotional state. *Journal of Cognitive Neuroscience*, 163-164.

Mériaux K, Kazzler P, Wartenburger I, Prehn K, Lammers CH, Villringer A, Heekeren HR (2005). Neural correlates of individual differences in cognitive processing of emotional stimuli: BOLD responses and effective connectivity measures. *Neuroimage*, 26, Suppl.1, S26.

**STATEMENT OF AUTHORSHIP**

I hereby certify that this dissertation has been composed by me and is based on my own work, unless stated otherwise. Ideas and thought cited directly or indirectly from other work have been cited accordingly.

-----

Date signed

Signature